THE IMPACT OF RAMADAN FASTING ON BIRTH OUTCOMES AND BREAST MILK CORTISOL IN RABAT, MOROCCO

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THE IMPACT OF RAMADAN FASTING ON BIRTH OUTCOMES AND BREAST MILK CORTISOL IN RABAT, MOROCCO

In this dissertation, I addressed questions about how maternal ecology affects fetal growth and the hormonal milieu the newborn is exposed to via early postpartum breast milk (colostrum). Drawing on Ramadan fasting as a natural experiment in Rabat, Morocco, I used a biocultural approach and the lens of life history theory to consider how differences between women shape maternal fasting behaviors during late pregnancy and explore the associations between maternal fasting, neonatal anthropometry, and colostrum cortisol.

Eighty-eight percent of participants engaged in some fasting and 57% fasted every day of Ramadan that passed before childbirth. Participants largely expressed family support for their decisions regarding participation in fasting. Women who fasted or fasted more days were lower in weight and higher in body fat. They were less likely to have diabetes, hypertension, or anemia, take vitamins, or receive advice not to fast by doctors or family members. Several variables associated with fasting behaviors also predicted infant anthropometry and colostrum cortisol.

Women who engaged in any fasting had infants with lower weight, length, and head circumference for gestational age. The number of days between cessation of fasting and birth was positively associated with neonatal weight, length, and head circumference, possibly suggesting in utero catch up growth. Although increased infant leanness was predicted from other situations of food restriction in late pregnancy, no associations were found between maternal fasting and neonatal ponderal index, arm circumference, or skinfold measurements. Ramadan fasting may be better modeled by situations of stress and dehydration.

Colostrum cortisol concentration was higher among women who opted out of some or all fasting, possibly indicating underlying differences in metabolic hormones between women who find fasting more difficult versus less. Fasting duration was positively correlated with colostrum cortisol, supporting the hypothesis that maternal fasting contributes to variation in colostrum composition.

This research elucidates some reproductive health consequences related to the religious fasting associated with Ramadan. The findings of this research contribute to the literature on fetal and lactational programming and our understanding of how the intrauterine and postnatal environments are shaped by the interplay between biology and culture in the maternal environment.

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Chapter 1: Introduction

Ramadan fasting is a cultural practice that has potentially profound effects on human biology, particularly that of pregnant and nursing mothers and their infants. During the month of Ramadan, many pregnant and nursing Muslim women around the world participate in a fast in which no food or water is consumed from sunrise to sunset for one lunar month. Little is known about how the physiological stress of Ramadan fasting influences the ecological and hormonal milieu the fetus is exposed to in utero or the infant is exposed to via breast milk. Although infants are not subject to fasting, maternal fasting could, in turn, affect fetal and infant growth and health in a variety of ways. In this dissertation, I provide a unique biocultural perspective on Ramadan fasting, exploring the relationship between this important cultural tradition and human biology.

The discussion of Ramadan's effect on infant growth, development and health can be enriched by approaching the topic through a biocultural lens. Biological impacts of maternal fasting which merit exploration include the effect on maternal physiology, the intrauterine environment, lactational physiology, and milk composition. While these biological aspects of maternal fasting are important to identify, it should be appreciated that Ramadan is a religious practice immersed in diverse cultural settings, observed around the globe by people from highly variable climates, socioeconomic strata, ethnicities, and lifestyles. Ramadan fasting provides a valuable cultural context that may increase our understanding of how culture guides maternal dietary options, constructs physiological stressors, influences fetal and infant growth, and encodes later life health of offspring.

This dissertation research addressed the question of whether maternal fasting from food and water for about 16 hours daily results in reduced fetal growth and increased postpartum milk cortisol concentrations when the month of Ramadan occurs during late pregnancy. This will be assessed through analysis of fetal growth, as ascertained by neonatal anthropometry and maternal postpartum breast milk endocrine composition approximately 48 hours post-delivery. Women and their infants will be compared based on maternal fasting behavior assessed by the total number of days fasted, non-fasting versus any fasting, and fasting every day of Ramadan that passed before labor versus opting out of fasting all or some of the month. The relationship between maternal fasting, fetal growth, and postpartum breast milk endocrine composition will be contextualized through a better understanding of maternal factors that influence fasting decisions, including maternal health and anthropometry. This study took place in Rabat, Morocco in 2017, when Ramadan occurred from late May to late June.

Rationale for Hypothesis

The sole source of nutrients and fluids are transferred from the mother to her offspring through the placenta during pregnancy and through breast milk for exclusively breastfed infants, along with other bioactive components (G. R. Bentley, 1998; Rutherford, 2009). The relationship between maternal ecology and fetal and infant life history strategies can be better illuminated with a deeper understanding of the cause and effects of variability in these conduits. Ramadan provides an ideal natural experiment to learn more about this relationship.

This religious fast presents a challenge that is different from caloric inadequacy or undernutrition, as it requires abstaining from food and liquids for several hours, but this often occurs in the absence of reduced caloric intake or dietary quality. Pregnant and lactating women often observe fasting during the month of Ramadan, but it is unclear how this affects maternal physiology, the intrauterine environment, breast milk composition, or growth and development during gestation and lactation. Much of what is known currently about the maternal nutrition and energetic stress of Ramadan fasting on pregnancy and lactation is based largely on the Gambian population studied by Prentice and Prentice, and more research is needed on other populations and under other conditions (Emery Thompson, 2013; Prentice, Lamb, Prentice, & Coward, 1984; Prentice, Prentice, & Lamb, 1983).

Life History Theory would predict that, in stressful or food restricted environments, it may be more beneficial for an infant to accelerate their life history trajectory by growing faster in order to reach maturation earlier and consequently achieve a smaller adult body size and other potential trade-offs in development. Maternal cortisol is one proposed mediator for this response (Dantzer et al., 2013; Hinde et al., 2014). Cortisol is an important hormone in regulating energy allocation and metabolism. It can be transferred from the mother to the fetus via the placenta and the infant via breast milk, and as such, this hormone may influence infant growth, development, and behavior (Hinde et al., 2014). Fetal programming of endocrine function resulting from fetal growth restriction may be related to changes in metabolic function that influence faster infant growth and earlier maturation (Adair, 2001). Since fasting constitutes a stressor for numerous physiological systems and has been associated with higher circulating maternal cortisol in pregnant women (Dikensoy et al., 2009; Herrmann, 2001), it is predicted that the developing fetus would perceive hormonal changes as cues about the maternal environment. If so, Ramadan fasting would be expected to elicit a faster life history trajectory in the developing fetus.

Research suggests that increased maternal cortisol alters offspring growth patterns, resulting in reduced fetal growth, faster growth in infancy, earlier maturation, and reduced size in adulthood. Increased maternal cortisol during pregnancy has been associated with reduced fetal growth, resulting in reduced birth weight (Bolten et al., 2011) and increased risk of preterm delivery, suggesting an accelerated life history trajectory (Field & Diego, 2008; Mclean et al., 1999). In studies on humans, growth restriction in utero, particularly when it is characterized by a low ponderal index, can result in rapid postnatal catch-up growth (Adair, 1989). Postnatally, higher maternal cortisol concentrations have been correlated with faster infant growth trajectories in animals, indicating that cortisol may be acting as a signal to prioritize growth, which may also result in deprioritizing other aspects of development, including behavioral temperament (Dantzer et al., 2013; Hinde et al., 2014). Faster infant growth has been associated with earlier age at menarche in females, further signifying a faster life history trajectory (Adair, 2001).

Theoretical Framework: Biocultural Approach

Biocultural approaches analyze the interplay between culture and human biology, which simultaneously influence each other. The term biocultural describes a uniquely anthropological approach to research, one that integrates the study of the human culture and human biology in order to create a more comprehensive, holistic picture of the human experience. The power of integrating biological and cultural anthropological approaches is in examining the ways in which biology and culture are interrelated by considering various levels of causal pathways. These levels of causality traverse the proximal level of the biological and cellular to the intermediary level of behavior to the more external environment, including the social environment (Dufour, 2006).

Adaptation is an important concept within biocultural research regarding human health and biology within suboptimal environments in which individuals or populations must deal with stressors such as nutritional deprivation, threat of diseases, extreme climates or high altitudes. Adaptations are traits that give an individual an immediate advantage to survival or reproduction and are shaped by selective forces within a specific environmental context, such as factors that threaten health, reproductive success, or survival (Wiley & Allen, 2012). These selective forces might include predation, infectious diseases, and pathogens, lack of access to food resources, extreme temperatures, or other stressors. Adaptations can be derived from the slow process of natural selection through heritable genetic changes that take place over generations, but human biological adaptability can also take place in form of physiological plasticity, which confers short term, non-genetic changes within an individual posed with an immediate survival challenge (Wiley & Allen, 2012).

Neither heritable nor non-heritable adaptation denotes an optimal or healthy state of being; rather, it is a compromise that is not cost-free or perfect (Fisher, 1985; Wiley, 1992). When physiological plasticity and adaptability occur during critical periods of development, they can result in developmental programming, wherein long-term, irreversible effects result from biological responses to stressors (Waterland & Michels, 2007). Physiological plasticity may include the use of external signals to make predictions about the future environment and to alter growth and development strategies accordingly, which requires reliable cues that the fetus, infant, or child is able to detect, interpret, and react to (Kuzawa & Quinn, 2009). Those alterations may be permanent, such as short stature from stunted growth due to undernutrition (Martorell, 1989; Wiley & Allen, 2012).

Regardless of potential immediate benefits of any perceived adaptation, the resulting growth impairment, pathology, and poor health consequences should be considered (Kuzawa & Quinn, 2009). Some adaptations, while immediately beneficial in surmounting survival challenges, have long term costs that challenge health and survival that might be impactful either immediately or later in life. This premise provides the basis for research on the Developmental Origins of Health and Disease (DOHaD) hypothesis, which is predicated on epidemiological evidence and animal studies suggesting that fetal and postnatal environment impact chronic disease risk, including various forms of cancer and metabolic diseases including coronary heart disease, Type 2 diabetes, and hypertension (Waterland & Michels, 2007). Some adaptations with long term costs may involve epigenetic mechanisms, which respond to extracellular signals such as paracrine, endocrine and nutritional stimuli and may cause heritable changes in gene expression (Waterland & Michels, 2007).

The Value of a Biocultural Approach in the Study of Ramadan Fasting Outcomes

In this dissertation, I looked at the cultural practice of religious fasting, which in the case of Ramadan imposes a strict set of rules about food consumption, water intake, and a variety of other behaviors. Fasting impacts human physiology in a variety of ways, including altering hormonal signals related to metabolism and fluid balance. Using a biocultural approach, I considered the effect culture has on human biology and the effect biology has on culture. I utilized theories, methods, and approaches that have been drawn from both biological anthropology and cultural anthropology. Combining methods and theory of the two subfields provides a deeper understanding and richer contextualization of the topic.

My central hypothesis draws from life history theory, a fundamental theoretical framework within biological anthropology to understand how an organism uses finite resources within a finite lifespan in order to optimize their energetic allowance for growth, development, maintenance, and reproduction. This framework contextualizes the trade-offs organisms make in their life history strategies in stressful environments to increase chances of survival to adulthood, along with the resulting long term consequences (Dantzer et al., 2013). Drawing from methodology from biological anthropology, specifically anthropometry and endocrinology, I will analyze maternal anthropometry, fetal growth via neonatal anthropometry, and the effects of Ramadan fasting on postnatal breast milk cortisol using hormonal assays.

I will also draw from cultural anthropology to contextualize the biological experience of fasting during pregnancy within the sociocultural experience. Through questionnaires, I will investigate reasons for fasting or for opting out of fasting, advice received from family members about fasting, and other lifestyle and environmental related questions that may affect maternal and infant health and wellbeing. Through these questionnaires, I hope to gain insight into how women experience this month of fasting.

Ramadan is not simply a biological experience of food and water abstinence. Whatever the biological implications of fasting during pregnancy and lactation, they are embedded in a complex practice deeply engrained in culture and religion, and therefore they cannot be fully understood apart of the sociocultural environment. Results from studies on the impact of Ramadan on maternal and infant health have been used to make recommendations about whether pregnant and lactating women should fast, and these recommendations come from many sources both locally and globally, including public health professionals and Islamic scholars. The fact that data resulting from this research could also be used in this way makes it even more critical to integrate important aspects of the religious, cultural experience of fasting.

Ramadan Fasting During Pregnancy

شَهْرُ رَمَضَانَ الَّذِيَ أُنزِلَ فِيهِ الْقُرْآنُ هُدًى لِّلنَّاسِ وَبَيِّنَاتٍ مِّنَ الْهُدَى وَالْفُرْقَانِ فَمَن شَهِدَ مِنكُمُ الشَّهْرَ فَلْيَصُمْهُ وَمَن كَانَ مَرِيضًا أَوْ عَلَى سَفَرٍ فَعِدَّةٌ مِّنْ أَيَّامٍ أُ رَ يُرِيدُ اللّهُ بِكُمُ الْيُسْرَ وَلاَ يُرِيدُ بِكُمُ الْعُسْرَ وَلِتُكْمِلُواْ الْعِدَّةَ وَلِتُكَبِّرُواْ اللّهَ عَلَى مَا هَدَاكُمْ وَلَعَلَّكُمْ تَشْكُرُونَ

The month of Ramazan is that in which the Quran was revealed, a guidance to men and clear proofs of the guidance and the distinction; therefore whoever of you is present in the month, he shall fast therein, and whoever is sick or upon a journey, then (he shall fast) a (like) number of other days; Allah desires ease for you, and He does not desire for you difficulty, and (He desires) that you should complete the number and that you should exalt the greatness of Allah for His having guided you and that you may give thanks.

-Quran 2:185 (Pickthall)

أُحِلَّ لَكُمْ لَيْلَةَ الصِّيَامِ الرَّفَثُ إِلَى نِسَآئِكُمْ هُنَّ لِبَاسٌ لَّكُمْ وَأَنتُمْ لِبَاسٌ لَّهُنَّ عَلِمَ اللّهُ أَنَّكُمْ كُنتُمْ تَ ْتانُونَ أَنفُسَكُمْ فَتَابَ عَلَيْكُمْ وَعَفَا عَنكُمْ فَالآنَ بَاشِرُوهُنَّ وَابْتَغُواْ مَا كَتَبَ اللّهُ لَكُمْ وَكُلُواْ وَاشْرَبُواْ حَتَّى يَتَبَيَّنَ لَكُمُ الْ َيْطُ الأَبْيَضُ مِنَ الْ َيْطِ الأَسْوَدِ مِنَ الْفَجْرِ ثُمَّ أَتِمُّواْ الصِّيَامَ إِلَى الَّليْلِ وَلاَ تُبَاشِرُوهُنَّ وَأَنتُمْ عَاكِفُونَ فِي الْمَسَاجِدِ تِلْكَ حُدُودُ اللّهِ فَلاَ تَقْرَبُوهَا كَذَلِكَ يُبَيِّنُ اللّهُ آيَاتِهِ لِلنَّاسِ لَعَلَّهُمْ يَتَّقُونَ

It is made lawful for you to go in unto your wives on the night of the fast. They are raiment for you and ye are raiment for them. Allah is Aware that ye were deceiving yourselves in this respect and He hath turned in mercy toward you and relieved you. So hold intercourse with them and seek that which Allah hath ordained for you, and eat and drink until the white thread becometh distinct to you from the black thread of the dawn. Then strictly observe the fast till nightfall and touch them not, but be at your devotions in the mosques. These are the limits imposed by Allah, so approach them not. Thus Allah expoundeth His revelation to mankind that they may ward off (evil).

-Quran 2:187 (Pickthall)

Fasting for the duration of the month of Ramadan is one of the five pillars of practicing Islam. Ramadan is the ninth month of the Islamic calendar, which follows a lunar rather than solar cycle and therefore occurs approximately 11 days earlier each year. Because it is practiced all around the globe and at varying latitudes, the time between sunrise and sunset varies extensively by location and year. Ramadan fasting includes abstinence from eating, drinking, sexual activity, immoral actions, and impure thoughts, among other things, from sunrise to sunset each day of the month. Children are not expected to fast but will often practice by fasting some days or partial days and gradually increase the number of days and duration that they fast. The ages at which they begin practicing and fasting throughout the month vary by region, but full fasting is expected around the age of puberty. Individuals who cannot fast, which may be due to illness, traveling, being elderly, or, for females, during menstruation, can make up the days they could not fast later. If the days cannot be made up, such as is the case with chronic illnesses, other options are available such as giving charity.

An exemption to maternal fasting comes from the Hadith Sharif, considered a primary source of Islamic law, which states: "If a pregnant women fears for herself (i.e., for her health) or the breastfeeding woman fears for her child in Ramadan, they should break their fast and feed a poor person for each day (they miss) and they do not have to make up the fast" (Hallaq (2007, p. 550) qtd. in Kridli (2011)). The passage specifies that this exemption is for women who believe fasting may be harmful to herself or her child. Some religious leaders and scholars argue that fasting is obligatory during pregnancy so long as the pregnancy is healthy (Joosoph, Abu, & Yu, 2004). It is generally understood that compensatory fasting later is still required, and charity is an option when fasting later is not possible, as with sick individuals. The requirement to make up fasting alone later is often given as a reason many women do not take the exemption (Kridli, 2011; Robinson & Raisler, 2005). These factors contribute to the high rates of maternal fasting in the Middle East and North Africa (MENA) region.

The exemption for fasting during pregnancy and lactation are different from the exemption against fasting during menstruation or after giving birth, which is related to religious purity (Ziv, 2006). Post-childbirth, a period of 40 days is usually given in which women are not permitted to fast. Menstrual bleeding and bleeding post-childbirth bleeding are considered events that break that fast, rather than grounds to abstain from fasting (Laway & Ashraf, 2015).

Ramadan Fasting as a Model for Food and Water Scarcity in Human Evolutionary History

The body has mechanisms in place to manage with periods of abstinence from food in order to make the most efficient use of stored energy and protect critical organ function for as long as possible. These mechanisms likely evolved long ago in our evolutionary history to deal with times of food scarcity (Bellisari, 2008). Therefore, it is clear that Ramadan fasting does not likely constitute an evolutionarily novel condition in terms of the body needing to adapt to a lack of access to food and water for several hours. Periods of food shortage and inability to access food or water for a prolonged period of time is likely a part of our deep ancestral biology. When these periods were experienced during pregnancy and breastfeeding, biological cues about maternal ecology that allow a developing fetus or a breastfeeding infant to adapt its life history strategy in preparation for the expected environment would be beneficial if the adaptations increased the probability of survival in the predicted environment (Gluckman, Hanson, & Beedle, 2007).

The practice of Ramadan fasting, however, is not a perfect model to represent past situations of food scarcity. Although some individuals who practice Ramadan limit their food consumption during the hours between sunset and sunrise, thereby consuming fewer overall calories than usual, the opposite is very often observed. Many people eat more during the month of Ramadan than their usual intake during non-Ramadan months. The increase in food consumption at night, along with a decline in activity during the day, is likely to reason weight gain is often observed during Ramadan fasting (Bakhotmah, 2011). Moreover, contrary to the psychological implications of food scarcity, Ramadan is not a psychologically stressful time for most people. It is a holy and peaceful time in which people are often diligent in completing their five daily prayers, which are reported to be mentally soothing and have similar neurological benefits to meditation (Newberg et al., 2014). Additionally, if at any point the fast becomes problematic for health reasons or if circumstances arise that make it difficult to fast such as traveling, the fast can be broken and the days of fasting that were missed can be made up later. This is in stark contrast to the psychological stress that might be experienced in circumstances of food and water scarcity.

It is difficult to assess the degree to which voluntary fasting behaviors were employed over the last 10,000 years or more. As an archaeological question, the practice of fasting is "invisible", as it requires the avoidance of the material culture associated with food (Dietler, 2011). Moreover, this voluntary food restriction is not typically extended to a length of time in which there would be evidence of osteological trauma, and even if there were, differentiating the effects of voluntary fasting from involuntary food insecurity would be impossible (Dietler, 2011). As a religious practice, Ramadan fasting has a history of 1,500 years or less depending on the population, and fasting has been studied by archaeologists when combined with historical evidence within this timeframe (Dietler, 2011; Harlow & Smith, 2001), but beyond a time in which historical evidence is available, what can be known about voluntary fasting practices is limited.

Therefore, it is possible that the stress of fasting in the absence of psychological stress and negative energy balance is evolutionarily novel. If similar situations have not existed in our evolutionary history, an infant may be unable to make a prediction about its future environment and may not have evolved ways to interpret signals that relate to voluntary fasting behavior. An argument for developmental programming requires that the infant receive reliable cues that are predictive of the environment. If signals of the physiological stress of the fasting state are mixed with the presence of an energy surplus and no psychological distress, maternal signals may become confounded and less conducive to programming infant life history strategies. If these deviations from what would be expected in situations of food scarcity characterize Ramadan as an evolutionarily novel dietary pattern, creating an evolutionary narrative for the effects of maternal fasting on fetal life history strategies becomes more complex. Consequences of maternal fasting for fetal growth and development may be obscured due to unexpected maternal signaling for fetal developmental programming from an evolutionary standpoint. Alternatively, if there are no alterations to infant growth trajectories, it is possible that the other aspects of religious fasting offset any signals intertwined with fasting stress.

Still, lack of access to food and water for several hours was likely experienced by many ancestral species throughout our evolutionary history. When it is experienced in lactating females, there were likely adaptations that evolved to help them conserve limited energy and sustain lactational processes. Removing the psychological stress and possibly the reduced caloric intake accompanying the fasting state does not change the physiological reality that the body must confront as it adapts to changing sources of fuel during fasting stages. Moreover, there are known risks associated with restricting caloric intake during the last trimester of pregnancy, including constrained fetal growth and lower birth weight, so Ramadan fasting may provide an ideal model to isolate biological mechanism involved in intrauterine growth restrictions when eliminating the confounding factors associated with maternal caloric restriction.

Some maternal physiological adaptions to fasting, including hormonal shifts, may also be perceptible to an infant in the breast milk. An evolutionary history in which these cues were recognizable and reliable may have allowed for these shifts in maternal physiology to develop into distinct signals and facilitate adaptations in infant physiology as well. The presence of identifiable and reliable signals from the mother may have allowed for infants to make predictive physiological adaptations to enhance their chances of surviving to adulthood (Kuzawa & Quinn, 2009).

Scientific Merit and Broader Impacts of the Present Research

Studying ways in which the fetal environment and milk composition respond to the stress of Ramadan fasting could help answer critical questions about fetal development and lactational biology. Research in this area can help detect maternal factors that influence inter- and intra-woman variation in the intrauterine environment and in milk composition, particularly endocrine and metabolic components, along with the mechanisms by which these channels connecting mother and offspring shapes growth and development during pregnancy and in infancy (Neville et al., 2012; Rutherford, 2009). Ramadan provides a unique context to better understand how the intrauterine environment and breast milk mediate the interaction between maternal socio-ecology and the development of life history strategies during fetal development and infancy, such as how much energy to allocate to growth versus other aspects of development, and how the intrauterine environment and lactational physiology may be adapted to respond to periods of food and water deprivation.

Discerning relationships between infant development and cultural practices bridges the intersection between anthropology and public health. Although the context of this study relates to Ramadan, it may also provide wide-ranging insights into maternal and infant health. It may increase our understanding of how the food and water insecurity, fasting, and the stress response influences fetal and infant growth and development via the intrauterine environment and milk composition. Bioactive components of milk can divert energy toward infant growth away from other areas of infant development, including behavioral development (Hinde, et al. 2014). If maternal fasting influences hormonal mechanisms involved in this process, Ramadan could elucidate key variables in this equation. If cortisol in breast milk increases due to fasting, Ramadan could provide an opportunity to study the association between breast milk cortisol and infant development, including behavioral temperament, a relationship which has been suggested from human and primate studies (Braithwaite et al., 2017; Glynn et al., 2007; Grey, Davis, Sandman, & Glynn, 2013; Hinde et al., 2014; Sullivan, Hinde, Mendoza, & Capitanio, 2011). Moreover, with the current popularity of intermittent fasting as a method to control body weight in the general population, further understanding of the physiological responses to fasting during various life cycles can contribute to the present literature on this topic. A better understanding of the interaction between maternal ecology and offspring growth and development may have implications for dietary recommendations and highlight other environmental constraints that can be addressed by public health policy to improve maternal and infant health.

Although previous research has analyzed relationships between maternal fasting during pregnancy and infant size at birth, these studies have largely focused only on birth weight as an indicator of fetal growth during fasting (Almond & Mazumder, 2011; Alwasel et al., 2010; Arab & Nasrollahi, 2001; Cross, Eminson, & Wharton, 1990; Yamauchi, Higuchi, & Suhaeti, 2009), with the exception of one study that included infant head circumference and length (Ziaee et al., 2010). None have assessed infant weight-to-length ratios or other measures of fatness. Previous studies have been unclear about whether gestational age was controlled for in the analysis, which is an important variable to consider in relation to birth size. They also have not controlled for the duration between the cessation of fasting and the onset of labor in the analysis of birth outcomes. The present study, therefore, expands the array of neonatal anthropometric measurements that have been examined in association with maternal fasting, which is important since infant birth weight does not provide a comprehensive picture of the intrauterine environment. This study also includes an analysis of postpartum breast milk cortisol, which may provide hints as to the maternal hormonal milieu an infant is exposed to postpartum and possibly in utero as well. This potentially adds an additional measure of the environment experienced by the neonate, and if it varies by fasting behavior, this may provide evidence that fasting impacts the fetal or neonatal environment. Increased postpartum breast milk cortisol may indicate that placental corticotropin-releasing hormone (CRH) was increased during pregnancy, as increased placental CRH triggers an increase in maternal cortisol. This has been hypothesized as a mechanism to respond to fetal stress, so elevated postpartum breast milk cortisol may indicate a suboptimal environment in utero (Mclean & Smith, 1999). Neither postpartum breast milk nor mature breast milk cortisol content has been studied in relationship to Ramadan fasting, so this is an additional novel aspect of this study. Additionally, maternal fasting decisions and birth weight in relationship to fasting have been studied in several countries, but this is the first study I am aware of to be done in Morocco.

Islam is one of the world's major religions, so each year many pregnant and nursing women around the world must make the decision about whether to fast or not. As more information becomes available about the biological effects of fasting during pregnancy and breastfeeding, this will aid religious leaders and medical professionals in making recommendations about maternal fasting. It will also increase women's understanding of the physiological processes and constraints she may face if she chooses to fast, providing more knowledge so that women and their families can make better-informed decisions.

Regardless of any effects, positive or negative, brought to light by research on Ramadan fasting on maternal and infant health, it should be recognized that religious fasting is a deeply personal decision that each woman has the right to make for herself and with her family. Public health initiatives can respect a woman's right to make this decision for herself and, for women who opt to fast, identify and encourage behaviors and circumstances that are conducive to safer and healthier maternal fasting. At the same time, they can aim to reduce environmental constraints, behaviors, and conditions that may increase the risk of detrimental outcomes. The holistic, biocultural approach of this study can aid in developing these culturally appropriate risk reduction strategies.

Broad Research Questions

The research that forms the basis of this dissertation broadly addresses the topic of the influence of maternal environment on infant life history strategies. Using Ramadan as a natural experiment, I explored the effects of over 16 hours per day without food and water for up to one month during late pregnancy. I considered the impact this might have on fetal growth and life history strategies. I also considered the possibility that this maternal environmental stressor might be experienced by a woman's offspring via changes in the hormonal milieu. Three specific hypotheses are addressed in this dissertation:

1. Mothers who fast or who fast for a greater number of days differ from women who do not fast or fast for fewer days. Moreover, these differences will also be associated with the outcome variables of interest in this study, particularly infant birth size and maternal milk hormones.
2. If maternal fasting from food and water for 16 hours per day creates a suboptimal intrauterine environment, increased maternal fasting during the third trimester will be associated with reduced infant birth size. Additionally, the duration between the discontinuation of fasting and birth will be associated with catch-up growth.
3. If environmental challenges are communicated to the neonate via variation in breast milk hormones, increased maternal fasting will be associated with increased postpartum breast milk cortisol concentration.

To contextualize the present study, a cultural and regional description of Ramadan and of Morocco follows in Chapter 2. This chapter includes a more detailed discussion of the religious practice of Ramadan fasting, along with relevant regional information from Morocco and the broader MENA region. Maternal and infant health in Morocco will be examined, including environmental and cultural considerations that may affect maternal health, infant health, and maternal fasting decisions.

In Chapter 3, I include a review of the literature to explore the potential biological effects of fasting during pregnancy, drawing on research on fetal and lactational programming. Current research on the effects of maternal fasting during Ramadan on pregnancy outcomes and lactation will be discussed. Ramadan fasting may have different effects on maternal physiology and fetal growth depending on infant sex, maternal anthropometry, and maternal health status, and this potential variation will be explored. Possible mechanisms for interactions between maternal fasting and fetal growth are explored, with an emphasis on cortisol, which has been implicated as playing a role as a mediator between maternal ecology and fetal and lactational programming.

Chapter 4 explicates the study design and methods of the present research, along with details from the preliminary research, an overview of the hospital that served as the primary study location, and an overview of the participants. To parse out the effects of fasting on postpartum infant birth size and maternal milk composition in the present study, the differences between women who choose to fast versus not fast and who feel they can sustain fasting versus those who cannot need to be understood.

Chapter 5 addresses the determinants of fasting behavior. Women who did not fast are compared to women who participated in any fasting, and women who fasted every day of Ramadan that passed before labor are compared to women who skipped days or did not fast. If breast milk cortisol or neonatal anthropometric measurements vary by maternal fasting behavior, it should be recognized that women who fast may be different from women who do not fast in several ways, and these confounding factors need to be accounted for in analyses of fasting outcomes.

If Ramadan fasting during the third trimester of pregnancy is a maternal environmental stressor, does it influence the intrauterine environment? This question is addressed in Chapter 6, which specifically addresses the hypothesis that maternal fasting behavior influences fetal growth or accelerates life history trajectory. This is assessed with gestational age at birth and neonatal anthropometry measurements were taken shortly after birth.

In Chapter 7, I explore whether cortisol appears to be a mediating hormone between maternal environmental stressors and fetal and infant life history programming. If Ramadan fasting during the third trimester of pregnancy is a maternal environmental stressor, information about this stressor would be expected to be perceived via maternal hormonal signaling by the fetus within the intrauterine environment or by the infant through breast milk. Cortisol has been identified as a possible mechanism in this equation for multiple reasons. It plays a role in metabolism and is increased when entering a physiological fasting state (Sareen & Jack, 2013). Animal studies have also identified cortisol as a potential messenger that relays information about maternal ecology to the infant and stimulates adaptations in infant biology in preparation for the maternal environment. Prior to birth, cortisol would be transferred to the fetus in utero, and after birth, it would be transferred to the neonate via breast milk. This study specifically looks at the amount cortisol in the breast milk at 48-72 hours post-partum to determine if it is increased in women who fasted in the days leading up to delivery compared to women who did not.

In Chapter 8, I discuss the interrelationship between maternal characteristics, maternal fasting behaviors, fetal growth outcomes, and variation in postpartum milk cortisol. As a biocultural anthropological study, I consider the interplay between culture and biology that is central to the study of religious fasting during pregnancy. I consider adaptations to maternal fasting during late pregnancy as evidenced by the milk cortisol analysis in Chapter 7 and birth anthropometry outcomes in Chapter 6. I also consider more broadly the social forces that shape women's fasting decisions, including the roles of men at the microstructural level of the home and macrostructural level of writers and interpreters of religious law (Inhorn, 2012). Recommendations for pregnant women considering fasting and their health providers will also be discussed. I will also discuss how these results contribute to the current research, directions for future research, study limitations, and concluding thoughts.

Chapter 2: Background: Ramadan and Morocco

Ramadan fasting occurs around the world, and as such, it is enmeshed in regional expressions of culture and experienced by highly diverse populations. Due to the high degree of variability in populations, environments, and timing of Ramadan, generalizing results of studies on the effects of Ramadan from one population to another is complex, but comparing outcomes across these different circumstances could lead to a rich understanding of human adaptability to food and water abstinence. As a natural experiment, Ramadan provides a unique opportunity to better understand biological adaptations to food and water abstention during pregnancy and lactation with cross-cultural data from a wide variety of environmental contexts.

I begin this chapter by exploring the ways in which the practice of Ramadan fasting varies by regional, seasonal, and cultural factors and an array of variables that relate to maternal fasting decisions around the world. After clarifying several reasons that the practice of Ramadan and fasting decisions can vary, I provide an overview of Rabat, Morocco, where this dissertation research took place. A full understanding of the practice of Ramadan depends on an understanding of the local context in which fasting is taking place, so I then consider population-specific maternal and infant health parameters, including maternal anthropometry, along with a discussion of the local and regional cultural context in which the experience of Ramadan fasting takes place.

Variability in the Practice of Ramadan Fasting

Ramadan is the ninth month of the lunar Islamic calendar during which Muslims around the world participate in a religious fast. Ramadan fasting is one of the five pillars of Islamic practice. The fast includes abstaining from food, water, smoking, and sexual intercourse from sunrise until sunset. Ramadan is about more than the physical experience of the fast. For Muslims, it is considered a time to purify thoughts and behaviors and to build a deeper connection with the divine (Ausma Zehanat, 2018).

In researching the effects of Ramadan on any aspect of human biology, it is important to understand this high degree of variability by year and region and in the populations that practice it. Ramadan is practiced throughout the Muslim world, but the local expression of religious practices can be highly variable as they are enmeshed in local culture and environment. Populations participating in Ramadan are rural and urban, are rich and impoverished, have highly variable diets, practice an array of subsistence strategies, live in diverse climates, and engage in different levels of physical activity. They also vary in how they alter their daily activities to accommodate Ramadan fasting, which leads to variability in work schedules, activity patterns, and sleep schedules. Some people continue with their typical work schedules, while others change them considerably. Due to variation in how work schedules shift to accommodate fasting, some people will sleep several hours during the daylight fasting hours while others will be involved in physically demanding activities.

Physiological implications of fasting are also susceptible to population differences. Populations vary in the prevalence of underweight and overweight individuals, rates of disease and infection, access to resources, access to medical care, and many other factors that can influence how they react physiologically to fasting, their health status, and their vulnerability to nutritional stress. They additionally vary in dietary choices during non-fasting hours, which may be responsible for inconsistencies in study results regarding weight gain versus weight loss during the Ramadan fasting.

Local practices and social norms also impact how this fast influences the health of mothers and children. Whether pregnant and lactating women fast is affected by the statements of regional religious leaders and local social norms. The effect of the fast on children also likely varies locally. They are not yet under a religious obligation to fast but experience an altered food environment during this time. In Morocco, children will often "practice" by fasting for an increasing number of days of the month until they are at an age in which they are expected to fast the whole time, which is generally around puberty.

Another important point of variability is the daily duration of fasting. Because the Islamic calendar is lunar, Ramadan begins approximately 11 days earlier each year and therefore can occur in the summer or winter, depending on the year. Because it is practiced all around the globe and at varying latitudes, the time between sunrise and sunset varies extensively by location and year. From 2015-2017, the month of Ramadan overlapped with the summer solstice, the longest day of the year, in the northern hemisphere. The last time Ramadan occurred over the summer solstice was between 1982-1984. When this occurs, fasting hours lasted about 14-16 hours throughout most of the MENA region, and in places closer to the North Pole, fasting might last for almost 24 hours unless the population decided to observe the same fasting hours as in Mecca, Saudi Arabia, as some do. Due to rising immigration to countries far north such as Denmark, this has been of increasing concern. Conversely, when Ramadan overlaps with the shortest day of the year in the Northern Hemisphere as it last did between 1998-2000, the sun may be up for 7-8 hours in the MENA region and only a couple of hours in locations closer to the North Pole. Table 2.1 lists the dates during which the month of Ramadan occurred or will occur between 2002 and 2022, with an approximate number of hours of fasting per day. When calculating daily fasting duration, note that daily fasting begins at astronomical twilight, which typically occurs one and a half to two hours prior to sunrise, and it ends at sunset.

Table 2.1: Dates of the month of Ramadan in the Gregorian calendar and duration of daily fast in Morocco between 2002-2022

Month of Ramadan	Year	Approximate Daily Fasting Duration in Morocco (hours)
November 5 - December 5	2002	11.5
October 26- November 26	2003	12
October 15- November 14	2004	12
October 4 - November 3	2005	12.5
September 23 - October 23	2006	13
September 12 - October 12	2007	13.5
September 1- September 30	2008	14
August 21- September 20	2009	14.5
August 10 - September 9	2010	14.5
July 31 - August 29	2011	15
July 19 - August 18	2012	15.5
July 8 - August 7	2013	16
June 28 - July 28	2014	16
June 17 - July 16	2015	16.5
June 6 - July 5	2016	16.5
May 26 - June 24	2017	16.5
May 16 - June 14	2018	16.5
(estimate) May 4 - June 4	2019	16
(estimate) April 23 - May 23	2020	15.5
(estimate) April 12 - May 12	2021	15
(estimate) April 1 - May 1	2022	14.5

Notes: The month begins at sundown of the given date and the first day of fasting begins the following morning.
Fasting hours were approximated based on mid-month.

As will be further discussed in Chapter 3, this variability in the duration of daily fasting is biologically significant because it typically takes 12 to 18 hours following a meal for the body to begin to adopt an early fasting state, marked by modifications in energy metabolism and altered hormonal signaling particularly with regards to glucocorticoids, insulin, and glucagon (Sareen & Jack, 2013). It is therefore important to indicate the amount of time spent fasting each day, along with other pertinent details such as the climate and activity level of the population, in studies of the effects of Ramadan. Pregnant and lactating women are under greater metabolic stress than the general population and may respond more quickly or differently to fasting with abstinence from food and water (Prentice, Prentice, Lamb, Lunn, & Austin, 1983; Sellen, 2006). Still, the effects of Ramadan fasting during pregnancy and lactation likely increase with increased fasting duration.

In other words, Ramadan fasting is not one precise practice. Given that the practice of Ramadan is so highly variable, it is understandable that research on its effects produces highly variable results, as will be demonstrated in Chapter 3. Generalizing research results of the effects of Ramadan fasting on any indicator is challenging due to this large variability in the practice by location, year, season, and population being investigated. Research demonstrating minimal effects of maternal fasting when daylight hours are short may not be an accurate representation of the entirety of the practice for all populations, although research results are often portrayed as such.

Rabat, Morocco

Morocco is the country that lies to the furthest northwest of the African continent. On its western coast lies the Atlantic Ocean and to its northern coast the Mediterranean Sea. It borders Algeria and the Western Sahara and is separated from Spain by the Strait of Gibraltar. Morocco is governed by a parliamentary constitutional monarchy and considered a developing country with high rates of unemployment, poverty, and illiteracy. For females, the literacy rate in the country is 59%, and for males, it is 79% ("CIA: The World Factbook: Morocco," 2014).

The country has been invaded and occupied multiple times over the past two millennia, including by the Romans in 50 A.D. and by Muslims from the Arabian peninsula in the 7th century A.D. (Gómez-Casado et al., 2000). The Arabization of the country at the time of the Arab conquest was relatively swift in many areas, with Islam becoming almost ubiquitous and with the introduction of Qur’anic education. Today, the Moroccan population is 99% Sunni Muslim, though the local expression of Islam in the country integrates religious aspects from its Berber heritage, which engenders an Islamic practice with elements of mysticism. Therefore, Moroccan Islam has been considered akin in many ways to Sufi Islam (Islamic mysticism), rather than a “pure” expression of Islam. Islam and Moroccan Islam are not generally considered to be two polarizing forces within the country; rather, they blend and separate to harmonize with the cultural backdrop of the country (Forster & Fenwick, 2015; Geertz, 1969). Even with the rapid Arabization of the country, there remains today a large proportion of Moroccans who identify as being of Berber rather than Arab heritage and linguistic tradition (Benmamoun, 2001). In 1912, the French occupation of Morocco began. French education systems overwrote the previous Islamic education systems, which had been focused on memorization of verses from Islamic texts. The French system introduced more modern academic subjects, such as the sciences (Benmamoun, 2001).

This history is reflected in the languages used within the country. Tamazight (commonly referred to as “Berber” by English-speaking peoples) refers to a set of dialects of the language of the indigenous peoples of Morocco and North Africa. The official languages of Morocco include Arabic, with the local dialect referred to as Darija, and Berber or Tamazight, which comprises several tribal dialects ("CIA: The World Factbook: Morocco," 2014). The country is roughly divided into Arabic-speaking and Berber-speaking regions, with urban areas more likely to be associated with Arabic speaking and rural areas more likely to be associated with Berber-speaking. The language divide in Morocco is entwined with status and power dynamics (Errihani, 2016). Classical Arabic is also used as a formal, institutional language, valued highly for its association with Islam. Since the French occupation, the French language is also used extensively, particularly in administrative centers, in the sciences and medicine, and in higher education (Benmamoun, 2001).

Rabat is the capital city of Morocco. It is located in theRabat-Sale-Kenitra Province on the Atlantic coast and lies 92 kilometers north of Casablanca (Lee, 2018). It is considered the administrative, educational, and cultural center of Morocco. It is home to the major national university, Muhammad V, along with many national research institutes ("Rabat," 2016). There are three main districts within the city, which include the modern quarter built by the French, the Medina or old city, and the Kasbah des Oudaia, which is a seventeenth-century Islamic fortress. The

Moroccan climate is generally subtropical, and as a coastal city, Rabat is dry with moderate temperatures throughout the year (Lee, 2018).

Figure 2.1: Map of Morocco (Htt, 2018)

Factors Affecting Maternal Fasting

During Ramadan, pregnant and nursing women can opt not to fast, but they are required to make up those days later, and many women prefer to fast with their families rather than fast alone later. When unable to fast, women have reported feeling that they are missing a deeply meaningful spiritual experience, disconnected from their communities, guilty, and unhappy about having to fast alone later to make up the days they missed (Robinson & Raisler, 2005). There are a number of factors that influence fasting behaviors, but research of Muslim populations around the world show that most pregnant and breastfeeding women participate in fasting, with rates that vary between 50-90% (Ertem, Kaynak, Kaynak, Ulukol, & Gulnar, 2001; Joosoph et al., 2004; Mubeen, Mansoor, Hussain, & Qadir, 2012; Ozsoy, Adana, & Hazar, 2014; Robinson & Raisler, 2005; Saleem, Afzal, & Saleemi, 2010).

One factor that increases variability in fasting behavior is that the exemption for pregnant and nursing women is interpreted in ways that give different degrees of flexibility to this population, depending on the area. In many places, it is interpreted as fasting being optional for this population (Robinson & Raisler, 2005; Saleem et al., 2010), whereas in others, it is largely considered obligatory to fast if otherwise healthy (Joosoph et al., 2004; Mubeen et al., 2012). In Singapore, religious leaders have stated that fasting is obligatory for pregnant women if healthy, and in surveying the population, 67% of women surveyed believed fasting during a healthy pregnancy was obligatory, 30% believed it was optional, and 3% were opposed to the practice of fasting during pregnancy (Joosoph et al., 2004). In Pakistan, most nursing women are aware that they are exempt from fasting (Saleem et al., 2010), and most (88%) of pregnant women believed fasting during pregnancy was obligatory if there were no complications (Mubeen et al., 2012). In one study, about half of the women reported fasting was harder during pregnancy than when not pregnant, while the other half did not report it to be more difficult, and most women (79%) did not believe fasting is harmful to mother or infant (Joosoph et al., 2004). A high frequency of adverse effects of fasting have been reported by pregnant women but only 24% of them stopped fasting (Joosoph et al., 2004; Mubeen et al., 2012).

In lactating women, even though studies have found that a large majority (59-91%) of women believe fasting causes a decrease in breast milk production (Ertem et al., 2001; Ozsoy et al., 2014; Saleem et al., 2010) and 65% believe that nursing women should not fast (Ertem, et al. 2001), many women who held these beliefs still fasted (Ertem, et al. 2001). A pilot study for the present research was conducted in preparation for the current study in Rabat in the summer of 2015. Nursing women with infants six months old or younger during Ramadan were included in the study. Of the participants, 81% of women fasted, 14% were restricted from fasting due to having an infant under 40 days old or due to vaginal bleeding, and 5% opted not to fast due to concern about milk production and infant health. Increased fasting has also been associated with increased supplemental feeding and reduced exclusive breastfeeding (Ertem et al., 2001), a trend that was observed in the feasibility study as well, as will be discussed in more detail in Chapter 4.

The effect of medical advice on fasting behavior is unclear. In the general population, medical advice against fasting is often ignored (Bachar, Walid, Fatima Al, Khalid Al, & Nico, 2017). However, research suggests that pregnant and breastfeeding individuals may take medical advice more seriously and self-report high compliance with medical advice (Firouzbakht et al., 2013). However, this seems to be more likely the case when medical advice is in reference to specific health risks, rather than general statements against fasting. Women tend to be less receptive if they believe the doctor does not understand their religious practice or are unconvinced of associated risks (Robinson & Raisler, 2005).

Previous research has found that many women who do not fast list health problems as the reason, and these health concerns may be responsible for variation in outcomes rather than maternal fasting behavior per se (Robinson & Raisler, 2005; Saleem et al., 2010). For example, a study from Pakistan found that 57% of nursing women fasted, and of those that did not, about 40% who chose not to fast did so due to health concerns (Saleem et al., 2010).

Family advice against fasting, particularly from the husband, has been predictive of reduced fasting (Joosoph et al., 2004; Robinson & Raisler, 2005). Multiparous women have been repeatedly found to fast more than primiparous women (Joosoph et al., 2004; Mubeen et al., 2012). Among pregnant women in Indonesia, lower maternal BMI, fear of adverse effects of fasting, husband support for not fasting, and having a higher gestational age at the time of Ramadan were predictors of less fasting (Van Bilsen et al., 2016). Reduced fasting has also been associated with increased education (Mubeen et al., 2012). In the United States, immigrants fast more than children of immigrants (Robinson & Raisler, 2005).

It is possible that infant sex may also be important in fasting decision. Culturally, during lactation or during pregnancy, if women are aware of the sex of the fetus in utero, they might make different decisions about fasting, as several populations in the MENA region have documented son preference (Obermeyer & Cárdenas, 1997). If this pattern is seen during pregnancy, it is also possible that it is related to biological rather than cultural influences, as research suggests that there are differences between male and fetal fetuses in terms of circulating maternal hormones, including cortisol (Dipietro, Costigan, Kivlighan, Chen, & Laudenslager, 2011), and fetal responses to intrauterine environment (Thayer, Feranil, & Kuzawa, 2012). It is, therefore, possible that either the maternal experience of fasting or the outcomes of fasting may vary by infant sex.

Maternal and Infant Health in Morocco

When considering possible outcomes of maternal fasting to maternal and infant health, it is important to first acknowledge the state of maternal and infant health for the population being studied. According to statistics from the World Health Organization (WHO), infant and childhood mortality has been declining steadily since 1990 in Morocco. In 2011, per 1000 live births, the neonatal mortality rate was 19, infant mortality before age 1 was 28, and the mortality rate before age 5 was 33. Premature birth was cited as the cause of neonatal mortality (within the first 27 days after birth) in 45% of cases and before 4 years of age in 27% of cases. (WHO, 2013). Percentage of low birth weight infants (defined as less than 2500g) was reported to be 15.3% in 2003 (WHO, 2013), though the reliability of this statistic is uncertain as most women who give birth at home, even those with clinics close by, wait at least a week to bring their children in to the clinic in cases of normal births.

Prevalence of maternal mortality in Morocco has also decreased, falling from about 300 to about 100 per 100,000 live births from 1990 to 2010. Over 80% of these deaths were considered avoidable and happened because of inadequate medical treatment due to insufficient medical follow-up, insufficient treatment, or waiting too long to access care. The leading cause of death directly related to pregnancy is hemorrhage (33% of maternal mortality), followed by pre-eclampsia and eclampsia (18%), infections (8%), and ruptured uterus (7%). Cardiovascular disease was the most frequent indirect cause, responsible for 39% of all maternal mortality, though it is not clear if this is related to pregnancy or preexisting conditions (Abouchadi, Alaoui, Meski, Bezad, & De Brouwere, 2013). This survey of maternal mortality includes an acknowledgment that data is likely missing because there is a high rate of home birthing in Morocco. Although this survey likely accounted for hospital deaths, up to 35% of maternal deaths likely occur at home and data for these deaths is largely unavailable. Deaths during home birth are most common in rural areas with inadequate access to medical care, including prenatal and postnatal care (Abdesslam, 2012).

Maternal and infant health is affected by several factors, including maternal anthropometry and nutritional environment. Morocco-specific details about these suites of variables will be explored. The current study took place in an urban hospital that served women from urban and rural surrounding areas, so the potential influences of urban versus rural living in Morocco will also be discussed as it interrelates to these variables.

Maternal Anthropometry

Maternal anthropometry is related to birth outcomes. The experience of fasting and outcomes of fasting may also be interrelated to variations in maternal body size and composition. Maternal body mass index (BMI), height, and gestational weight gain are important indicators of nutritional status and are associated with pregnancy outcomes. Anthropometry in Moroccan populations varies by urban versus rural living. An overview of what is known about these variables in Moroccan women is provided here.

Pre-Pregnancy BMI

In Morocco, there are high rates of obesity and overweight and the prevalence increases with age. Rates of overweight and obesity increased from 21.7% for those 15-25 years to 36.7% for women 25-35 and to 53.5% for women over age 35. Underweight is much less prevalent, with 6.3% in women between 15-25 years of age and 3.0% in the over 35 age group (Belahsen, Mziwira, & Fertat, 2004; El Rhazi et al., 2010).

Rates of overweight and obesity have increased substantially in the last few decades, especially in urban areas, which will likely lead to new challenges in maternal and infant health (Benjelloun, 2002; El Rhazi et al., 2010). Women living in urban settings are more likely to be overweight or obese, with 50% of urban women having a BMI over 25 compared to 37% of rural women. Twice as many women who live in rural settings compared to urban settings are underweight, categorized as a BMI of less than 18.5, at 7% compared to 3.5%. (Benjelloun, 2002; El Rhazi et al., 2010). Still, risks associated with maternal overweight and obesity are expected to be more prevalent than underweight in either population.

Because women in urban settings are more likely to be overweight or obese, they are more likely than women in rural areas to have large-for-gestational-age (LGA) infants. Obesity and overweight also increase the risk of developing gestational morbidities such as gestational diabetes, hypertension, and preeclampsia. The prevalence of both Type 2 and gestational diabetes in this population is believed to be around 12% (Utz et al., 2017). Due to a higher prevalence of underweight women in rural areas, rural women are at greater risk for delivering SGA infants. Low pre-pregnancy BMI has been modestly associated with an increased risk of preterm birth, and spontaneous abortion is less frequent in women with a high BMI (Behrman & Butler, 2007, p. 93; Kramer, 2003).

Maternal Height and the Consequences of Stunted Growth

One study of maternal anthropometry of women of childbearing age from the El Jadida Province found that rural women averaged about 2 cm taller than urban women (160.5 ± 5.9 cm compared to 158.5 ± 6.0 cm) (Belahsen et al., 2004), but more studies are needed to confirm this trend in other regions of the country. An area of previous concern regarding height is growth stunting, defined as less than 2 standard deviations below the median height for age. Although there have been steady decreases in the prevalence of stunted growth during childhood, previous high rates of growth stunting may have affected many women currently of childbearing age.

Percentages of children under 5 years of age that experienced growth stunting fell from 29% in 1996-1997 to 23% in 2003-2004 to 15% in 2010-2011, according to the surveys from the Moroccan Ministry of Health (Abdesslam, 2012; WHO, 2013). Most of the women currently of childbearing years would have been born prior to this improvement, so a substantial proportion of Moroccan women may be dealing with consequences of stunted growth on pregnancy outcomes.

Maternal stunting has costs for health and growth of offspring. In low and middle-income countries, shorter maternal stature, used as a proxy for lifetime nutritional status, causes excess intrauterine growth restriction, which has been cited as the primary cause of low infant birth weight in these countries (Kramer, 2003). Maternal height is also significantly negatively associated with higher rates of infant and childhood mortality, underweight and stunting (Ozaltin, Hill, & Subramanian, 2010). Maternal height is positively correlated with infant length for age through the first year of life and negatively correlated with rates of childhood stunting (Dekker et al., 2010; Hambidge et al., 2012). The negative outcome of undernutrition includes short adult stature, impaired cognitive development, and reduced economic productivity. An undernourished individual also has an increased likelihood of having infants with low birth weight, thus perpetuating this cycle (Victora, De Onis, Hallal, Blossner, & Shrimpton, 2010).

Gestational Weight Gain

Adequate maternal weight gain during pregnancy is important for normal fetal growth and development (Stein, Ravelli, & Lumey, 1995), but gaining adequate weight during pregnancy may be a challenge for a large portion of the Moroccan population. In a sample of Moroccan women giving birth in a maternity hospital in the Rabat-Sale-Kenitra region, Mochhoury, Razine, Kasouati, Kabiri, and Barkat (2013) found that 37.6% of pregnant women gained less than 8 kg, as recommended. Most women gained adequate weight, with 55.2% gaining 8-16 kg, and a smaller proportion gained more than recommended, with 7.2% gaining over 16 kg during pregnancy. This may increase the risk of lower birth weight infants. Whether the research on the prevalence of inadequate gestational weight gain in the population was assessed at a time that overlapped with Ramadan is not indicated, but Ramadan fasting as a contributing factor is possible. If the timing of the study did not overlap with Ramadan, clarifying if there are additional impacts of Ramadan fasting would be of interest.

The risk of delivering small for gestational age infants may be exaggerated by a preference for delivering small babies, which has been noted in the Middle East and tends to result in behaviors that may discourage fetal growth, even when recommended by doctors (Good, 1980; Inhorn, 1994). Because of the preference for delivering smaller babies and the ability to act upon this preference to some degree, such as through dietary restriction, there is an increased chance that fetal growth restriction in this population.

Rural Versus Urban Living

In Morocco, there is a disparity between urban and rural health, nutrition, and healthcare access (Abdesslam, 2012). In Morocco, there is an obvious gap in opportunities, health, and nutrition profiles between rural and urban populations. Women from rural regions are almost twice as likely to be uneducated, with an illiteracy rate of 66.2%, compared to 34.7% in urban areas, and have less access to health services, including during pregnancy and birth (Abdesslam, 2012). Data on health and nutritional intake of Moroccan women would suggest that women from rural areas tend to have lower intakes of energy, protein, and several micronutrients (Belgnaoui & Belahsen, 2006) and have higher rates of intestinal parasitic infections (El Guamri et al., 2011; El Idrissi, Lyagoubi, Barkia, Ayoujil, & Mahjour, 1999). It has been acknowledged that preschool children from rural areas are more likely to experience malnutrition-related underweight, wasting and stunting (El Hioui, Farsi, Aboussaleh, Ahami, & Achicha, 2010). However, urban preschool children were more likely to be anemic, and 72.2% of anemic children also experienced stunted growth (El Hioui et al., 2010).

Because of the different ethnic groups in Morocco, genetic differences could hypothetically result in variations in maternal anthropometry and health risk, but genetic evidence does not support this. Morocco is divided linguistically between areas that speak Arabic and Tamazight, a language commonly called Berber. Though both Arabic and Tamazight speaking individuals can be found in rural or urban settings, Tamazight is associated with rural areas (Bureau, 2004). However, genetic sampling has not been able to show any difference between Arab-speaking and Berber-speaking populations in Morocco (Choukri, Chakib, Himmich, Raissi, & Caillat-Zucman, 2002; Gaibar, Esteban, Harich, Kandil, & Fernáández-Santander, 2011; Gómez-Casado et al., 2000). Gómez-Casado et al. (2000) found that the majority of Moroccans are genetically closest to Berbers, and, despite the huge cultural transformation left by Arab invasions in the 7th century A.D., the genetic evidence suggests limited gene flow from the Arabian Peninsula.

Relevant Cultural Considerations

In the MENA region and Morocco specifically, several cultural factors may be important in research on Ramadan, maternal fasting decisions, and fetal and infant growth. Men's roles in maternal fasting decisions may take place at various levels of society, from regulations set by religious leaders to the advice of husbands and family members. Style of dress varies from highly conservative and traditional to European-inspired trends, and choices about dress might have implications for fetal and infant growth. Son preference can influence parental behaviors, and if sex is known in utero, it is possible that variation in behaviors based on infant sex may start in utero. Of course, Ramadan fasting is a religious practice, so it should be contextualized with an understanding of it as a spiritual experience that permeates the mind, body, and spirit. These cultural considerations are discussed more broadly based on the region but data from Morocco specifically is incorporated.

Men's Roles in Women's Health, and Health-Related Decisions

In *The New Arab Man*, Marcia Inhorn maintains that "men's relative superior power and privilege in most societies may have dire consequences on women's lives and reproductive well-being" (Inhorn, 2012, p. 12). The patriarchal structure may influence many women's access to health-related information and health care and their autonomy over health-related decisions. It can also influence the social support and support in childcare that a woman might receive from her husband.

Patriarchy affects women's reproductive health on multiple levels, as men are more often the policymakers, healthcare administrators and service providers within the society and more likely to engage in extramarital sex and to make reproductive decisions within the household (Inhorn, 2012). One of the ways this patriarchal structure can affect women at the macrostructural level is through religious scholars, who continually interpret religious texts and research to make rulings on health-related concerns, which can vary widely between different regions and religious sects (Rispler-Chaim, 1989). Religious leaders and scholars, a domain dominated by men, can have a strong impact on the way their followers view health concerns. Moreover, during Ramadan, scholars often make statements about who should and should not fast.

The gender divide creates a need for different strategies when implementing healthcare and family planning programs. Family planning programs are sometimes seen by men as a threat to the patriarchal system (Hasna, 2003). This reality has been overlooked by externally imposed family planning programs across the Middle East. These programs have often taken a feminist approach, making women the concentration of family planning services and encouraging women to make "independent choices", and overlooking the importance of men's roles in reproductive decisions. After accounting for this factor, many programs began targeting men, demonstrating that a responsible, caring husband protected the health and future of their wives and children through family planning (Ali, 1997). This approach, too, has been criticized as reinforcing the inegalitarian structure (Obermeyer, 1994). However, positive change in women's health may be more likely to result from working with the societal structure instead of fighting against it. By acknowledging men's roles in women's access to care and education and by encouraging awareness and cooperation with men as well as women, more rapid improvements can be made in women's health.

At the microstructural level, men have a lot of influence over medical treatment within the family. Access to medical care is additionally limited for women because a wife often must have permission from her husband to leave the house, including to seek medical care (Manhart, Dialmy, Ryan, & Mahjour, 2000). Because men have more access to resources and more freedom to travel, they are more likely to have access to medical treatment, and their symptoms are often treated with more seriousness than women's, even if they are less significant (Morsy, 1981). Moreover, individual family members typically have less influence over decisions regarding their own medical treatment than the man of the family (Graaff & Francke, 2003).

Compared to men, women also tend to have fewer rights regarding their own knowledge of their diagnosis and less control over their treatment options, which often fall into the domain of the husband or man of the family. The nations of the Sahara have such strong historical roots within this "inegalitarian gender system" that attempting to break this tradition is met with resistance from the state and the family (Obermeyer, 1994). Although in America and Europe, autonomy and full disclosure of diagnosis and treatment are considered a patient's right, this principle is distinct to Western ethics. In many cultures, it is seen as more ethical not to inform patients of their diagnosis, especially if it is terminal or stigmatized, and the family is usually told instead (Lapine et al., 2001). How people handle concerns of patient disclosure and autonomy vary by culture and social context. In Morocco, the patriarchal structure shapes the way medical information is provided to the patient. An example of this is in the case of STIs. Men often insist that a doctor treat their wives for a sexually transmitted infection (STI) without telling her why she is being treated.

However, neither husband nor wife is likely to disclose their diagnosis to their partner because of the seriousness of the repercussions. For one partner to admit to the other that they are infected with an STI is equivalent to admitting adultery. Women stand to lose their economic security, home, and status, even though in Morocco married women's risk of STIs are more often indicative of their husbands' extramarital activities. For that same reason, they often don't view themselves as susceptible to STIs (Manhart et al., 2000).

The role of men in fasting decisions has been observed at various levels. Religious leaders are predominantly men and often advise on and make statements about whether pregnant women should fast. An Islamic religious leader of Singapore, for example, ruled that it is obligatory for pregnant women to fast if the pregnancy is healthy (Joosoph et al., 2004). Previous studies on determinants of fasting have noted that advice of husbands is significantly predictive of fasting during pregnancy and breastfeeding (Joosoph et al., 2004; Robinson & Raisler, 2005; Van Bilsen et al., 2016). In the feasibility study, the only participant who broke fast for a considerable number of days for reasons other than vaginal bleeding said she did so at the request of her husband when she became sick. Many women also said that their husbands told them that they should do whatever felt right to them regarding their decision to fast during breastfeeding.

Conservative versus Modern Dress, Veiling, and Vitamin D

Conservative clothing covering most of the skin is typical for females, but this varies regionally and from rural to urban setting throughout Morocco. In Rabat, one is likely to see a full range of clothing styles on women, from tank tops and tight jeans, more modest and loosely fitting European-style clothing, to the traditional conservative Moroccan jilaba, with or without a hijab (the veil that covers the head), and, although rare, fully garbed in a niqab, which covers her entirely with only a small slit for the eyes. The style of dress a woman chooses can have a wide range of meanings that may speak of her personal beliefs and worldview, her interest in modernity and

European lifestyles, her family environment, her social circle, and her job, to name a few. There is quite a bit of regional variability in ideals of modesty, especially in larger cities where the entire range of dress is used, but the traditional jilaba with the hijab, which leaves the hands and face exposed, is most common.

The interplay between European trends and conservative Moroccan dress, between Western influence and Islamic ideals, between modernity and convention, and between mass media and tradition have generated a unique expression of fashion in contemporary Morocco that is intimately tied to sociocultural constructions of identity, a topic explored in detail by anthropologist M Angela Jansen (2015) in *Moroccan Fashion: Design, Culture and Tradition*. While living in rural Morocco as a Peace Corps Volunteer, the women I knew who wore a full niqab did so because their husbands required it, although (or perhaps because) prior to marriage they were not known to be especially conservative in their dress or behavior. Other women who commented on this told me that they did not consider these women's husbands to be good men because of their strictness toward their wives. Although almost all women in the rural area where I lived wore the hijab, some women I knew from cities did not wear it for a variety of reasons. For example, one woman I knew who did not wear it said she simply had no family pressure to do so, so it was just not something she ever had to decide to do. This woman is fluent in English and French, has family that lives internationally, and has spent much of her adult career working with American and Europeans in Morocco. She also grew up in Rabat, which is a more liberal city where it is not uncommon to see Moroccan women without the hijab and where there is very little harassment compared to other cities. Another woman told me that she knew too many women who wore the hijab and used it to cover inappropriate behavior, and she would rather symbolically wear it in her heart and with her actions.

The issue of dress may have implications for the present research. There are some areas of Morocco where it is more common to see women wearing less conservative clothing, which is more common in some cities. In Rabat specifically, while the city center has areas that are less conservative, there are also areas within the city and in the surrounding region where it is less common to see women in non-traditional clothing. Conservative dress has been demonstrated to predict serum levels of vitamin D, along with supplemental vitamin D intake (Alagol et al., 2000; Javaid et al., 2006; Mishal, 2001; Nabulsi, Mahfoud, Maalouf, Arabi, & Fuleihan, 2008). In the Middle East and North Africa, vitamin D deficiency has been the subject of some concern due to limited sun exposure with traditional styles of dress. Maternal vitamin D deficiencies may impact childhood health and growth.

Middle Eastern dress has been associated with poor infant growth outcomes. A study by Nabulsi et al. (2008) found that maternal veiling and socioeconomic status affected skeletal development in sons, as measured by bone mineral content and bone mineral density of the lumbar spine, femur, and total body. Lower socioeconomic status was strongly correlated with veiling and was the strongest predictor of poor skeletal growth in all children but after controlling for socioeconomic status, male children were significantly affected by veiling. The reasons for this significant finding for boys but not girls may have been due to the low power of the study, but the results are consistent with other research that suggests a gender difference in the role of vitamin D on development of bone mass, including sexual differentiation in vitamin D receptors that impact gains in fetal and infant weight and length (Suarez, Zeghoud, Walrant, Garabédian, & Rossignol, 1997). Rickets is the result of severe vitamin D deficiency and has seen a recent resurgence in North America among infants of darker-skinned or veiled mothers who breastfeed exclusively. This further suggests that veiling plays a role in maternal vitamin D status and offspring growth (Dror & Allen, 2010).

Maternal vitamin D deficiency has a prevalence of 30-70% in veiled populations at various latitudes (Dror & Allen, 2010). In Morocco, veiling was one of the strongest predictors of vitamin D deficiency (Fadoua et al., 2009). One study from Turkey found that 60% of women wearing this hijab and 100% of women covering everything including the face and hands had hypovitaminosis D (Alagol et al., 2000). In Jordan, the prevalence of hypovitaminosis D was significantly related to the conservativeness of dress. In the summer, women wearing the niqab had an 83.3% prevalence, among women wearing the hijab had 54.5% prevalence, and women wearing "Western-type dress styles" had a 30.8% prevalence. All women had comparable risk in winter of 75-82%. For comparison, men's risk was 18.2% in the summer and 45.5% in the winter. The prevalence of hypovitaminosis D was lower in the summer in all groups except the group of women remaining fully covered (Mishal, 2001). In a Lebanese population, 83.9% of women had hypovitaminosis D, and 61.8% of veiled women had severe hypovitaminosis D (Gannagé-Yared, Chemali, Yaacoub, & Halaby, 2000).

Consequences of maternal vitamin D deficiency during pregnancy may impact both pregnancy and long-term infant growth. Low serum vitamin D status may increase the risk of poor pregnancy outcomes and fetal development. Correlational studies suggest that vitamin D deficiencies may be related to the development of preeclampsia, gestational diabetes, birth complications, and poor childhood health outcomes (Dror & Allen, 2010). Research has also correlated maternal vitamin D status during pregnancy to long-term outcomes in her offspring's bone development. In a longitudinal study of maternal vitamin D status and bone mineral content of children, women with vitamin D deficiencies during pregnancy had children with significantly lower bone mass by age 9, along with lower weight, fat mass, and lean mass (Gale et al., 2008; Javaid et al., 2006). However, studies on the effect of maternal vitamin D status during pregnancy have been correlational, so other factors may play the causal role, and the mechanism behind the associated risks may not have a direct mechanism involving vitamin D (Brannon, 2012).

As increased fasting and conservative dress may both be expressions of religious devotion, they are predicted to be connected. This is suggested by research of Muslim populations in the United States. Kopp (2002) found a direct relationship between religious practice and modest dress. Fahmy and Mohamed (2018) found that the importance placed on religious practice was predictive of fasting behavior during Ramadan. Given the associations between dress, vitamin D and fetal growth, the possibility that dress may be variable that is related to both fasting behavior and fetal growth should be accounted for when considering the effects of fasting on outcome variables.

Son Preference

Obermeyer (1996) demonstrated a moderate preference for sons exists in Morocco. Drawing from data from the Demographic and Health Surveys, son preference quantified by mothers' ideal number of children, stated a preference for having sons, desire for additional children based on the existing children, and reported contraceptive use in relation to the number of existing children of each sex. For any given family size, the proportion of women who wanted more children was always lower if there were more boys than girls, suggesting that the desired number of sons may be more prominent than the desired number of total children. Urban living, exposure to television, a higher standard of living, and more modern marriage practices (for example, married couples that were not first cousins) all decreased the degree of son preference as indicated by these proxies. In Morocco, the mother's education was negatively associated with son preference, but the father's education was positively associated.

Based on my own experiences living in rural Morocco, I believe son preference may not be well-captured by the proxies used in this population and therefore that it may be stronger than the study results suggest. In my experience, although mothers often expressed a strong desire for daughters, this was because daughters help around the house, but it was still the sons that received preferential treatment. Mothers wanted daughters because if they have no daughters, they must do all the housework themselves. The more sons they have, the larger the household and the more work they have. So, although sons are often given preferential treatment, parents may not overtly express a preference for male infants, especially mothers. Son preference may be indicated in other ways, such as access to resources and treatment, rather than an overt expression of parental preference. Also, the expected behaviors of sons versus daughters differed, even at very young ages. For example, I rarely saw male toddlers told "no", but the behavior of females was more contained at the same age. In the area where I lived, it was also customary to refer to women by the names of their first son as a title (similar to "Mary Mother of Jesus"), suggesting their sons are an important part of their identity.

Son preference can have significant effects on infant health, as resulting preferential treatment may influence access to nutritionally adequate diet or medical care, for example. Although there is increased fetal and infant mortality in males when faced with environmental stressors, cultural practices may be moderating exposure to stressors in males. This may be why many studies have found little difference between male and female morbidity in preschool years and a greater difference in morbidity in developed than underdeveloped countries (Stinson, 1985). With contemporary access to technologies allowing fetal sex to be known prior to birth, differential treatment could begin during pregnancy.

Religious considerations

Ramadan fasting takes place within the local sociocultural environment in which it is practiced. Therefore, the practice should be contextualized within religious ideals that permeate local worldviews, the concept of the body and the local ethnomedical structure. Fatalistic attitudes and the interconnectedness of body and spirit have been considered part of Arab culture and influence how medicine is practiced. Islamic fatalism, which ascribes events and outcomes to divine will with limited ability to alter circumstances through the will or actions of individuals, has been cited as an obstacle to progress, passive, irrational, and anti-science, but Hamdy (2009) argues that fatalism is not laziness or a passive outlook but an active approach that must be continuously practiced, and that people must constantly remind themselves, or be reminded by others, that will of God is never without purpose. Rather than feelings of anger, frustration, and helplessness, the reminder that God is behind all struggles and submission to God's will helps create "steadfastness, fortitude, and ultimate gratefulness" (Hamdy, 2009). As an example, some religious interpretations say that there is no fault in being sick and that a person who is sick is not responsible for their condition. They are being tested and purified and will be rewarded if they "bear their ordeal patiently" (Adib, 2004).

Pregnancy and infertility are no exception to this viewpoint. In her ethnographic analysis of infertility treatment in Egypt in *Quest for Conception*, Inhorn (1994) describes the dominant belief is that it is God's will whether or not a woman will become pregnant and whether any ethnomedical or biomedical remedy will work. However, this doesn't stop women from pursuing every available option, because it is accompanied by the belief that God created the medicine and leads people to it, and it is their responsibility to exhaust all possibilities. "To cease this quest prematurely is, in effect, to admit doubt in God's wisdom and his ability to grant children to whom he wishes at times designated only by him" (Inhorn, 1994, p. 244).

This example also illustrates a viewpoint that is important in the debate about whether Islamic fatalism facilitates anti-science rhetoric, particularly within the arena of health and medicine. In the Western medical model, which is concerned with the physical body but not the soul, spiritual beliefs and spiritual healing are considered valuable so far as they do not deny or delay medical treatment or cause physical harm (Adib, 2004). However, the soul and body are not clearly distinguished in the Islamic view of health and the body, Western medicine is often seen as valuable so far as it does not harm the soul. Hamdy (2009) argues that this attitude is not anti-science because it is not in direct opposition with science, and her ethnographic work demonstrates that patients want the best treatment options available, so long as they are in the permissible constructs of religious law. Inhorn and Sargent (2006) also argue that as a whole, the Islamic religion has been pro-biomedicine and encouraging of the use of many medical technologies (Inhorn & Sargent, 2006). "Muslims' attitudes to both types of ethical issues often prove that pragmatism prevails and the aim is to seek a compromise between Islamic heritage and the achievements of modern medicine, as long as basic Islamic dogma is not violated" (Rispler-Chaim, 1989).

Religious leaders are influential in the way their followers view health concerns. Muslims often seek medical advice from their religious leaders, in order to find out what their religion says about a method of treatment or medication. It is important that their medical decisions are in accord with the religious ruling (Rispler-Chaim, 1989). Doctors will also often first consider the spiritual aspects, and their decisions about medical treatment "will sometimes be guided more by ethics derived from Islamic law than by purely medical considerations" (Rispler-Chaim, 1989).

The interconnectedness of the body and soul is a theme that becomes readily apparent in this discussion. "For most of human history, medicine was a branch of religion and its practice a deep and sacred mystery" (Paul, 1977). In Western biomedicine, physical health and spiritual health are most often treated as distinct entities. There are hospitals for bodies and places of worship for the soul. However, in the Middle East, the interconnectedness of spiritual and physical health cannot be overstated; the mind-body duality that permeates Western medicine is nonsensical from this conceptualization of the body (Morsy, 1981). Though not typically considered part of the Islamic faith, this health belief model has ancient roots in indigenous beliefs in the supernatural, which still play a part in the concept of health in much of the Arab world. It is why people wear amulets to protect against the evil eye or malevolent spirits, which are believed to cause all sorts of maladies (Darity, 1965; Masquelier, 2009). When doctors are inaccessible or if a health problem is believed to be especially related to the spirit realm, traditional healers are often sought.

The spiritual realm constantly influences the physical. This is an important part of understanding the experience of Ramadan: it is a time of cleansing and purifying the spirit. Although an obligation, fasting is not viewed as a hardship. Rather, it is valued as an important part of spiritual, psychological, spiritual and social wellbeing (Robinson & Raisler, 2005). Research suggests that most women (79%) believe that fasting does not pose a risk to mother or infants (Joosoph et al., 2004) and are often unconvinced of risks associated with fasting (Robinson & Raisler, 2005). Most (67%) women also report believing that fasting is obligatory in healthy pregnancies if no risk is perceived (Joosoph et al., 2004). This is probably why blanket prohibitions against fasting during pregnancy are often rejected (Robinson & Raisler, 2005). Fasting is expected as the norm, so unless there is a reason to perceive fasting poses a risk before attempting to fast, most women will at least try and see how they feel (Robinson & Raisler, 2005). For Muslims, spirit and body are interconnected, and the impact of the fast on the body is interrelated to the purifying effect of the soul. Anyone interested in the expression and practice of the Ramadan fast should be aware of these powerful themes of acceptance of divine will and the interconnectedness of body and spirit that permeates this religious experience.

Summary

Several variables influence biological outcomes associated with fasting, including the duration of daily fasting, which varies by year and location, and populations that practice Ramadan vary in the climate they are exposed to, health concerns, and cultural norms. With an appreciation for the variability of the practice of Ramadan fasting around the globe and local factors specific to Morocco, discerning potential biological effects of maternal fasting on birth outcomes and lactation is more effectual. In Chapter 3, I discuss potential biological implications of maternal fasting, framed by research on fetal and lactational programming, and research currently available on pregnancy, birth outcomes, and lactation in relation to Ramadan fasting.

Chapter 3: Biological Implications of Fasting during Pregnancy and Lactation: A Review of the Literature

Understanding how life history strategies and health risks are shaped by culture is a central question within biocultural anthropology (Wiley & Allen, 2012). In early growth, including in utero and through childhood, under what conditions is it more beneficial to grow faster and possibly reach maturity earlier? What biological mechanisms are responsible for shifting the allocation of energy toward growth in these circumstances, and what are the short-term and long-term consequences? Specifically, when pregnant and lactating women enter a fasting state prompted by food and water abstinence, is this physiological stressor perceived by their infants via biological signals, and if so, does this result in a corresponding alteration in the infant's life history trajectory?

When confronted with challenges and stressors, the body adapts. However, adaptations that help survive immediate threats do not necessarily come cost-free. Adaptation does not imply a perfect fit with the environment; it requires trade-offs. Environmental stressors experienced during early life, including pregnancy and infancy, may lead to trade-offs and adaptations with long-term consequences, particularly if the trade-off causes a disruption in critical periods of fetal and infant growth and development. Moreover, many early-life critical periods coincide with stages when the fetus is supported by the placenta and the exclusively breastfed infant by breast milk, so these mediums provide an opportunity for information about maternal ecology to be transferred from mother to infant (Kuzawa & Quinn, 2009).

During maternal fasting, resources may be temporarily compromised, and short-term adaptation may be necessary to conserve energetic reserves, maintain physiological function, and support reproductive success. Research on maternal fasting during Ramadan can provide a valuable opportunity to further understand fetal and lactational programming, including a more in-depth understanding of mechanisms at play.

In this review of the literature, I first provide an overview of the theoretical framework that forms the basis of these questions, drawing primarily on the literature concerning fetal and lactational programming, including how these frameworks may give insight on expected outcomes of maternal fasting during Ramadan. I then explore the ways in which this fast is likely to impact biological function, with an emphasis on pregnancy and lactation. Physiological responses to fasting, water deprivation, and reduced nutritional quality of the diet are discussed in detail. Along with other religious facets of the fast and variation in the local culture, environment, and timing of the fast discussed in Chapter 2, these variables comprise several ways in which altered physiological responses and biological outcomes may be predicted vary with Ramadan fasting.

Next, I discuss more specific outcome variables that may be of interest in relation to maternal fasting as indicated by the literature on fetal and lactational programming. During pregnancy, these outcomes include early pregnancy loss, variation in the length of gestation, and fetal growth as assessed by birth anthropometry. During lactation, these outcomes include the influence of fasting on milk nutrient content, milk endocrine content, with an emphasis on the role of cortisol, and milk production. Finally, I review the current research on the effects of Ramadan fasting during pregnancy and lactation and contextualize these findings within the milieu of other literature on fetal and lactational programming.

Fetal Programming

Fetal programming refers to the concept that the intrauterine environment influences fetal development, and when stressors arise during critical periods of development, there can be long term consequences for health (Godfrey & Barker, 2007). This work arose from the Developmental Origins of Health and Disease (DOHaD) literature, which provides insight into what responses might be observed when other nutritionally and physiological stressors overlap with critical periods of development during gestation and early life.

Barker (1992) first proposed that adverse environments during critical periods of development, which include in utero and during infancy, have long-term adverse effects. This was demonstrated through the relationship between adult risk of cardiovascular disease and reduced growth in utero and during infancy. He further proposed that risk factors were dependent on when during pregnancy or infancy exposure to a stressor (such as growth restriction) occurred and which critical period of growth and development it coincided with. He demonstrated that markers of cardiovascular disease varied by the timing of the exposure to a stressor, such as reduced growth. Blood pressure in infancy and adulthood is inversely associated with infant birth weight, maternal gestational weight gain, smoking, physical activity, height, parity, and body fat (Barker, 1992; Barker, Osmond, & Law, 1989; Wadhwa, Buss, Entringer, & Swanson, 2009). Barker (1992) also identified a critical period of liver development during the first year of life based on alterations in plasma marker controlled by the liver.

Research on the outcomes of the Dutch Hunger Winter provides evidence of trimester-specific exposure outcomes of maternal stressors and malnutrition that may be relevant to studies of maternal fasting (Heijmans et al., 2008; Lumey & Van Poppel, 1994; Stein et al., 1995). First-trimester exposure did not result in low birth weight offspring, but in adulthood, these individuals had increased risk obesity, and for females, of delivering preterm and having offspring with lower weight at birth (Lumey & Van Poppel, 1994). Epigenetic changes were also observed in individuals who were exposed to the famine early in utero. Heijmans et al. (2008) found less DNA methylation of the insulin-like growth factor II (IGF2) gene was observed in individuals exposed periconceptually compared to their unexposed siblings. Alternatively, third-trimester exposure resulted in infants with lower birth weight but lower risk of other consequences in adulthood, including obesity or epigenetic changes in IGF2 (Heijmans et al., 2008; Lumey & Van Poppel, 1994). Studies on exposure to stressors in the prenatal period further demonstrate an increased likelihood of developing the suite of characteristics associated with metabolic syndrome and altered immune, endocrine, and cognitive functions (Wadhwa et al., 2009).

Since the data demonstrates that disruption at different points in fetal and infant development present different risk factors later, this evidence of fetal programming demonstrates that exposure to similar stressors can have wide-ranging effects, the most severe of which may be suffered by those exposed in early pregnancy. It also provides an explanation for why indicators of chronic diseases, such as blood pressure and plasma glucose concentrations, often correlate to each other but do not coincide. This body of research further demonstrates that stress influences fetal programming, but that birth weight, although easily accessible and a valuable indicator of fetal growth, is not an adequate proxy to understand the intrauterine environment or the consequences of in utero exposure to stress and malnutrition.

Developmental responses to stressors may have benefits to immediate survival, even if there are long term consequences. For example, elevated fetal blood pressure could increase placental perfusion and then persist after birth (Barker et al., 1989). Although some responses may be immediately beneficial for survival, other adaptations may be in anticipation of the future environment. Gluckman and Hanson (2006) propose that the fetus develops adaptively in response to environmental cues in utero based on what may be most helpful to survival in an anticipated environment. If cues are indicating reduced nutrient availability, it may be more beneficial to be smaller in size, for example.

Research from this field allows for some hypotheses about the effects of maternal fasting during pregnancy. As demonstrated by studies of the Dutch Hunger Winter and other situations of maternal exposure to suboptimal environments during pregnancy, there may be long-term effects of exposure to maternal fasting while in utero, and these consequences will not necessarily be captured by studies of birth weight (Heijmans et al., 2008; Lumey & Van Poppel, 1994). If Ramadan influences fetal development similarly to studies of famine, in utero exposure to maternal fasting during the first trimester is not expected to be correlated with low birth weight but may have several consequences for later adult health, including cardiovascular function, epigenetic changes that influence growth and glucose metabolism, risk for obesity, diabetes risk, neurocognitive function, and later reproductive success (Brown & Susser, 1997; Heijmans et al., 2008; Lumey & Van Poppel, 1994; Stein et al., 1995). Birth weight would be more likely to be reduced if exposure occurs during the third trimester (Lumey & Van Poppel, 1994). Evidence from the Dutch Hunger Winter would also imply that the consequences of fasting on birth outcomes may be moderated by maternal weight gain (Stein et al., 1995). If maternal weight gain is restricted during Ramadan, as was observed by Prentice, Prentice, Lamb, et al. (1983), or if birth weight is reduced due to maternal fasting, it would be predicted that infants would be at a greater risk of fetal programming for higher blood pressure and associated health risks. If Ramadan triggers an endocrinological stress response, this may increase the risk for later life development of metabolic syndrome and less efficient immune, endocrine, and cognitive functions (Wadhwa et al., 2009). Length of gestation and fetal growth are influenced by placental corticotrophin-releasing hormone (Wadhwa et al., 2009), so if Ramadan triggers an endocrinological stress response, this may increase risk for shorter gestation period and preterm birth, defined as labor prior to 37 weeks gestation. These findings and other will be explored further throughout this chapter to contextualize current research on maternal fasting within the broader literature of fetal programming.

Sex Difference in Fetal Response to Exposure to Stressors

Birth outcomes vary by infant sex. Male fetuses are more vulnerable to spontaneous abortion, defined as fetal deaths prior to the 28th week of gestation. Females are more likely than males to survive stressful conditions in early gestation (Stinson, 1985). This forms the basis of the Trivers-Willard Hypothesis, which predicts in times of stress, the sex ratio will move away from 50/50 split in favor of females, while in times of plenty, the ratio would favor males, as it would be more advantageous to produce female offspring for parents in poorer conditions, whereas male offspring would be more advantageous for parents in better conditions (Trivers & Willard, 1973). Interestingly, evidence from the Dutch Hunger Winter does not suggest this famine caused altered birth ratios. By analyzing birth records from three birthing institutions in the western Netherlands from 1943 through 1947, Stein, Zybert, and Lumey (2004) found that there was not a decrease in the male-to-female ratio of live births during the Dutch Hunger Winter, as would be suggested by the Trivers-Willard hypothesis. In fact, the ratio increased somewhat.

Maternal anthropometric differences influence male size at birth more than females (Stinson, 1985), but research indicates that response to maternal nutrition during pregnancy varies by sex as well. Height approximates lifetime nutritional status and body mass index (BMI) signifies current nutritional status. Males appear to be more responsive to a mother's current nutritional status, reflected in maternal BMI, and more affected by malnutrition during pregnancy, while females appear to be more responsive to lifetime nutrition, reflected in height (Alwasel et al., 2011). Studies of the prenatal period support the hypothesis that males are less buffered than females against environmental stress during growth and development. During fetal growth, males respond more strongly to nutritional supplementation, and females usually have greater postnatal catch-up growth (Stinson, 1985). This suggests that female fetuses may fare better during nutritional deprivation of Ramadan than male fetuses. Males are also more strongly affected by intrauterine exposure to nutritional deficits. For example, spina bifida, normally more prevalent in girls, affected males more often if in utero when their mothers were pregnant during the Dutch Hunger Winter (Brown & Susser, 1997). In healthy pregnancies, however, males are overall larger in size at birth compared to females (Dipietro et al., 2011; Van Ewijk, 2011).

Additionally, in the first week after birth, male mortality exceeds female mortality. One reason for this may be the fact that males have less mature lungs for gestational age than females (Stinson, 1985). Male and female infants have different growth curves, but their growth may also be impacted differentially by environmental factors. Studies of high SE class children suggest that female growth may be more impacted by genetic factors while male growth, including male body fat levels, may be more strongly related to environmental factors (Stinson, 1985).

Cortisol is one possible hormone linking maternal stress and metabolism to differences in birth outcomes by sex since circulating maternal cortisol follows a different pattern depending on infant sex. In females, maternal cortisol is lower early in pregnancy and higher in late pregnancy, whereas in males, the inverse is true (Dipietro et al., 2011). High maternal cortisol levels are strongly associated with risk of spontaneous abortion, delayed fetal growth and development, low birth weight, attention and temperament problems in infancy, and illness in adulthood (Christian, 2012; Field & Diego, 2008). This may be one mechanism behind sex differences in risk of early pregnancy loss and spontaneous miscarriage. It may also play a role in sex differences in birth anthropometry, higher cortisol is associated with reduced growth and females tend to be smaller at birth (Dipietro et al., 2011).

Lactational Programming

Lactational programming refers to the ways that mother's milk contains biologically active components can act as signals for the offspring and shape offspring development (Grey et al., 2013). Breast milk is an intermediary between mother and infant and its components may play a role in infant life history programming. Maternal physiological adaptions to fasting may alter the non-nutritional components of breast milk in a way that influences fetal and infant metabolism, appetite, immune response, development, behavior, and growth. Mother's milk is more than just liquid with essential nutrients. The milk of each species is unique and reflects the evolutionary history, current ecology, and infant growth and developmental trajectories specific to that species (Hinde & German, 2012). Macronutrient composition differs across species, but milk also contains immunoglobulins, minerals, vitamins, hormones, bacteria and oligosaccharides, and these micro-constituents are important in the neurobiological, cognitive, somatic, metabolic and immune development in infants. An example of co-evolution can be seen with mammalian milk in the case of an important intestinal bacteria for the mammalian gut microbiota, the growth of which is supported by certain oligosaccharides present in mammalian milk (Hinde & German, 2012).

In infancy, mother's milk not only transfers essential nutrients but also acts as a pathway for glucocorticoid signaling which may impact infant growth (Hinde, et al. 2014). Breast milk nutritional composition and endocrine factors, such as cortisol, are intricately related to maternal ecology, including diet, and simultaneously influence infant life history strategies. Breast milk composition is known to be sensitive to maternal diet (Bronner & Auerbach, 2005; Lonnerdal, 1986), but factors responsible for the inter- and intra-women variation are not yet fully understood (Neville, et al. 2012).

Research on Ramadan can help elucidate ways in which distinct maternal dietary patterns influence breast milk composition, but infant growth could be influenced by maternal fasting in various other ways. For example, fasting may alter the quantity of milk produced due to water abstention or shift supplemental feeding practices. Research on the effect of fasting on the nutritional and endocrine composition, quantity of breast milk, and supplemental feeding will be discussed, along with potential influences on infant growth.

Avenues for Biological Impacts of Ramadan Fasting on Pregnancy and Lactation

There are multiple pathways through which Ramadan fasting may result in physiological responses. These include adaptations to abstinence from food for several hours via metabolic hormones associated with the fasting response, physiological adaptations to dehydration due to abstinence from water, and altered diet during non-fasting hours. Abstention from food leads to a physiological fasting response characterized by alterations in metabolic hormones. Of these, cortisol is one metabolic hormone that has been implicated in fetal and lactational programming, so the role of this hormone will be highlighted in the following discussion of the fasting response. Additionally, the water abstinence and associated dehydration that occurs during Ramadan fasting will cause physiological adaptations to maintain homeostatic fluid balance. Although diet during non-fasting hours of Ramadan is not delimited and could potentially remain similar to the typical diet, studies suggest the nutritional quality of the diet is often reduced during this month, so the effects of predicted nutritional alterations on pregnancy and lactation during fasting will be discussed. Diets vary locally and alterations in dietary quality have different implications for pregnancy and lactation. Therefore, the following discussion about variation in nutritional quality during Ramadan will first address pregnancy, with an emphasis on specific concerns within the Moroccan population, and then lactation, with a general discussion about consequences of short-term reductions in maternal dietary quality during lactation.

The Role of Cortisol and Stages of Fasting

One of the main functions of cortisol during fasting is to help maintain blood glucose levels. In its role in the stress response, this function is useful in mobilizing energy in case immediate action is needed (such as fight or flight), and during long periods of exercise, cortisol increases to mobilizes energy stores after others have been depleted (Christiansen et al., 2007). During weight loss and fasting, increased cortisol helps balance blood glucose to protect against hypoglycemia which can negatively affect physiological functions (Breakey, 2015). During fasting, there is an increase of circulating cortisol and in the half-life of cortisol in plasma, and reduced HPA sensitivity to negative feedback (Breakey, 2015).

Cortisol is a metabolic hormone, with direct effects on fat, protein, and carbohydrate metabolism, as increased cortisol can increase the availability of each of these substrates for use as fuel sources (Christiansen et al., 2007). Cortisol stimulates lipolysis, the breakdown of lipids into free fatty acids (Hinde, 2013). Cortisol promotes catabolism of muscle protein as a substrate for gluconeogenesis, so exposure to high levels of cortisol over time may contribute to decreases in lean body mass (Christiansen et al., 2007). In the presence of high glucagon and low insulin levels, such as would occur in the fasting state, cortisol increases the rate of conversion of amino acids to glucose (Sareen & Jack, 2013). During fasting, insulin activity decreases, but increased glucagon, catecholamines, and glucocorticoids promote fatty acid mobilization from adipose tissue, production of ketones, and proteolysis (Sareen & Jack, 2013).

During fasting, there are marked physiological changes that take place within the body. For the first few hours after a meal, the body is able to derive energy directly from the ingested macronutrients. After that, the body enters a post-absorptive state, followed by the fasting state and finally the starvation state.

- *Post-absorptive state* (begins about 3 hours post-meal): During this stage, new sources are needed for fuel. Hepatic glycogenolysis, or the breakdown of glycogen to glucose in the liver, is a major glucose supplier. The onset of gluconeogenesis, the de novo synthesis of glucose, is also seen during this state. Lactate and the amino acid alanine are important sources of fuel. This state ends when glycogen reserves from the muscle and liver are depleted, which occurs approximately 12-18 hours after a meal (Sareen & Jack, 2013).
- *Fasting state* (begins about 12-18 hours post-meal): Glycogen stores have been depleted, so gluconeogenesis is the primary source of glucose during the fasting state. Muscle protein is broken down for amino acids to provide the primary fuel for gluconeogenesis, a shift that is marked by increased nitrogen loss through the urine. Lactate and lipid breakdown also provide some fuel. This shift is mediated by increased glucagon and glucocorticosteroid hormones and reduced insulin levels (Sareen & Jack, 2013).
- *Starvation state* (begins about 48 hours after a meal): When the previously discussed sources of fuel have been exhausted, the body enters a starvation state. During this state, a physiological shift occurs in order to spare body protein, which is critical to prolonging

body functionality. To do this, gluconeogenesis from amino acids subsides and lipolysis is the major energy-generating processes with fat stores becoming the preferential fuel source. There is a sharp increase in the blood levels of fatty acids, which are oxidized by the heart, liver, and skeletal muscle, and of ketones, which are used to fuel the brain. Glycerol is used for gluconeogenesis for red blood cells. Survival during starvation depends on fat stores, though ketosis is toxic and limits how long one might survive even with above average fat stores (Sareen & Jack, 2013).

Many studies on Ramadan fasting simply ask if Ramadan fasting affects the variable of interest, without specifying the time spent fasting, even though it can range from less than 7 hours in the winter to over 16 hours during the heat of summer in the MENA region. Much of the research on Ramadan fasting has taken place when daily fasting duration was less than 12 hours and therefore may be investigating the post-absorptive state, which may be different from results when fasting duration is increased. Therefore, it is important to specify the duration of fasting per day and discuss the generalizability of the results based on variability in fasting duration.

As the body goes through phases when food is restricted, and there will be individual variation for exactly how long it takes to enter a fasting state. Because it takes at least 12 hours and often longer for humans to enter into this early fasting state and the fast can last anywhere from 7-16 hours per day in the MENA region, it is not surprising that studies on "the effects of Ramadan" have not had shown consistent results on metabolic changes accompanying fasting. Results on the "effect of Ramadan" on any indicator is not meaningful without specifying the amount of time spent fasting for the given location and year, which often goes unmentioned. In the study of energetic stress and dehydration, it is also important to specify the climate during Ramadan and the activity patterns of the population, which are also greatly variable.

The fasting state begins after approximately 12-18 hours without food, when the body shifts away from utilizing glycogen stores to primarily amino acids derived from muscle protein. One hormonal change that facilitates this process an increase in cortisol. This fasting state is also marked by elevated circulating glucagon, low circulating insulin, and high urinary nitrogen. This physiological shift out of the post-absorptive state distinguishes what might be considered a normal break between meals and entry into an early fasting state. Individuals will vary in the amount of time after a meal before experiencing this shift in hormonal output and metabolism. Some individuals will experience this shift from the post-absorptive state to the fasting state during a 16 hour fast while others will not.

Due to the fact that pregnant and lactating women are already under greater metabolic stress (Prentice, Prentice, Lamb, et al., 1983; Sellen, 2006), it is likely that they would enter this early fasting state more quickly than other individuals. Research supports this hypothesis. Prentice, Prentice, Lamb, et al. (1983) found indications of accelerated starvation in pregnant and lactating women when fasting for Ramadan, particularly in late pregnancy. A 2006 study of pregnant women in Turkey, when fasting time would have been about 11-12 hours, found that Ramadan fasting increased maternal serum cortisol levels (Dikensoy et al., 2009). Another study on a population in the U.S. suggested that for pregnant women in their second and third trimesters, this shift may take place after an average of 13 hours after a meal. Women whose overnight inter-meal fast lasted over 13 hours had increased levels of corticotropin-releasing hormone (CRH), which stimulates a rise in cortisol (Herrmann, 2001).

Because pregnant and lactating women would be expected, on average, to enter this fasting stage closer to the 12-hour mark, these physiological changes would be expected to be observed after fasting for 16 hours for much of this population. However, considering natural human variation, and this transition may not be observed in all individuals. Therefore, there is a possibility that some individuals, including lactating women, do not enter a clearly marked fasting state with the anticipated increase in cortisol during fasting, even when Ramadan fasting occurs during times of the year when fasting hours are longer than average.

Biological Regulation of Water Balance

Studies of the biological effects of water deprivation are lacking (Wutich & Brewis, 2014) and this research allows for some study of water deprivation and resulting maternal and infant health consequences. Sawka, Cheuvront, and Carter (2005) called water "the quintessential nutrient of life", as it is the primary component of the human body, making up 50-70% of body weight. Unlike any other nutrient, death occurs within days of lack of water (Popkin, D'anci, & Rosenberg, 2010). Dehydration can result from loss of water or salt, together or independently, and the type of dehydration necessitates different strategies for rehydration. Inadequate water intake to replace water loss results in hypertonic dehydration, in which water is lost in excess of salt loss (Jéquier & Constant, 2009), and is, therefore, the type most likely associated with Ramadan fasting.

Water balance can be maintained with high precision regardless of variations in fluid intake or hydration stressors. This is due to neuroendocrine and renal responses to minute changes in body water volume and tonicity and due to behavioral to biological urges, such as the urge to drink due to thirst (Sawka et al., 2005). Homeostatic mechanisms respond to slight changes in plasma osmolarity, stimulating neuroendocrine responses that prompt fluid intake via the sensation of thirst and through the role the kidneys play in regulating water loss and reabsorption and altering urine osmolarity. Negative water balance leads to an increase in osmotic pressure of extracellular fluid (ECF), which stimulates the hypothalamic osmoreceptors and causes the posterior pituitary gland to release antidiuretic hormone (ADH). The sensation of thirst is triggered with both the increased ECF osmotic pressure and secretion of ADH. Kidneys can regulate water loss and reabsorption and can alter osmotic pressure of urine to a considerable degree to respond to slight changes in plasma osmotic pressure (Jéquier & Constant, 2009).

Studies of the effects of dehydration are complicated by the fact that the effects are difficult to separate from heat stress or physical activity or other possible confounders (Popkin et al., 2010), and the interrelatedness of food and water deprivation. Studies of water scarcity are often complicated by the fact that water scarcity tends to be intertwined with food scarcity, and both food and water scarcity occur within the broader framework of resource scarcity (Wutich & Brewis, 2014). However, research has demonstrated several effects of dehydration on cognitive performance and biological function. Cognitive effects include influences on consciousness, alertness, mood, memory, speech incoherence, headaches, and delirium. Effects on physical performance and biological function include influences on the gastrointestinal tract, kidney function, reduced blood pressure, slowed heart rate, reduced blood flow to muscles, extremity weakness, reduced intraocular pressure, and possibly contributes various chronic diseases (Jéquier & Constant, 2009; Popkin et al., 2010). Dehydration also creates osmotic stress, which results in plasma hypernatremia and can result in nutritional stress due to dehydration-anorexia (Ross & Desai, 2005), one of many reasons food and water deprivation are highly interrelated and the effects are often difficult to separate.

Healthy adults regulate water balance well but infants and elderly people are at greater risk for dehydration due to less ability to regulate water balance as precisely (Jéquier & Constant, 2009). Dehydration may also more strongly influence a fetus, as the fetus takes longer to recover from dehydration during pregnancy than the mother. Even after pregnant mothers rehydrate and rebound from the effects of dehydration and both maternal and fetal plasma osmolarity has returned to basal levels, fetal responses to maternal dehydration are prolonged and include elevated hematocrit, plasma arginine vasopressin (AVP), and urine osmolarity (Ross, Sherman, Ervin, Castro, & Humme, 1988).

Although more research is needed, some effects of dehydration during pregnancy on birth outcomes have been observed. Animal studies have found that dehydration stress during pregnancy contributes to reduced fetal growth and small for gestational age offspring independently of nutritional and energetic stress (Ross & Desai, 2005). Animal and human studies also suggest that water restriction during pregnancy may have long-term consequences for the developing fetus, as it may cause alterations in fetal programming to prepare for a water restricted environment. Studies of water-restricted mothers show that offspring have increased salt appetite and blood pressure, more efficient water retention, and reduced physiological responsiveness to AVP due to reduced AVP binding sites on the kidneys, indicating in utero adaptations with permanent effects (Ross & Desai, 2005).

These adaptive mechanisms may be particularly useful in infancy and childhood if there is an increased risk of dehydration in the environment, as young infants are at increased risk of dehydration compared to adults. They have a higher percentage of body water weight at about 75% of weight at birth, less developed ability to excrete solutes and concentrate urine, a high metabolic rate, higher surface area to body mass ratio, and they cannot express their sensation of thirst (Jéquier & Constant, 2009). They also have a lower rate of sweating, although they may be able to dissipate more body heat via dry heat, which may help conserve body water during heat stress. Dehydration may also result in higher increases in core body temperature compared to adults (Popkin et al., 2010). Urine osmolarity of breastfed infants is very low, about 120 mOsm/kg, indicating hyperhydration. This may be due to evolutionary pressure to prevent infant death from dehydration due to diarrhea (Sawka et al., 2005) or the other factors that contribute to a higher risk of dehydration in infants.

Climate plays an important role in water balance and hydration needs, but more information is needed about individual and population-level differences in water intake, water requirements, and the consequences of suboptimal water intake. Research I needed on the effects of living in varied environments and the differential impacts of suboptimal water intake during pregnancy and lactation on maternal and infant health (Popkin et al., 2010; Sawka et al., 2005).

Researching the impact of Ramadan on pregnancy and lactation in the North Africa region, where populations may be better adapted to hot, water-restricted, desert environments, may help to understand how populations better adapted to arid environments respond to water deprivation physiologically, including during pregnancy and breastfeeding (G. Bentley, 1998; Ross & Desai, 2005). Considering Morocco specifically, the Saharan desert and the Atlas mountains cover much of the country; temperatures are moderate near the coast but are otherwise extreme, and the country receives an average of 346 mm of rainfall per year, with almost no rain in the summer months and very little through the rest of the year (Pearson, 2015; World Bank Group, 2015). Although the present research takes place in a coastal region of Morocco, people living in this city come from all around the country, and it is possible that much of the Moroccan population is better adapted to an arid climate and has a better tolerance for water abstention than other populations. Populations that have been acclimatized to desert regions may be better adapted to withstand lower water intake than other populations (G. Bentley, 1998).

On average, lactating mothers produce over 750 ml per day of milk. Peak lactation is considered about three months, at which point 785 ml/day is the average output. Lactation promotes thirst which has been shown to result in a 12-16% increase in fluid intake in American women. Increased fluid intake may be prompted by increased thirst during lactation mediated by oxytocin since it is structurally similar to vasopressin. However, total water intake per unit of energy ingested has not been found to be significantly different between lactating women and nonlactating controls (G. Bentley, 1998).

Adaptations to water abstention during lactation could be further clarified by research on water turnover rates, body composition, milk composition of dehydrated lactating women, and hormonal data, particularly circulating arginine vasopressin (AVP), plasma oxytocin (OT), and serum prolactin (PRL) in relation to thirst and dehydration during nursing. Variation in nursing patterns and behaviors also need to be considered (G. Bentley, 1998). Researching the impact of

Ramadan on lactation may help to understand how populations better adapted to arid environments respond to water deprivation physiologically, including the regulation of lactation (Bentley 1998), and provide insight into lactational responses under conditions of water insecurity (Wutich & Brewis, 2014). It may also provide much-needed insight into biological adaptations under conditions of water insecurity (Wutich & Brewis, 2014), including their effect on the intrauterine environment, fetal programming, and lactational responses.

Reduced Nutritional Quality of the Diet

During Ramadan, there is a potential for decline in micronutrient intake, as those who opt to fast for Ramadan are often observed to have an altered diet during this month and to eat a larger portion of their calories from sugar and fats, leading to a less nutritionally dense diet with fewer micronutrients (Aoyama, 1999; Belgnaoui & Belahsen, 2006; Rakicioglu, Samur, Topcu, & Topcu, 2006). Therefore, exploration of the effects of micronutrient deficiencies during pregnancy may help to identify potential mechanisms that account for variation in birth outcomes in research on maternal fasting. During lactation, milk nutritional composition remains highly stable during temporary reductions in dietary quantity and quality and are therefore less likely to be compromised by maternal fasting than other components of milk or milk production.

Nutrition during Pregnancy in Morocco

Morocco is not a food deficit country (WHO, 2013). On average, pregnant women in both urban and rural areas have adequate caloric intakes; one study estimated energy intakes averaged 3111 kcal in urban areas and 2708 in rural areas, and both populations met or exceeded the RDA for protein consumption (Belgnaoui & Belahsen, 2006). Eighty percent of the average caloric intake in Morocco consists of cereals (primarily wheat), oil and refined sugar (Mokhtar et al., 2001). Although caloric intake is sufficient, the consumption of some micronutrients may be inadequate during pregnancy. Using statistics from national surveys and the results of a food frequency questionnaire and epidemiological statistics on disease prevalence, micronutrients that are potentially deficient in the diet of pregnant women include folate, calcium, zinc, iron, and iodine (Belgnaoui & Belahsen, 2006; Musaiger, Hassan, & Obeid, 2011). An overview of these micronutrients of interest and their associated risks of deficiencies are described in Table 3.1, and they are described in more detail below.

Table 3.1: Overview of micronutrients of potential concern for pregnant women in Morocco during Ramadan fasting and associated risks.

Micronutrient	Prevalence of Deficiencies*	Intake during Ramadan fasting**	Risks of deficiencies
Folate	Unclear, high prevalence of folate deficiencies prior to national implementation of a fortification program[1]	Not reduced	Preterm birth, intrauterine growth restriction, placental abruption, repeated miscarriages, preeclampsia, and reduced bone mineral content and health in offspring throughout childhood (Molloy, Kirke, Brody, Scott, & Mills, 2008)
Calcium	Intake of calcium is generally low, but not low enough to be associated with negative birth outcomes [1, 2]	Not reduced	Eclampsia, hypertension, or preterm delivery (Zijp, Korver, & Tijburg, 2000).
Zinc	High prevalence, particularly in rural Morocco [1]	Declines	Reduced gestational length, increased risk of preterm labor, appetite suppression, low caloric intake, low gestational weight gain (Scholl et al., 1993)
Iron	High prevalence [1]	Declines	Maternal anemia, higher rates of preterm births, lower birth weight and delayed maturation and cognitive development (Ribot et al., 2013)
Iodine	High prevalence, but not in coastal regions such as Rabat [3]	N/A	Premature delivery, low birth weight, miscarriage, preeclampsia, fetal death, placental abruption, and impaired fetal neurocognitive development (Obican, Jahnke, Soldin, & Scialli, 2012)

*Micronutrient status for pregnant women in Morocco is based on research from;

1. Belgnaoui & Belahsen, 2006;
2. Zijp, Korver, & Tijburg, 2000
3. Musaiger et al., 2011

**Study took place in Turkey and assessed changes in diet during Ramadan compared to non-fasting months in lactating women (Rakicioglu et al., 2006)

Iodine deficiencies are the cause of the high prevalence of goiter in Morocco (Musaiger et al., 2011). Iodine deficiency during pregnancy can have severe consequences for birth outcomes, including premature delivery, low birth weight, miscarriage, preeclampsia, fetal death, placental abruption, and impaired fetal neurocognitive development (Obican, Jahnke, Soldin, & Scialli, 2012). Iodine deficiencies are probably not implicated in birth outcomes in Rabat; however, deficiencies are common in the mountainous regions of Morocco, due to the iodine depleting effect of altitude on soil (Abuye, Berhane, & Ersumo, 2008; Aquaron et al., 1993), rather than coastal regions such the region in which Rabat is located.

Calcium deficiencies are also not likely highly problematic in Morocco. Although one study reported daily calcium intake for pregnant women generally low (Belgnaoui & Belahsen, 2006), they were not low enough to significantly impact risk factors for eclampsia, hypertension, or preterm delivery (Zijp, Korver, & Tijburg, 2000). If dietary trends are similar to what was observed in Turkey, calcium intakes and associated complications are not predicted to be significantly affected during maternal fasting (Rakicioglu et al., 2006).

Folate deficiencies are of more concern for Moroccan women, but the associated risks are not likely worsened by maternal fasting. Maternal folate deficiency may result in higher risks of preterm birth, intrauterine growth restriction, placental abruption, repeated miscarriages, preeclampsia, and reduced bone mineral content and health in offspring throughout childhood (Molloy, Kirke, Brody, Scott, & Mills, 2008). Average folate intakes were found to be below the RDA for pregnant women and insufficient to meet estimated daily turnover rates, particularly in rural areas (Belgnaoui & Belahsen, 2006), but this was prior to the implementation of a national folic acid fortification of flour initiative that began in 2007. Therefore, current folate intake is probably higher, although in rural areas it may be less common depending on whether they rely on commercial flour. Still, it not predicted that the alterations in diet during Ramadan would lead to significantly further reduced intake of folate, so deficiencies should not be exacerbated by maternal fasting (Rakicioglu et al., 2006).

Zinc and iron deficiencies are likely more prevalent in this population and may be affected by fasting. Research suggests that plasma zinc concentrations are directly correlated with gestation length (Scholl, Hediger, Schall, Fischer, & Khoo, 1993). Zinc deficiency may suppress appetite, which may account for its strong associations with low caloric intake and low weight gain throughout pregnancy, along with increased risks of preterm labor and other negative birth outcomes (Scholl et al., 1993). In Morocco, there was found to be a high prevalence of low zinc intake among pregnant women in rural areas (Belgnaoui & Belahsen, 2006), and dietary changes during Ramadan may result in reduced intake of zinc, so the effects of deficiencies may be intensified during maternal fasting (Rakicioglu et al., 2006).

Iron and Iron Inhibiting Factors

Iron deficiency is associated with maternal anemia, higher rates of preterm births, lower birth weight and delayed maturation and cognitive development (Ribot et al., 2013). Iron-deficiency anemia is considered a contributing factor in the prevalence of low birth weight infants within the Middle East and North Africa (Musaiger et al., 2011). Iron deficiency is postulated to lead to negative birth outcomes due to insufficient oxygenation of fetal tissue, which increases norepinephrine and triggers the release of CRH (Ribot et al., 2013).

Iron deficiency is common among pregnant women in Morocco, with average iron intake reaching only 64.8% and 61.9% of the RDA in urban and rural populations, respectively (Belgnaoui & Belahsen, 2006). In 2000, 39% of pregnant women had iron-deficiency anemia (Musaiger et al., 2011). Intake of iron is predicted to decline during maternal fasting (Rakicioglu et al., 2006), so the prevalence of iron-deficiency induced complications may be increased during the month of Ramadan.

Iron deficiency anemia is associated with a low intake of iron-rich food, but the bioavailability of iron also fluctuates due to the type of iron (heme or non-heme) and inhibiting and enhancing factors (Musaiger et al., 2011; Zijp et al., 2000). Non-heme iron is less readily absorbed than heme iron (Zijp et al., 2000). Calcium inhibits iron bioavailability by about 50% (Zijp et al., 2000), though intake of calcium is generally low in Morocco. Phytates are found in the Moroccan diet in legumes and whole wheat flour, and these also inhibit iron absorption (Zijp et al., 2000).

Along with low iron intake, iron absorption may be reduced by a high intake of polyphenols, which are found in tea, coffee, vegetables, grains, herbs (including oregano) and spices (including cinnamon). The inhibitory effect of drinking 150mL or more of coffee is 40% and of tea, 60% (Zijp et al., 2000). Because iron deficiency is common in Morocco, concern has been expressed over the central role of tea within the diet due to its marked inhibitory effect on iron absorption (Musaiger et al., 2011). Coffee and tea are important in Moroccan culture and are consumed several times throughout the day in most homes and in cafes. This may be especially problematic for women and children whose iron needs are higher, individuals with iron deficiencies, and people in poor, rural areas where the diet is more plant-based and already low in iron (Musaiger et al., 2011). However, the effect may be smaller than suggested. Green tea is often brewed with mint, which improves iron bioavailability somewhat (Zaida et al., 2006). Drinking coffee and tea between meals also attenuates the effect on iron absorption. Typically, the only meal during which tea and coffee are consumed together with the meal is breakfast, but the time between drinking tea and other meals is variable (Musaiger et al., 2011).

Another contributing factor to the high prevalence of iron deficiency in Morocco is parasitic infections. It has been estimated that about two-thirds of the rural population and half of the urban population in Morocco have intestinal parasitic infections. Studies have found *Entamoeba histolytica*, *Blastocystis hominis*, and *Giardia lamblia* to be very common pathogenic species, and various species helminths have been found with inconsistent frequency (El Guamri et al., 2011; El

Idrissi et al., 1999). All of these infections, and particularly *Entamoeba hisolytica*, are regarded as hidden risk factors the development of iron deficiency anemia in pregnant women, particularly if their iron status is already low (Deeb, Salah-Eldin, & Khodeer, 2012; Haider, Humayun, & Bhutta, 2009; Weigel et al., 1996). Women with pathogenic intestinal parasitic infections have higher rates of spontaneous abortions, stillbirths, and preterm delivery than uninfected women (Czeizel, Hancsok, Palkovich, Janko, & Zoltai, 1966; Reinhardt, 1979). These outcomes relate to both the negative influence of the parasitic infection on the pregnancy via disruptions in nutritional status but also likely reflect access to sanitation, medical care, adequate diet, and financial resources, among other confounding factors (Reinhardt, 1979).

Maternal Diet and Nutritional Composition of Breast Milk

Human breast milk provides infants with a rich supply of energy, proteins, lipids, lactose, vitamins, minerals, growth factors, immune factors, enzymes, and hormones, among other substances. It is about 85-90% water. Milk composition is influenced by many factors, including infant age, whether the infant was born at term, whether it is foremilk (the milk expressed at the beginning of the feed) or hindmilk (milk expressed toward the end of the feed), and feeding frequency. However, the composition of human breast milk is very stable across our species and this variation typically remains within a relatively narrow range (Riordan, 2005).

It is hypothesized that lactation evolved as a means of buffering infants against disruptions in the food supply (Sellen, 2006). Evidence supports this; although lactating women are typically recommended to eat an extra 400-500 calories per day (Bronner & Auerbach, 2005), reduced maternal dietary intake or dietary quality does not generally have significant effects on breast milk composition. Studies of captive animals show compromised lactation performance only with severely restricted food intake. Although animal studies show that milk yield can be compromised to the point that infants stop growing in situations of very restrictive caloric intake (Hinde, 2013), lactational physiology is otherwise highly resilient to maternal undernutrition, which suggests infant needs supersedes maternal needs in times of scarcity. (Sellen, 2006).

Lactation carries a high energetic burden to maternal physiology, but there are mechanisms to accommodate this energetic demand and to offset inadequate food availability. One way the body prepares for this energetic burden happens during pregnancy, as maternal fat stores increase to be readily available for use in milk production (Sellen, 2006). During breastfeeding, healthy women are expected to lose approximately 0.8 kg per month over the course of the first 6 months of lactation. During this time, her body mobilizes the fat stores that accumulated during pregnancy, which often largely accounts for this gradual weight loss (Bronner & Auerbach, 2005). There are no known negative effects of moderate weight loss during breastfeeding, and since, from an evolutionary perspective, fat gained during pregnancy is likely allocated for milk production, adverse effects would not be expected. It also does not appear that lactation is influenced by whether energy for lactation is derived from the diet or maternal fat stores (Sellen, 2006).

Potential Impacts of Maternal Fasting on Birth Outcomes and Lactation

Prior to reviewing the research that has been done on maternal fasting during Ramadan specifically, I discuss more generally the effects of variations in cortisol, nutritional status, and, when applicable, dehydration on pregnancy and lactational outcomes that may be of concern during maternal fasting. During pregnancy, early pregnancy loss, length of gestation, and fetal growth may be influenced by maternal fasting, and during lactation, milk nutritional composition, milk cortisol, and milk production may be affected.

Pregnancy Loss

Estimates of the total rate of pregnancy loss, including early pregnancy loss and spontaneous abortion of clinical pregnancies, have varied widely, with estimates ranging from 30-

80% of all conceptions (Vitzthum, 2008; Wang et al., 2003). In a study by Wang et al. (2003), 25% of pregnancy losses were categorized as early pregnancy loss (EPL), occurring prior to clinical pregnancy and detectable only by a highly sensitive hCG assay. Most pregnancy losses take place within the first 3 weeks of conception, and only about half of these are the result of genetic abnormalities or pathology, so other causal mechanisms likely account for many spontaneous abortions (Nepomnaschy et al., 2006; Vitzthum, 2008). Because many pregnancies are lost before they can even be detected, studying causal mechanisms is exceedingly difficult. As possible conditions through which Ramadan may impact pregnancy loss, the role of cortisol and nutrition are considered.

Cortisol and Pregnancy Loss

Negative energy balance, increased physical activity, and weight loss have been shown to decrease luteal progesterone and lead to a decrease in fecundability and increasing risk of amenorrhea (Baird, 2013). The means by which energetic stress alters LH via a hypothalamic/pituitary response and ovarian suppression is complex, involving androgens, insulin, IGF-1, and stress hormones (Baird, 2013).

Nepomnaschy et al. (2004) found evidence of a relationship between stress (using cortisol as a biomarker) and female reproductive function (based on estrone conjugates, pregnanediol glucuronide, luteinizing hormone and follicle stimulating hormone) in a population living in rural Guatemala. During the follicular phase, increased cortisol levels were associated with increased gonadotrophin and progestin levels, and, between days 4 and 10 after ovulation, increased cortisol levels were associated with lower progestin levels. Increased gonadotrophins and decreased mid-luteal progesterone have previously been shown to disrupt ovulatory and luteinizing functions and decrease the likelihood of successful implantation (Ferin, 1999; Nepomnaschy et al., 2004).

Nepomnaschy et al. (2006) also found a direct association between increased levels of maternal urinary cortisol and risk of pregnancy loss in the first three weeks after conception (or five weeks after the last menstrual cycle). The data are correlational, but the authors propose a causal explanation for the results. From an evolutionary perspective, the costs of early pregnancy loss are low compared to potential costs of pregnancy under stressful conditions, such as drought, infection, social conflict, or other environmental or health stressor (Nepomnaschy et al., 2006; Vitzthum, 2001; Wasser & Barash, 1983).

Nutrition and Pregnancy Loss

Nutrition also plays a role in the risk of spontaneous abortion in the first trimester (Cintio et al., 2001). One study found that risk of miscarriage in the first 12 weeks was related to the composition of the diet, with a decreased risk associated with increased daily intake of fruits, vegetables, and chocolate (Maconochie, Doyle, Prior, & Simmons, 2007). In a study by Cintio et al. (2001) dietary patterns of women who aborted spontaneously before the 12th week of pregnancy were compared to that of women whose pregnancies proceeded normally. An increased risk was associated with poor intake of green vegetables, fruit, milk, cheese, egg, and fish. Risk also increased with higher intake of butter and oil. No association was found with meat, liver, ham or carrots (Cintio et al., 2001). Diets low in nutrients and energy often correspond to low BMI, which is also known to increase risk (Maconochie et al., 2007). Vitamins, particularly multivitamins, iron, or folic acid were associated with decreased risk of miscarriage (Maconochie et al., 2007), and deficiencies of specific micronutrients impair embryonic development (Cintio et al., 2001). Given the decreased intake of micronutrients during Ramadan observed in other studies (Aoyama, 1999; Belgnaoui & Belahsen, 2006; Rakicioglu et al., 2006), a decline in the nutritional quality of the diet may be of concern if early pregnancy loss is occurring with Ramadan fasting.

Length of Gestation and Preterm Delivery

Evidence that maternal cortisol may act as a signal for developing life history strategies is reflected in its potentially causal role in regulating the length of gestation. Maternal CRH and cortisol levels in the second trimester are highly predictive of preterm delivery (Field & Diego, 2008; Mclean et al., 1999), which may signify accelerated fetal development. Preterm labor has been associated with increased stress, CRH and cortisol in some situations. For example, it has been hypothesized that the increase in CRH in cases of maternal depression is responsible for higher rates of premature delivery (Field & Diego, 2008). However, it is unclear if the length of gestation would be affected by the physiological stress of fasting (Christian, 2012).

How cortisol influences length gestation has not been determined. Increased maternal cortisol may increase susceptibility to infection, and intrauterine infection may account for 25-40% of preterm births (Christian, 2012). Uterine artery vasoconstriction, which is associated with perinatal developmental problems, preeclampsia, and premature delivery, can be triggered by increased cortisol and is another potential mechanism (Field & Diego, 2008; Walker, Connacher, Webb, & Edwards, 1992).

Cortisol may play a more direct role in regulating the length of gestation. Stress, including metabolic stress, may activate a placental cortisol-corticotropin-releasing hormone positive feedback loop that promotes reduced length of gestation (Siega-Riz, Herrmann, Savitz, & Throp, 2001). Cortisol may serve to signal the metabolic needs of the fetus and if they are being met by the mother. This possibility relates to the hypothesis that gestation length and neonatal size are limited by maternal metabolic constraints rather than the obstetric dilemma (Dunsworth, Warrener, Deacon, Ellison, & Pontzer, 2012). The energetics of gestation and growth (EGG) hypothesis is based on data indicating that the energetic demands of pregnancy approach the limit of maternal energetic capacity and that the energetic requirements of extending gestation by even one month would exceed this capacity (Dunsworth et al., 2012). The EGG hypothesis is an expansion of the "metabolic crossover hypothesis" proposed by Ellison (2001), which proposed that the trigger for birth is inadequate resources reaching the fetus, and that in providing energy to the fetus in the third trimester, a pregnant woman's body uses mechanisms similar to which "a starvation victim's body employs to stay alive" (Ellison, 2001). The crossover point is when the mother can no longer meet the energetic demands of the fetus. Ellison points to the increasing fetal production of cortisol late in pregnancy as a signal that it is becoming difficult for the fetus to meet its energetic requirements.

This hypothesis would appear to be supported by the strong relationship between low maternal gestational weight gain and an increased risk of preterm delivery, but the direction of causation is contested. Kramer, Mclean, Eason, and Usher (1992) and Berkowitz and Papiernik (1993) have concluded that lower gestational weight gain is an effect of shortened gestation, rather than the cause, as the association disappears when weight gain is expressed as a net rate or when the data is corrected for infant birth weight. This is supported by studies which have found no evidence of an association between preterm birth and caloric intake except in more severe cases, such as the Dutch Hunger Winter. Exposure to the famine in the first trimester of pregnancy resulted in a slight increase of preterm deliveries, and exposure during the third trimester was associated with a slightly shortened gestational period but not with an increase of preterm deliveries (Berkowitz & Papiernik, 1993). Low pre-pregnancy BMI, which would also indicate maternal nutritional status and metabolic constraints, is often considered a contributing factor in preterm labor, (Berkowitz & Papiernik, 1993; Kramer, 2003), but this finding is not consistent across studies. Moreover, obesity does not seem to decrease the risk for preterm delivery, so Berkowitz and Papiernik (1993) argue that the relationship between BMI and preterm delivery is inconclusive. Obesity also appears to increase the risk of delivering preterm until controlling for hypertension, after which the relationship is no longer significant (Cnattingius, Bergström, Lipworth, & Kramer, 1998).

Fetal Growth and the Intrauterine Environment

Infant size at birth is more strongly determined by the intrauterine environment rather than genetics (Cameron & Bogin, 2012). The intrauterine environment is affected by many factors, including maternal anthropometry as a proxy for current and lifetime nutritional status, health conditions and diet. Intrauterine growth restriction (IUGR) is difficult to identify in individuals, so birth weight is currently used as a crude measure of IUGR and perinatal mortality risks (Goldenburg & Cliver, 1997; Stein & Susser, 1984). One roadblock to understanding IUGR is that it is not currently possible to determine growth potential in order to determine whether or not intrauterine growth was restricted, so methods for distinguishing pathological growth restriction from non-pathologically smaller infants are not well established (Goldenburg & Cliver, 1997; Zhang, 2010).

Infants with low birth weight for gestational age are at a greater risk of death than premature infants of normal weight for their gestation age (Bogin & Smith, 2012). Infant and child mortality before age 5 is strongly related to stunting (low length or height for age), underweight (low weight for age), wasting (low weight for length or height), and IUGR, which are estimated to be responsible for 2.2 million deaths and 21% of disability-adjusted life-years lost (Victora et al., 2010).

Maternal Anthropometry and Health

Maternal body size is correlated with neonatal size. Maternal height and weight, particularly when considered together, are strong predictors of risk for giving birth to small-for-gestational-age (SGA) and large-for-gestational-age (LGA) infants (Voigt et al., 2010). Low pre-pregnancy BMI and shorter stature increase the likelihood of delivery of an SGA infant (Kramer, 2003; Voigt et al., 2010). Higher pre-pregnancy BMI and taller stature reduce the risk of delivering SGA infants but increase the risk for LGA infants (Cnattingius et al., 1998; Voigt et al., 2010).

The role of socioeconomic variables in determining maternal anthropometry is a crucial point which should not be overlooked. Because maternal anthropometry tends to differ by socioeconomic classes and education, maternal anthropometry may be a mediating factor that creates a differential risk of perinatal mortality among socioeconomic classes (Cnattingius et al., 1998). Stein and Susser (1984) argue that maternal undernutrition is the most important environmental factor in IUGR, both during pregnancy and over the course of the mother's own growth and development. For example, poverty is associated with stunted growth resulting in shorter adult stature, typically resulting from poor nutrition and infection (Martorell, 1989). Females who experience growth stunting and grow up to be shorter adults have an increased likelihood of delivering growth-stunted infants (Martorell, 1989), so this could create a cyclical pattern in IUGR that carries on to the next generation. Pelvic size may be a limiting factor in fetal growth, given the established relationships between female height and pelvic size (Merchant, Villar, & Kestler, 2001) and between shorter maternal stature increases the risk for IUGR and SGA infants (Kramer, 2003; Merchant et al., 2001).

In affluent populations, the relationship between height and health is not as strong and the likelihood of positive pregnancy outcomes and infant survival are better overall (Pollet & Nettle, 2008). Height is more likely to signify health status and therefore reduced height is often associated with reduced reproductive success in high stressed environments, such as poverty (Pollet & Nettle, 2008). One large-scale study found the protective benefits of height on child mortality were most prominent for women with the least education across 42 developing countries and that maternal height had a strong, negative effect on child mortality (Monden & Smits, 2009).

In a study of malnourished Guatemalan Indian women with little variability in socioeconomic status, Martorell, Delgado, Delgado, Valverde, and Klein (1981) found maternal stature positively correlated the with number of surviving offspring; taller women had more surviving offspring, even though shorter women had higher parity. One of the reasons proposed for this observation is the correspondence between height and birth weight. Taller women tend to have larger babies, and in this study, the tallest third of the women had significantly larger babies than the shortest third of women. Impaired growth and short adult stature had a detrimental impact on the reproductive health of these women.

Short maternal stature is strongly associated with an increased incidence of complications and cesarean deliveries, more so than newborn head circumference or birthweight (Merchant et al., 2001). Taller women are at less risk for gestational diabetes, which is a risk for adverse pregnancy outcomes and for chronic diseases later in life for the infant (Brite et al., 2014). In light of the importance of maternal height, some have suggested that maternal height is what needs to be addressed rather than fetal size in order to improve maternal and infant health outcomes. In other words, maternal and infant health initiative should aim to optimize female growth in early life, as increases in maternal height are expected to be accompanied by increases in fetal size. Moreover, increasing fetal size without increasing maternal size could put both the mother and infant at risk (Merchant et al., 2001).

Nutrition during Pregnancy and Gestational Weight Gain

Maternal weight and BMI are often considered proxies for current maternal nutritional status. Alternatively, height is an indicator of nutritional status during growth and development. With the increasing prevalence of overweight and obesity all over the world, including Morocco, conditions related to high BMI are also rising. Overweight and obesity increase risks for adverse pregnancy outcomes. While some of this risk is due to increased risk for gestational morbidities, such as hypertension and preeclampsia, these do not always account for the increase in risk for overweight and obese mothers. For example, risk of hypertension increases consistently with maternal weight, and this condition potentiates a large risk for adverse pregnancy outcomes, including preterm delivery (Cnattingius et al., 1998). However, higher pre-pregnancy BMI increases the risk of late fetal death, independently of hypertensive disease (Cnattingius et al., 1998). Very obese women are at a greater risk for gestational diabetes, hypertension, wound or episiotomy infection, giving birth to excessively large infants, and giving birth to infants who were more obese by the age of one compared to controls (Edwards, Dickes, Alton, & Hakanson, 1978). Women who are lean prior to conception are at much lower risk for preeclampsia and perinatal or infant death (Cnattingius et al., 1998).

Moreover, studies have shown that the response of the reproductive system to nutritional stress varies by BMI. Alvero et al. (1998) found lean women (defined as having a BMI of 20 or less) who were fasting, but who were not energetically stressed prior to fasting, seem to have a more pronounced changes in neuroendocrine function, disruptions in follicular development, a significantly lengthened follicular phase, and a higher incidence of anovulation than women with a BMI between 21-25 (Alvero et al., 1998; Olson, Cartledge, Sebring, Defensor, & Nieman, 1995).

Anthropometry and body composition vary greatly in populations practicing Ramadan, and since it is likely that fasting impacts women of different based on BMI, population differences in the prevalence of overweight and underweight may contribute to different fasting outcomes. Variation in body size by ethnicity may also be relevant in comparing populations that practice Ramadan, as the BMI ranges at which different pregnancy risks appear are not static across populations. In Taiwan, for example, women with pre-pregnancy BMI of between 18.5-24 have the lowest frequency of pregnancy complication, compared to Caucasian women whose lowest risk is associated with a BMI of 19.8-26 (Tsai, Chen, Sun, Wu, & Yeh, 2012).

Comparing the effects of Ramadan across populations on gestational weight gain and fetal growth may be further complicated given the variation in recommendations for gestational weight gain during pregnancy by ethnicity and pre-pregnancy weight. Ethnic-specific and BMI-specific recommendations have been made based on research demonstrating changes in risk of preterm labor, preeclampsia and Cesarean deliveries at different BMIs (Tsai et al., 2012). Variation in healthy BMI ranges by ethnicity and the prevalence of overweight and underweight within populations likely causes differences in what constitutes healthy gestational weight gain. For example, the Institute of Medicine recommends Caucasian women of a moderate BMI (19.9-26) to gain 11.5-16 kg, compared to 12-18 kg for women with a lower BMI and 7-11.5 kg for women with a higher BMI. A moderate BMI for Chinese women is 19-23.5, and the weight gain recommendation for these women is 11-16.4, and for women with a lower or higher BMI, the recommendation is to gain 13-16.7 and 7-14.4 kg respectively (Wong, Tang, Lau, & Wong, 2000). Taiwanese women are recommended to gain 10-14 kg for women with a moderate BMI of 18.5-24 (Tsai et al., 2012). If Ramadan fasting poses a challenge to adequate weight gain, this may be more impactful for women in demographics that are recommended to gain more weight.

Late Gestation and Fetal Fat Gains

Barker (1992) proposed that adverse environments during critical periods of development in utero and during infancy have long-term adverse effects and studies on the Dutch Hunger Winter show that nutritional deficiencies have trimester-specific effects on birth outcomes, including infant birth size. Exposure during the first trimester did not correspond to low infant birth weight, but later pregnancy exposure did (Stein, Zybert, Van De Bor, & Lumey, 2004). Infant size at delivery was most strongly influenced by maternal weight gain when exposure occurred later in pregnancy. Maternal weight gain was also most constrained when exposed to the famine during the third trimester, averaging 0.05 kg per week, but it was also reduced during the second and first trimesters. Only 3% of women exposed to the famine in their third trimester gained more than 0.5 kg per week, which resulted in a corresponding reduction in infant length, weight and ponderal index (Stein et al., 1995). Low gestational weight gain has been associated with increased risk of delivering an SGA infant and a slight increase in the risk of early neonatal death but was not found to influence the risk of late fetal death (Cnattingius et al., 1998).

Low birth weight is one tradeoff that is often observed when resources are scarce during fetal development (Stein et al., 1995). This is primarily true if the scarcity takes place in the third trimester (Stein et al., 1995; Aryeh D Stein et al., 2004). Given that infant body fat at birth is dependent on the maternal diet (Garn, 1952), this association is likely related to the substantial gained by the fetus during the final weeks of pregnancy, which demands over half of the energetic costs of pregnancy during that period (Hrdy, 1999b). Humans infants are the fattest infants of any species recorded and are especially fat compared to other primates (Hrdy, 1999b; Kuzawa, 1998). This high body fat composition in human infants does not seem to protect against hypothermia (Hrdy, 1999b), and human infants have a large amount of white adipose tissue (12-14% of birth weight) as opposed to brown adipose tissue (1-3% of birth weight), which is abundant and useful in thermoregulation in baby seals, reindeer, caribou, and walruses (Kuzawa, 1998). It has been hypothesized that the buildup of fat right before birth is essential for the development of brain growth which attains about 70% of its final mass within the first year after birth (Hrdy, 1999b) and consumes 50-60% of total metabolic expenditure during infancy (Kuzawa, 1998). These fat stores appear to be an energetic buffer that allows a newborn to maintain blood sugar levels in the absence of being fed for long periods of time and are therefore protect the infant from a disruption in resources during infancy (Hrdy, 1999b; Kuzawa, 1998). This may be particularly advantageous in times of infections when evidence suggests that infant fat stores are mobilized (Kuzawa, 1998).

Nutritional Composition of Breast Milk

As previously discussed, there is not a strong basis for predicting that maternal fasting would compromise the nutritional composition of milk. Although maternal fasting may influence breast milk and infant growth in a similarly to caloric restriction and undernutrition, Ramadan fasting does not necessarily mimic a situation of food scarcity based on total calories consumed. Even if minor changes in the nutritional quality of the maternal diet was observed, the nutritional composition of breast milk is largely buffered against short-term changes in maternal nutritional quality (Emery Thompson, 2013). Although milk nutritional composition remains highly stable during temporary reductions in dietary quantity and quality, some milk constituents being more resilient against changes to maternal diet than others, as will be explored in greater detail.

Milk Macronutrients

The total amount of calories an infant can access is important for infant growth, and the number of calories obtained by an infant from breast milk depends on the macronutrient composition and quantity of milk consumed. Fat is the main source of energy in human breast milk, but the fat content is also most sensitive to maternal nutrition. Milk fat accounts for about half the energetic value of the milk; it is the most variable component and the most affected by maternal diet (Riordan, 2005). Population-level differences have also been noted; lipid content of milk tends to be higher in affluent populations than developing countries (Nikniaz, Mahdavi, Arefhoesseini, & Khiabani, 2009). Milk fat content is significantly related to maternal dietary carbohydrate consumption and maternal BMI (Nikniaz et al., 2009). Research suggests that milk fat content may be important for infant growth, as one study found it to be positively correlated with infant weight-for-age Z-scores (Nikniaz et al., 2009). Although total maternal dietary fat does not affect the total amount of fat in milk, types of dietary fats influence milk fat composition. Considering fatty acid composition in breast milk, DHA, a long-chain polyunsaturated fatty acid, and AA, arachidonic acid, are of particular importance in brain development, visual acuity and cognitive ability in infants. In the United States, DHA is of concern because of its low levels in American women and by extension in breast milk (Bronner & Auerbach, 2005; Riordan, 2005).

However, the fat content of maternal milk is not necessarily an indicator of the amount of milk fat and milk energy an infant will consume. Milk fat is typically lowest in foremilk and highest in hindmilk, and longer intervals between breastfeeding may mean the infant is less likely to fully empty the breast in order to access the high fat hindmilk, which may lead to the infant consuming higher quantities of lower fat, lower energy milk (Riordan, 2005). Though infants who are fed on-demand thought to be adept at regulating their intake of fat and energy, scheduled breastfeeding may negate their ability to self-regulate (Riordan, 2005; Woolridge, 1995). Scheduled breastfeeding sessions limit an infant's ability to regulate their own intake and can lead to a reduction in an infant's consumption of fat- and energy-rich hindmilk, and large quantities of low-fat milk can cause digestion problems and colic (Woolridge, 1995).

The milk protein content is also sensitive to the maternal diet but to a lesser degree than fat (Lonnerdal, 1986). High milk protein content has been associated with excessive weight gain in infancy, increased infant plasma concentrations of insulin and IGF-1, and increased risk of obesity later in life (Grunewald, Hellmuth, Demmelmair, & Koletzko, 2014). The amount of lactose in breast milk is thought to be the macronutrient least sensitive to maternal diet (Lonnerdal, 1986) but it did decrease during Ramadan in a study on dehydration and breast milk when it occurred in the summer in the Gambia (Prentice et al., 1984). As this was accompanied by an increase in milk osmolarity and sodium content and a decrease in the sodium/potassium ratio, decreased lactose likely resulted from dehydration rather than other dietary changes. The effects of water abstinence will be discussed further later. Overall, there is not strong evidence to support predictions of changes in milk composition that such that infant growth would be influenced by an altered nutritional composition of milk during maternal fasting unless milk quantity is also reduced.

Milk Micronutrients

Fasting might influence the micronutrient content of breast milk, and this would most likely occur in the case that the mother was already deficient in these vitamins. Maternal micronutrient stores are usually depleted before milk is compromised, indicating a preferential investment in the infant's immediate needs (Sellen, 2006). During temporary reductions in dietary quality, milk quality is largely buffered against micronutrient deficiencies, especially fat-soluble vitamins.

Nevertheless, maternal deficiencies can cause deficiencies in breastfed infants. Early growth faltering has been hypothesized to be caused by inadequate concentrations of micronutrients in breast milk, especially if micronutrient deficiencies were acquired in utero (Neville et al., 2012).

Vitamin A and zinc deficiencies have been found to be some of the most common vitamins and minerals attributed to infant morbidity and mortality (Black et al., 2008). Micronutrient deficiency may increase the risk of infectious disease in infancy, which is a determinant of growth stunting. Infectious diseases that cause diarrhea are particularly implicated in growth stunting (Black et al., 2008), and diarrheal diseases have a high prevalence in infants in Morocco (Bourrous, Elmjati, Amine, El Omari, & Bouskraoui, 2010).

Milk nutritional content changes with infant age. Water-soluble vitamin content tends to increase while fat-soluble content, which draws on stores in the body, tends to decrease (Riordan, 2005). Folate is an exception; this vitamin typically remains at a stable level throughout all stages of breastfeeding (Riordan, 2005). Also, milk mineral content is primarily derived from maternal body stores and as such is likewise typically fairly constant, declining slightly with infant age but overall varying little within feedings or with maternal diet, parity or age (Riordan, 2005). Zinc has an important role in infant growth, but milk zinc is not typically impacted by maternal nutritional status. Deficiencies are usually associated with preterm births rather than maternal nutrition (Riordan, 2005).

Water-soluble vitamins in breast milk are more closely tied to current maternal diet. Breast milk content of water-soluble vitamins can reach a plateau in which additional maternal intake of those vitamins will not increase their concentration in the milk (Bronner & Auerbach, 2005). On particular water-soluble vitamin of interest is vitamin B12, which is important for the development of the central nervous system and possibly for infant growth, because there is a tendency for deficiency in breastfed infants of women following strict vegetarian and vegan diets (Riordan, 2005; Stabler & Allen, 2004). Vitamin B6, which is necessary for neural development, is also of concern because deficiencies in breastfed infants are also possible if there is a maternal deficiency (Bronner & Auerbach, 2005).

Fat-soluble vitamins are stored by the body in fatty tissues for long periods, so fat-soluble vitamins for breast milk can be derived from maternal stores, which do not need to be regularly replenished like water soluble vitamins. The exception is Vitamin D, which has an important role in skeletal health and growth but is present only in very low quantities in breast milk. Maternal intake of vitamin D does correlate with its concentration in breast milk and with the incidence of vitamin D deficiencies in breastfed infants, so infants may be vulnerable to maternal deficiencies of this micronutrient (Riordan, 2005).

Breast Milk Cortisol

Life History Theory would predict that, in stressful or food restricted environments, it may be more beneficial for an infant to grow faster in order to reach maturation earlier and consequently achieve a smaller adult body size. This prediction has been supported by animal studies, which suggest that cortisol may be one mediator of this interaction (Dantzer et al., 2013; Hinde et al., 2014). Cortisol is an important hormone in regulating energy allocation and metabolism, which can be transferred from the mother to the fetus via the placenta and the infant via breast milk and may influence infant growth, development and behavior (Hinde et al., 2014).

Cortisol passively diffuses into milk. Because of this, there is a high correlation between maternal cortisol and milk cortisol; human studies have found maternal milk cortisol to positively correlate with maternal serum cortisol with r=0.5-0.7 (Breakey, 2015), and maternal serum cortisol concentrations have been shown to account for about 35% of the variance in cortisol concentrations in milk of other primates (Sullivan et al., 2011). This could mean that breast milk production evolved such that infants are able to remain acutely aware of their mother's cortisol status at all times via breastfeeding, which could serve to send information to an infant about maternal ecology. Alternatively, there may have been no selective advantage in terms of maternal reproductive success and infant survival, and if so, there was no evolutionary pressure to reduce, increase or otherwise regulate milk cortisol.

It is improbable that maternal cortisol is under the control of the infant and more likely that it responds to maternal energetic resources, physiological stress, and psychological stress. So, unlike milk fat content which is responsive to infant-driven variations in on-demand breastfeeding (Woolridge, 1995), an infant's ability to control the amount of cortisol it receives is likely negligible. Variations in cortisol, therefore, most likely respond to maternal factors, such as the need to adapt to a given stressor.

Evidence from animal studies supports the hypothesis that maternal energetic status and environment are communicated to an infant via milk cortisol and that infant growth responds to this signaling. Primate studies suggest that increased maternal cortisol in breast milk may alter infant life history strategies. Higher cortisol concentrations have been correlated with increased infant growth trajectories, indicating that cortisol may be acting as a signal to prioritize growth. Prioritizing growth may, in turn, result in deprioritizing other aspects of development, including behavioral temperament (Hinde et al., 2014). In squirrels, Dantzer et al. (2013) found that cortisol was also positively associated with environmental stress and increased offspring growth, and offspring of mothers with experimentally elevated glucocorticoids grew significantly faster. This experimental study indicated that increases in maternal glucocorticoid transferred via milk may serve as a hormonal cue that in the future environment may be high risk and therefore trigger an adaptive increase in investment into growth. The resulting faster life history strategy increases chances of survival to adulthood in stressed environments, but it may have negative long term consequences (Dantzer et al., 2013).

Although animal studies suggest this link, it is not clear if similar results will be found in humans and data is not currently available to link milk cortisol to infant growth. In one study done on humans, Breakey (2015) found primiparity to be positively associated with both milk cortisol and faster gains in infant weight and length, but a direct link between cortisol and infant growth was not found, possibly due to unaccounted effects of milk energy or volume. It is also not clear how maternal fasting may influence infant growth during lactation, although increased growth may be predicted based on animal studies. Three small studies reported no difference in growth between infants with fasting mothers compared to non-fasting controls (Haratipour et al., 2013; Khoshdel et al., 2007; Rakicioglu et al., 2006), although these studies were limited by small sample sizes, unclear methodology, and variables that were not controlled for that may have confounded results, such as supplemental feeding practices (Rashid, 2007).

Further research is needed to clarify this relationship in humans. The rationale for extending the hypothesis to humans includes evidence that milk cortisol is an indicator of maternal energetic status and that it is biologically active in the infant. Moreover, there is evidence that milk cortisol may play a role in mediating adaptive responses in times of energetic stress to maintain the integrity of the lactational process while conserving maternal energetic resources and allowing growth-promoting components of milk to increase. The potential for cortisol to be diverted towards infant growth may be further supported by studies suggesting milk cortisol may divert energy away from behavioral development.

Milk Cortisol as an Indicator of Maternal Environment and Energetic Status

Maternal cortisol in milk may serve as a signal of maternal energetic status to the infant. One study demonstrated that maternal energetic status, as indicated by BMI, is related to non-nutritive components of breast milk, specifically milk cortisol. Although weight change during lactation was not related to cortisol, maternal BMI and milk cortisol were negatively related. This study did not find any association between change in maternal BMI and milk cortisol, though higher BMI and maternal weight gain resulted in a significant likelihood of reduced cortisol (Breakey, 2015).

Although elevated milk cortisol may indicate the presence of a maternal stressor to the infant, animal studies show that the infant's physiological response to this is altered based on other hormones that also likely serve as signals of maternal ecology. For example, elevated leptin levels can indicate adequate maternal body fat stores and a positive energy balance. Animal studies suggest that in the presence of elevated leptin, infants more quickly return to baseline following a physiological stress response (Hinde, 2013). Therefore, maternal nutritional status may mediate any effects of maternal fasting.

Is Cortisol Bioactive in Infants?

Demonstrating that cortisol serves as a signal for infant life history strategies requires evidence that it retains its biological activity once ingested by the infant and that there is a direct effect of exposure on infant physiology, metabolic function, growth, or development (Peaker & Neville, 1991). If these criteria are not met, increased cortisol is probably adaptive primarily for maternal physiological adaptation to stress, possibly reducing the energetic demand of the infant, and feasibly enhancing her own reproductive fitness via maintenance of lactation (Peaker & Neville, 1991). The gastrointestinal tract of the neonate is highly permeable to many bioactive substances, and while it is thought that this probably extends to glucocorticoids, it remains to be demonstrated that this is true of cortisol in particular (Hinde et al., 2014; Peaker & Neville, 1991). Glucocorticoid receptors in the gastrointestinal tract are most abundant during infancy and decline to adult levels after weaning, which suggests a bioactive role of ingested glucocorticoids (Hinde, 2013). However, one study with rhesus monkeys did not find a correlation between milk cortisol and infant plasma cortisol, which may suggest otherwise (Sullivan et al., 2011).

Although the explicit roles of milk cortisol for the infant have yet to be fully elucidated (Riordan, 2005), current evidence does suggest a bioactive role for cortisol. One known bioactive role of breast milk cortisol is its critical functions in normal infant development, including the development of the gastrointestinal tract (Riordan, 2005). In human neonates, milk cortisol stimulates maturation of the intestinal tract and intestines (Riordan, 2005). It has also been hypothesized that milk cortisol has a role in the growth of the pancreas and in the transport of fluid and salts in the infant's gastrointestinal tract (Riordan, 2005). As previously discussed, animal studies also suggest a role for cortisol in infant growth (Dantzer et al., 2013; Hinde et al., 2014), although one study on humans did not observe this trend (Breakey, 2015).

Still, these roles of cortisol do not necessarily mean its presence in milk is transferring information about the maternal environment and programming life history strategies. It is also important to consider the costs and benefits of observed adaptations and whether they reflect pathology, poor health consequences, or impairment of growth or development (Kuzawa & Quinn, 2009). More research is needed to determine how maternal ecology may influence infant life history strategies through alteration of non-nutritive components of breast milk composition.

Maternal Cortisol: Roles in Lactational Physiology and Energy Conservation

It is likely that both mother and infant experience physiological adaptations in response to a stressor such as maternal abstinence from food and water, the goals of these adaptations may not always be mutually supportive (Hinde et al., 2014) and the scale and duration of these adaptations may vary. Elevated cortisol is the body's response to food restriction; after glycogen supplies are depleted, the body needs another source of fuel to convert into energy, and increased cortisol is one mechanism by which alternative food sources are made available for glucose synthesis. This hormonal shift is important in mobilizing stored energy in order to maintain physiological function. Research suggests that increased cortisol may help maintain lactational processes to aid in reproductive success, but it also may help to conserve maternal resources by allowing for a "cheaper" infant that could sustain with fewer of her resources (Breakey, 2015; Hinde et al., 2014).

During maternal fasting, elevated maternal cortisol may help counteract some of the consequences of long periods of abstinence from energetic resources via its effects of lactational physiology, as research suggests it plays an active role in the process of maternal milk production.

Glucocorticoids prevent apoptosis of epithelial cells, including mammary glands, thereby maintaining the structural integrity of the mammary glands (Breakey, 2015). This may be one reason that milk of primiparous mothers tends to be substantially higher in cortisol than multiparous mothers, averaging 38.6% higher milk cortisol in one human study (Breakey, 2015), which is similar to the results of primate studies (Hinde et al., 2014). The mammary glands of primiparous mothers are relatively underdeveloped, so increased cortisol may be present to help establish proper functionality. Elevated cortisol may be a mechanism by which primiparous mothers are able to compensate for underdeveloped mammary glands (Breakey, 2015).

Research suggests that cortisol also plays a role in the accumulation of nutritive components of milk (Hinde, 2013; Hinde et al., 2014; Sullivan et al., 2011). Cortisol has a direct effect on milk energy production in the mammary glands, as it promotes protein production for milk (Hinde, 2013) and may have a role in the synthesis of milk fat (Hinde et al., 2014). Therefore, maternal cortisol may be one mediator of variation in macronutrient composition. Notably, both fat and protein content of breast milk are associated with increased infant growth (Grunewald et al., 2014; Nikniaz et al., 2009). The influence of maternal cortisol on milk protein and fat content could be a mechanism through which maternal cortisol leads to an increased infant growth during maternal fasting, independent of milk cortisol or the degree of bioactivity of cortisol in the infant.

Although glucocorticoids may help maintain lactational processes, they also may be important in conserving maternal energetic resources. Reduced maternal energy reserves may create a temporary situation in which a woman cannot invest as much in offspring quality. Energy-sparing mechanisms include the possible role of increased maternal glucocorticoids in suppressing milk synthesis and milk letdown (Neville et al., 2012). Milk cortisol may also play a role in reducing infant appetite. For example, in dairy calves, exposure to exogenous glucocorticoids resulted in elevated leptin, which is an appetite suppressant that may lead to reduced infant suckling. Glucocorticoids, therefore, may attune infant demand of energetic resources to the maternal resource availability. More research is needed on the role of milk hormones in regulating infant appetite, but if human milk glucocorticoids act similarly, increased milk cortisol may trigger a mechanism that reduces the energetic demands of an infant during maternal energy deprivation or stress, allowing mothers a method to decrease energy expenditure (Hinde, 2013).

Maternal cortisol may increase maternal reproductive success via its ability to enhance lactational processes and to increase the milk energy content and macronutrients that most strongly influence infant growth. Therefore, it is also possible that during Ramadan fasting, when the production of breast milk may become disturbed (Prentice et al., 1984), increased maternal cortisol may mitigate the consequence of such disturbances in milk synthesis thereby conferring adaptive benefits when environmental stressors present a risk to the lactation processes. However, adaptations do not imply optimal functioning as they usually require trade-offs that carry costs, and increased maternal glucocorticoids may also result in energy-sparing mechanisms via reduced investment in offspring quality.

Possible Adaptive Benefits and Costs of High Cortisol to Infant

Milk cortisol may confer some benefits to infants in times of maternal energetic stress by increasing infant access to milk energy in various ways. Various aspects of Ramadan fasting, including increased maternal cortisol, may influence milk macronutrient composition in a way that impacts infant growth. Since my previous work and the work of others in Morocco leads me to expect that much of the population practices on demand feeding (Komodiki E, M, Volaki P, Sm, & Iacovidou, 2014), it is possible that Ramadan fasting increases feed frequency. Probably due to the dehydration from water restriction during Ramadan, research suggests that women often reported feeling that their milk production has was reduced or that their infant is not satisfied after feeding (Ertem et al., 2001; Ozsoy et al., 2014). If an infant really is getting less milk per feed, the infant may also elicit feeding more often. If mothers perceive infants to be unsatisfied, they may also feed them more often. Increased feed frequency also increases milk fat content, and because fat is the primary contributor to milk energy, infants may actually consume the same or more calories (Woolridge, 1995). In this case, if increased maternal cortisol is associated with fasting, increased infant weight gain might be caused by milk components other than cortisol.

Abnormally high protein content of breast milk may lead to increased weight gain and increased risk of obesity in the infant (Grunewald et al., 2014). Maternal cortisol promotes protein production within the mammary glands (Hinde, 2013), so if maternal milk cortisol is elevated for long periods of time, this could lead to atypically high protein content in the milk as well and potentially result in increased weight gain in the infant. However, other studies of Ramadan fasting, even when fasting was over 12 hours, have not observed any significant changes in milk protein (Bener et al., 2001; Prentice et al., 1984; Rakicioglu et al., 2006). However, a 24-hour fast resulted in increased protein and decreased lactose (Zimmerman, et al. 2009), so the fasting hours during previously studied Ramadan fasts may be too short to significantly impact protein.

Increased milk cortisol may also have costs to infant development. For one, cortisol depresses the immune system, which may make it more difficult to fight illness (Breakey, 2015), breaks down lean muscle mass (Sareen & Jack, 2013), and delays wound healing due to its anti-inflammatory effects (Cooper, Segal, Diegelmann, & Reynolds, 2015). If maternal cortisol and milk cortisol increase during maternal fasting, the immunosuppressive effects could leave both mother and infant more vulnerable to infections and diseases, which could have negative impacts on infant growth. Increased maternal cortisol may have other long-term health effects. Cortisol also has an effect on DNA transcription, which has led to hypotheses on its role in developmental programming, particularly the diseases associated with metabolic syndrome, when it is present in abnormal levels during critical periods of growth and development (Anagnostis, Athyros, Tziomalos, Karagiannis, & Mikhailidis, 2009).

Another possible cost of increased milk cortisol is behavioral development. Evidence from animal studies suggests that cortisol may increase the allocation of resources put toward growth and indicates that resources may then be allocated away from other aspects of infant development. Research on humans and other animals suggests that one potential trade-off is in behavioral development, which also requires energetic investment (Hinde, 2013). Animal studies indicate a link between maternal cortisol, infant growth, and infant behavioral development. A study of rhesus monkeys by Hinde et al. (2014) found that milk cortisol levels were positively correlated with offspring growth rates, suggesting that cortisol may act as a signal to the infant to prioritize investment in growth. In this study, increased glucocorticoids in milk were also associated with more nervousness and timid temperaments and less confident, exploratory, playful temperaments in infants. Cortisol had sex-specific effects on growth and behavior, with daughters being more sensitive to absolute concentrations of milk cortisol and sons being more impacted by changes in cortisol in milk across time. Lower parity mothers produced milk with higher cortisol concentrations. BMI had little influence on milk cortisol. Sullivan et al. (2011) found that milk cortisol was not related to infant plasma cortisol levels in rhesus monkeys but higher cortisol was predictive of male infant temperament in the researcher's measurement of confidence. This relationship remained significant after controlling for nutritional composition of the milk. Cortisol concentrations in milk were positively correlated to maternal plasma cortisol concentrations and with the protein content and the fat content of the milk. Although maternal plasma cortisol did not differ by sex of the infant, the milk cortisol concentration was higher in mothers of male infants than female infants.

Research on human infants and children also supports the hypothesis that cortisol might play a role in behavioral development. A study by Grey et al. (2013) provided evidence that hormones in human breast milk influence offspring behavioral development. Milk cortisol concentrations were positively associated with more negative infant temperament, specifically with regards to fear and sadness and this association remained significant after controlling for maternal demographic characteristics and psychological distress. After segmenting the results by infant sex, this effect was only significant for female infants. Though this may have been due to small sample size, sex differences in the effects of glucocorticoids have been seen in other animals studies. In formula-fed infants, there was no relationship between infant temperament and maternal cortisol. Glynn et al. (2007) also tested behavior and maternal cortisol by comparing breastfed to formula-fed infants. Although there was no association between maternal cortisol levels and fear behavior in the formula-fed infants, increased maternal cortisol was significantly related to increased infant fear behavior in breastfed infants.

Another study by De Weerth, Hees, and Buitelaar (2003) provides evidence that prenatal exposure to maternal cortisol may program behavioral development in infancy. The researchers found a correlation between higher maternal cortisol levels in late pregnancy and, based on maternal reports, higher incidence of crying, fussing, and negative facial expressions in the infant over the first 20 weeks of life and more engagement in behaviors categorized as difficult. These associations were strongest during the earlier post-natal period and crying in particular lessened by 4 to 5 months, except for fussing and negative facial expressions. However, explanations other than fetal programming are possible. Given that these were maternal reports, a mother's perceptions may have been influenced by variations in her own cortisol and stress reactivity, for example. More research is needed to assess the effect of maternal cortisol during pregnancy and behavioral programming.

Studies of children have also found evidence of relationships between cortisol, behavior, and growth. Linking birth weight with later behavioral outcomes and serum cortisol levels, Wadsby, Nelson, Ingemansson, Samuelsson, and Leijon (2014) found that VLBW children had more behavioral problems at ages 7 and 9, social and attention problems, (but still within normal range) and lower cortisol levels compared to NBW children, indicating decreased HPA function. Hatzinger et al. (2007) found that in kindergarten children, baseline HPA activity, assessed by morning cortisol, significantly increased in kindergarten girls compared to boys, and this was predictive of a high hormonal response to stress. Increased HPA activity was associated with hyperactivity/impulsivity and emotional problems in boys but with positive emotions in girls. Smider et al. (2002) found increased cortisol linked to withdrawal in girls and externalizing difficulties in boys. In a study of boys by Perez-Edgar, Schmidt, Henderson, Schulkin, and Fox (2008), high cortisol at 4 was strongly associated with withdrawal (but not with acting out), but this was only significant in boys who had high levels of negative temperament in infancy. Tout, Haan, Campbell, and Gunnar (1998) found decreased cortisol in boys was linked to internalizing difficulties.

Findings that maternal cortisol may be one mediator between maternal ecology and infant behavior in human and animal studies are logical from an evolutionary perspective. Behavioral programming based on indicators of maternal environmental and emotional stressors, such as cortisol, may increase infant survival in situations of maternal stress and resource scarcity (Hrdy, 1999a). From mothers, offspring attain a sense of whether or not they have support and security, what will be provided for them, what their social status would be, how wanted they are, among other aspects of social development. Mothers give varying degrees of support to children. Leaving offspring with other caretakers, giving less than ideal care, and infanticide would have all been common practices in human evolutionary history. A wanted child will grow up in a very different environment and expect very different treatment than an unwanted one (Hrdy, 1999a). Hrdy (1999a) proposed that avoidance behaviors in infants may be adaptively employed to conceal reactions that might endanger the relationship with the care provider. It might be beneficial for children who are given less support and care to develop more self-reliance and less emotional empathy (Hrdy, 1999a).

Although the physiological mechanisms for alterations in behavioral development and the specific role of milk cortisol are not yet fully understood, there is evidence that brain development and brain activity are affected by reductions in the energy budget and in maternal investment.

Glucocorticoid exposure early in life can result in altered development of the amygdala, which is important in emotional experience and has the potential for long-lasting impacts on neurological function, as negative temperament in infancy can lead to increased risk of psychiatric conditions later, including eating disorders, depression, and anxiety (Grey et al., 2013). Animal models also demonstrate that hippocampal volume and low birthweight are directly related in individuals with low levels of parental bonding (Wadhwa et al., 2009). In rats, increased maternal care (licking and grooming) increased hippocampal expression of glucocorticoid receptor mRNA protein, decreased corticotrophin-releasing factor, and reduced the hypothalamic-pituitary-adrenal stress response. There is a direct correlation between maternal care and DNA methylation in the hippocampal glucocorticoid receptor and the programming can be reversed in adulthood by central infusion of methionine (Wadhwa et al., 2009). Cognitive impairment also contributes to a cycle of poverty and disease throughout the world, so optimizing neurological and behavioral development is an important public health concern (Neville et al., 2012).

Dehydration and Milk Production

During Ramadan, the quantity of breast milk produced may be reduced and milk composition may be altered due to abstinence from water. Not enough is currently known about the role of hydration in lactation to determine whether or not this is the case, particularly when it comes to populations that may be adapted to desert regions where extreme heat is a climatic norm (G. R. Bentley, 1998). Several hours of maternal abstinence from water could reduce the quantity of milk produced, but the “moderate” water restriction associated with Ramadan fasting may have only modest effects on breast milk volume (G. Bentley, 1998), especially since lactating women may “superhydrate” during non-fasting hours (Prentice et al., 1984).

Decreases in maternal milk production could lead to infants having an inadequate supply of milk. Inadequate milk intake by the infant could lead to inadequate macronutrient and micronutrient intake, the ramifications of which were discussed previously (G. R. Bentley, 1998). Dehydration of the infant is also a critical factor to consider if milk quantity and composition is reduced. Breast milk provides exclusively breastfeeding infants with their sole source of nutrients and fluids. Infants are particularly susceptible to dehydration; they experience greater evaporate loss and do not yet have the full ability to control urine osmolarity. Some cases of dehydration have been linked to a lack of sufficient milk production by mothers and other cases have been linked to an abnormally high sodium content in milk (G. Bentley, 1998).

Summary

Ramadan fasting may hypothetically influence the intrauterine environment and breastfeeding due to endocrine changes associated with the fasting state, dehydration and biological mechanisms to regulate water balance, and reduced nutritional quality of the diet during the month. Other research on consequences to pregnancy and lactation via alterations in these pathways suggests that maternal fasting might increase the likelihood of early pregnancy loss or reduce gestational length when Ramadan occurs early in gestation. Throughout gestation, fasting could create challenges in the intrauterine environment that could impact fetal growth and development. After birth and during lactation, fasting unlikely influences many nutritive components of milk, but fasting may alter non-nutritive components such as cortisol and other hormones, reduce milk production, and alter breastfeeding practices. During gestation and lactation, alterations in growth and development, exposure to alterations in hormone levels, and altered infant feeding practices could result in fetal or lactational programming with long-term costs for offspring. Having explored potential mechanisms for maternal fasting to generate these outcomes during gestation and lactation, what does the current research on maternal fasting on Ramadan suggest? In the following section, I described current research on maternal fasting for the month of Ramadan.

Studies of Ramadan Fasting During Pregnancy and Lactation

Having reviewed potential biological challenges of maternal fasting during Ramadan with regards to nutrition, endocrine changes, and challenges to water balance and how these stressors may impact pregnancy and lactation, I now turn to the research on maternal fasting during Ramadan. First, research on the effects of maternal fasting on pregnancy and birth outcomes are described and situated within other research on fetal programming. Studies of the effects on lactation are then summarized and considered in terms of potential consequences on infant health, growth, and development.

Ramadan Fasting: Pregnancy and Birth Outcomes

Consequences of maternal Ramadan fasting have been studied during different stages of pregnancy to maternal and infant health. Research has been conducted on Ramadan's influence on pregnancy loss and altered sex ratios at birth, length of gestation, and fetal growth as indicated by birth anthropometry. Although findings are not always consistent, overall the results of many studies support the hypothesis that Ramadan fasting is physiologically stressful for pregnant women and results in consequences to birth outcomes. Contextualizing these data with other research on fetal programming can generate valuable insight into the consequences of maternal fasting with regards to modified female reproductive strategies and the effects of in utero exposure on fetal growth and development.

Pregnancy Loss & Ramadan Fasting

Evidence from several studies suggests birth rates decline around the time of Ramadan. Some studies provide clear evidence that this association is due to early pregnancy loss (Almond & Mazumder, 2011; Hoffmann, 2014; Van Ewijk, 2011), but for others this is less clear and reduced conception rates (Friger, Shoham-Vardi, & Abu-Saad, 2009; Johnson, Tan Boon, & Palan, 1975). Changes in rates of conception may involve cultural and behavioral changes around the month of

Ramadan or other seasonal factors, but these do not adequately explain the evidence early pregnancy loss in several studies. Some studies have indicated cortisol and dietary factors in early pregnancy loss. Early pregnancy loss due to Ramadan fasting may result from various mechanisms, but previous research has indicated cortisol and dietary factors as potential causal mechanisms (Cintio et al., 2001; Nepomnaschy et al., 2006). As these may be reasonably expected to be altered during Ramadan in ways that may encourage early pregnancy loss, they will be explored in further detail.

Evidence suggests early pregnancy loss may be a consequence of Ramadan fasting, though separating the effects of fasting from other potential seasonal influences is complicated (Almond & Mazumder, 2011; Friger et al., 2009; Hoffmann, 2014; Johnson et al., 1975). Hoffmann (2014) provides compelling evidence of early pregnancy loss in a large-scale data analysis across multiple Muslim countries and several decades based on data from Demographic and Health Surveys (DHS). She demonstrates a consistent trend in decreased male to female birth ratios eight months after Ramadan, leading to a 2.5% increased chance of being female if born at this time. Comparing Muslim and non-Muslim populations with similar son preference, Hoffman further demonstrated that this contributed to an overall higher percentage of females in the Muslim populations. Based on her analysis, she estimates that 2 million men would be alive today if it were not for Ramadan fasting.

Data from in Muslim populations in Michigan and Uganda also provide strong evidence for early pregnancy loss associated with Ramadan fasting (Almond & Mazumder, 2011). In Michigan, a decrease in male births was highest when Ramadan fell during years of highest daylight hours; when Ramadan overlapped with early pregnancy, odds of delivering a male decreased 12%. During this study, daily fasting duration would have been just over 12 hours. In an analysis of total full-term births to Muslim women in Uganda, there was a 13% decline in total births observed when conception would have occurred one month prior to Ramadan. A 26% decrease in male birth was seen at this time, along with an insignificant decrease in female births. The authors note that early pregnancy loss is most common if the fetus is male, which is supported by evolutionary hypotheses (Trivers & Willard, 1973; Wasser & Barash, 1983). This evidence suggests an increase in early pregnancy loss when the first few weeks of pregnancy overlap with the month of Ramadan "since it is difficult to imagine an alternative mechanism which impacts sex-specific fertility" (Almond & Mazumder, 2011). However, this data is from only one year, so other seasonal effects could also be at work.

A study that spanned multiple generations of individuals in Indonesia by Van Ewijk (2011) had similar findings regarding sex ratios. Exposure to Ramadan in utero reduced the likelihood of the infant being a male by 2.6%. Contrary to the previous studies, though, this exposure included any time during pregnancy and was not limited to early gestation.

Other studies have not considered sex ratios in seasonal birth patterns and have interpreted findings of seasonality in birth rates around Ramadan to be the product of other factors. Johnson et al. (1975) examined birth rates in Malaysia between 1964-1969, comparing the predominantly-Muslim Malay population with the non-Muslim Chinese population. The Malay had more dramatic seasonality in births. Malays had their lowest birth rates from September to December, which corresponded to a conception time that coincided with Ramadan, and an increase in births in January (Johnson et al., 1975). However, the Islamic calendar is based on lunar months and shifts about 11 days earlier compared to the Gregorian calendar each year. However, Ramadan shifted approximately two months from the start to the end of the study period, so if seasonality was associated with Ramadan fasting, the timing of the lowest birth rates would be expected to shift over the course of the study. The authors noted that they did not observe this expected shift, suggesting that this was seasonality may have been an artifact of other seasonal influences.

An interesting case of seasonality was found in a study by Friger et al. (2009) when births increased during Ramadan in the Muslim population but not in the Jewish population living in the same geographical area of southern Israel over several years. As they did not find a larger incidence of preterm births during Ramadan than at other times, they concluded that Ramadan did not induce earlier labor. Therefore, more pregnancies occurred two to three months after the previous Ramadan. The authors proposed that the reason for this trend was cultural variation in sexual activity. The trend was found only in multiparous mothers, whereas first births clearly followed a yearly cycle around spring and summer wedding trends. Birth seasonality trends became more prominent following increased wealth in the country that may have allowed for increased participation in the Hajj, a 10-day religious pilgrimage that occurs 38 weeks prior to the first day of Ramadan during which sexual activity is not permitted. It is not known what portion of this population participates in the Hajj each year, but daylight hours were longer prior to the increase in wealth in this population. The authors argue that stronger effects should be seen when Ramadan occurs in years when daylight hours are longer if the effect was biological. Given these observations, the authors ruled out biological causes to the observed birth patterns.

Still, it is possible that early pregnancy loss during Ramadan followed by increased rates of conception is a contributing factor. Following early pregnancy loss, fecundity is often disrupted for one month but quickly returns (Donnet, Howie, Marnie, Cooper, & Lewis, 1990), which would also correspond to the observed pattern. Moreover, the fact that the relationship between fasting during Ramadan and the likelihood of having offspring with reduced birth rates intensified after wealth increased within the country would be predicted by the Flexible Response Model proposed by Vitzthum (2001). There would be no advantage to suppress reproductive effort under normal conditions, even if these conditions are challenging. Only conditions that are suboptimal compared to normal conditions would be expected to result in a delayed reproductive effort. This means that women who were living in already challenging environments may not experience fasting as much more stressful than normal conditions, whereas women who in more “luxurious” conditions would find fasting to be considerably more stressful than usual and more likely to suppress reproductive effort (Vitzthum, 2001).

Cultural Hypotheses for Reduced Conception Rates

Studies of birth seasonality around Ramadan provide compelling evidence of suppression of reproductive effort and of physiological stress caused by fasting, but alternative explanations should be considered. Other cultural, environmental, demographic, and economic variables could account for seasonality coinciding with Ramadan in different populations. Increased risk of early pregnancy loss may be due to environmental conditions other than Ramadan, as environmental factors like temperature and fluctuations in food availability cause seasonal variation in conception rates and birth rates in almost all populations (Bronson, 1995). Reduced conception during Ramadan may be explained by family planning strategies to avoid pregnancies that overlap with Ramadan, sexual behavior during the month, marriage patterns, and other religious activities.

With increasingly effective and available family planning methods available, it is also possible that women are making decisions that affect their reproduction so that pregnancy does not coincide with Ramadan. In Indonesia, after birth control methods became widely available, rates of contraceptive use were high during Ramadan and declined sharply after Ramadan (Karimova, 2015). This led to a small increase in post-Ramadan conceptions. This pattern of contraceptive use would likely result in a short delay before reproductive function returned to normal (Baird, 2013), so conceptions rates might appear to be lower during Ramadan and increase a few months after.

Frequency of intercourse may decline during Ramadan. Decreased frequency of intercourse and decreased sexual desire during Ramadan fasting has been reported among married men (Talib, Canguven, Al-Rumaihi, Al Ansari, & Alani, 2015). As with food and water, intercourse is only forbidden during the hours between sunrise and sunset. However, Ramadan is also a time of purification when many behaviors are ideally supposed to be moderated, and because practices and interpretations vary greatly regionally, sexual behavior during the month may differ across populations.

Sexual practices during other religious observances may influence birth rates. As previously discussed, a possibility suggested by Friger et al. (2009) for birth seasonality relating to Ramadan is that the Hajj pilgrimage rather than Ramadan fasting could have caused the seasonality observed in Israel, since more births occurred during the month of Ramadan and sexual intercourse is forbidden during the Hajj, which occurs about 38 weeks prior (Friger et al., 2009). Another example is marriage patterns, which may influence birth patterns. In some populations, women are expected to conceive relatively soon after marriage, and marriages often take place in seasonal patterns (Friger et al., 2009). Friger et al. (2009) found seasonal patterns in primiparous birth to follow a yearly cycle corresponding to the wedding season. As primiparous birth may follow distinct patterns in populations with similar customs, it may be beneficial to separate primiparous and multiparous births when looking at seasonality.

Although cultural practices may explain variation in conception rates occurring around the time of Ramadan, they do not adequately explain findings that clearly highly early pregnancy loss. The most plausible explanation for the decreased ratio of male to female birth when conception would occur shortly before the onset of Ramadan is early pregnancy loss. Seasonal factors other than Ramadan could be at play, such as variations in the food supply. If Ramadan fasting induces early pregnancy loss, causal mechanisms can be hypothesized. As discussed previously, increased cortisol and reduced micronutrient quality of the diet have both been implicated in early pregnancy loss and are likely to result from Ramadan fasting.

Summary of Pregnancy Loss and Maternal Fasting

These studies provide compelling evidence that Ramadan fasting during early pregnancy is physiologically stressful to the extent that maternal reproductive effort is reduced. This includes an increased change of pregnancies being spontaneously terminated. It is possible that changes in overall birth rates around Ramadan observed in some studies may be caused by cultural behaviors and other factors that reduce rates of conception around that time. However, the evidence from multiple studies of altered sex ratios corresponding with Ramadan fasting and the evidence that this effect is stronger when daylight hours are longest is strongly suggestive of early pregnancy loss. Although exposure to other environmental factors could be at play, the repeated observances of altered sex ratios at birth over multiple years when Ramadan falls at different times throughout the year would indicate that fasting plays a causal role. The mechanism may be related to maternal stress responses resulting from fasting, but it could also be related to a reduction in the nutritional quality of the diet. The mechanism that is causing higher rates of spontaneous abortion in early pregnancy is likely at work and with effects specific to gestational age. It is particularly interesting that the Dutch Hunger Winter did not prompt changes in sex ratios, yet maternal fasting during Ramadan may. This disparity supports the assertion that outcomes of exposure to this fast may not be well captured by other situations of food scarcity and malnutrition.

Ramadan, Length of Gestation and Preterm Delivery

Although the effect of maternal nutritional status on length of gestation may not be clear, some studies have found relationships between fasting and increased cortisol and between reduced meal frequency and reduced length of gestation. Evidence suggests that maternal fasting increases maternal cortisol. One study found that Ramadan fasting increased maternal cortisol in pregnant women (Dikensoy et al., 2009) and another study found that pregnant women whose overnight fast lasted 13 hours or more had increased maternal CRH, which stimulates a rise in cortisol (Herrmann, 2001).

Reduced frequency of eating and fasts other than Ramadan have been associated with earlier initiation of labor. One study found that women who eat less frequently have a greater risk of delivering preterm than women eating three meals and two snacks per day (Siega-Riz et al., 2001). Also, evidence from the 25 hour Yom Kippur fast demonstrated that the day following the fast, births increase significantly in number, indicating fasting may prompt the initiation of labor (Wiser et al., 1997).

As fasting has been linked to increased maternal cortisol and as increased maternal cortisol has been linked to preterm birth, cortisol may play a mediating role, although there are other potential mechanisms that might mediate this relationship. Due to findings from other scenarios, it is reasonable to hypothesize that Ramadan fasting may cause a reduction in the length of gestation. However, the research thus far has been contradictory (Awwad et al., 2012; Hefni, 1993; Kavehmanesh & Abolghasemi, 2004; Tith, Bilodeau-Bertrand, Lee, Healy-Profitós, & Auger, 2019). Awwad et al. (2012) found no significant differences between the incidence of preterm labor in fasting versus non-fasting controls when Ramadan occurred during the second or third trimester. However, it is possible that fasting could lead to a reduction in gestational age while still maintaining the timing of birth within the range of full term, so this study does not rule out the possibility of fasting being associated with reduced length of gestation. However, in a study in Iran when fasting was approximately 13 hours per day, Kavehmanesh and Abolghasemi (2004) did not find fasting associated with reduced gestational age at birth. However, a more recent study from Quebec that spanned 36 years found that when the month of Ramadan overlapped with the second trimester, the relative risk of delivering very preterm (28-31 weeks gestation) increased, and exposure later in the second trimester was associated with greater risk (Tith et al., 2019). Tith et al. (2019) found that when Ramadan overlapped weeks 15-21 of pregnancy, the risk of delivering very preterm (at 28-31 weeks gestation) increased by 33%. When Ramadan overlapped with weeks 22-27 of pregnancy, the risk increased by 53%. The risk of delivery earlier than 28 weeks did not increase, nor did the risk of later preterm delivery (32-36 weeks).

Studies of Ramadan and Fetal Growth and Development

Studies of Ramadan fasting during pregnancy have incongruent findings regarding the effects of Ramadan on birth size, and most have only used birth weight as an outcome variable.

Although birth weight is a valuable indicator of fetal environment, it does not provide a comprehensive picture of intrauterine stress or possible trade-offs made in fetal development. Findings on the effects of Ramadan fasting on birth weight have not been consistent, and it is difficult to compare non-fasting and fasting women within a population for multiple reasons. Fasting women have been found to differ from non-fasting women ways that are also significant to infant birth weight, including factors such as education, socioeconomic status, and health concerns such as diabetes. Moreover, even non-fasting women may experience an altered food environment if the rest of their household and communities are fasting (Yamauchi et al., 2009).

Studies that have assessed the effect of fasting on fetal growth have largely focused on infant birth weight as the outcome variable. In a study based in Michigan that spanned 18 years, Almond and Mazumder (2011) found a significant decrease in birth weight associated with Ramadan fasting, particularly when fasting occurred during the first and second trimesters but not the third trimester. This study took place between 1989 and 2006 when Ramadan did not overlap with summer months and daily fasting durations fluctuated between about 9 hours and 14 hours. In a population of Lebanese women, Awwad et al. (2012) found that average birth weight of infants of fasting mothers was significantly lower than infants of non-fasting mothers (3094 ± 467 g versus 3202 ± 437 g, $p<0.024$) when fasting hours were about 15 hours per day and Ramadan began between 20-34 weeks gestation. Fasting mothers in this study sample also had higher rates of ketosis and ketonuria. A study by (Yamauchi et al., 2009) compared regions with primarily Christian populations to those with predominantly Muslim populations in Indonesia. Daylight hours in Indonesia do not very greatly and are about 12 hours throughout the year. The researchers found that infants born shortly after Ramadan had lower birth weights. Whether Ramadan played a causal role is unclear, because the study spanned only one year, and because other factors may account for the difference, including seasonal and regional variation in crop production, poverty, and clean water.

In a study of Muslim immigrants in the Netherlands when daylight hours were about 14 hours per day, birth weight was lower in infants of mothers who fasted in the first trimester of pregnancy but not in the second or third trimesters after adjusting for confounding factors (although not maternal anthropometry or gestational age at birth) (Savitri et al., 2014). In Iran in 2004 when daylight lasted about 12 hours per day, Ziaee et al. (2010) also found maternal fasting in the first trimester to be associated with a relative risk of 1.5 for having low birth weight offspring. This study included head circumference in its analysis but found no association with head circumference and fasting.

Other studies found no effect of Ramadan fasting on birth weight. None of these studies stated if gestational age was controlled for in their analyses. Kavehmanesh and Abolghasemi (2004) found that fasting was associated with infant birth weight until controlling for maternal BMI, which although was not stated, appears to be based on pre-pregnancy weight. Therefore, the potential for fasting to influence gestational weight gain was not a confounding factor in this analysis. Across a 20 year period in England, Cross et al. (1990) found no significant changes in birth weight regardless of the trimester fasting occurred, though there was a non-significant increase in low birth weight infants when Ramadan occurred during the second trimester. This study spanned 1964, when Ramadan occurred in winter and 7-8 hours of daylight, to 1984 when Ramadan occurred during the longest days of the year with about 16-17 hours of daylight. In a study that began shortly after Ramadan and spanned 9 months, Arab and Nasrollahi (2001) also found no association between birth weight and fasting in utero in Iran when daylight lasted about 9 hours. There was again a non-significant increase in low birth weight infants born when fasting occurred during the second trimester. It is unclear whether they controlled for other maternal variables. Given the time period of the study, only pregnancies that overlapped with the month of Ramadan were included in this study; pregnancies that did not overlap with the study were not used for comparison.

Several articles reporting on birth weight or gestational age that did not find associations with Ramadan fasting have concluded that Ramadan fasting is, therefore, safe during healthy pregnancies or safe other than the trimester in which there was a significant reduction in birth weight. However, birth weight does not give a complete picture of the effects of fasting. Results of other studies that have focused on outcome variables other than birth weight suggest growth and developmental differences in infants were exposed in utero to Ramadan fasting and provide evidence of fetal programming due to variation in placental development during fasting.

Alwasel et al. (2010) did not find differences in birth weight resulting from Ramadan but they did find reduced placental weight and reduced placental to birth weight ratio in infants of mothers who had fasted in the second and third but not first trimesters, which suggests reduced placental transfer during fasting. However, uterine artery blood flow was not reduced during Ramadan fasting when daily fasting duration was about 15 hours in Iran when fasting hours (Moradi, 2011) or nine hours in the United Arab Emirates (UAE) (Mirghani, Salem, & Weerasinghe, 2007), which challenges this hypothesis, although the authors specify that this finding may not apply to longer fasting durations. In the UAE sample, Ramadan fasting was found to contribute to reduced fetal heart rate (Mirghani, Weerasinghe, Al-Awar, Abdulla, & Ezimokhai, 2004), reduced fetal breathing movements (Mirghani, Weerasinghe, Smith, & Ezimokhai, 2004), increased incidence of gestational diabetes, induction of labor, cesarean section, and admission of the infant to the special care unit (Mirghani & Hamud, 2006), but did not result in a difference in Apgar scores at birth (Mirghani & Hamud, 2006).

There is also evidence that fasting increases the risk of child mortality. In a study spanning 20 years and including over 40,000 children in Burkina Faso, child mortality before the age of five was substantially higher among the Muslim population in children of mother that were fasting during the month of conception or the first or second trimesters. There was no difference in Muslim and non-Muslim populations when Ramadan fasting happened during the third trimester or did not overlap with pregnancy (Schoeps et al., 2018). Given the span of the study, it was possible to differentiate the effects of seasonal variation from Ramadan fasting. This study took place in a location with high rates of mortality before five years of age, largely due to infectious disease, so the authors hypothesize that one potential link between Ramadan fasting and increased mortality includes alterations to the immune system.

Exposure to fasting in utero may lead to a difference in anthropometry and reproductive outcomes in adulthood. In Indonesia, adults that had been in utero during Ramadan were thinner and those whose estimated conception dates were during Ramadan were shorter in stature as adults (Van Ewijk, Painter, & Roseboom, 2013). In Tunisia, Alwasel et al. (2013) found that women who had been exposed to Ramadan fasting in utero had infants who had lower birth weights, lower ponderal indexes, and smaller placentas. These results did not vary by the trimester of the mother's exposure, infant sex, or parity. In a study from Saudi Arabia of pregnant women who had been exposed to Ramadan in utero, if maternal exposure occurred during the second trimester, male infants were longer in length and female infants were born at earlier gestational ages (Alwasel et al., 2011).

Fasting during pregnancy may have implications for cognitive development. In children, academic performance has been found to be lower in offspring of fasting mothers. One study found that each additional week of exposure to Ramadan in utero corresponded with reduced grades in school (Oosterbeek & Van Der Klaauw, 2013), while another found a significant reduction in test scores when fasting occurred in early gestation (Almond, Mazumder, & Van Ewijk, 2015). In Uganda, Almond and Mazumder (2011) found that fasting in early pregnancy was associated with an increased incidence of cognitive disabilities and hearing and sight impairment.

Fasting may contribute to lower birthweight by constraining maternal weight gain during pregnancy. Prentice, Prentice, Lamb, et al. (1983) found that all pregnant and lactating women lost weight even when given nutritional supplements and determined that fasting induced accelerated starvation during late pregnancy. Although the effects of fasting on gestational weight gain in Morocco is unclear, research on a sample of Moroccan women giving birth in a maternity hospital in the Rabat-Sale-Kenitra region by Mochhoury et al. (2013) suggests that, in general, gaining adequate weight during pregnancy may be a challenge for over a third of the population. They found that 37.6% of pregnant women gained less than 8 kg, 55.2% gained 8-16 kg, and 7.2% gained over 16 kg during pregnancy. In a study in the Gambia when fasting hours were over 14 hours.

The difficulty of maintaining adequate daily caloric intake and nutritional quality while fasting may vary by population and duration of daily fasting and may contribute to difficulties achieving appropriate gestational weight gain in some populations. Normally, the average caloric intake is thought to be adequate for pregnant women in Morocco (Belgnaoui & Belahsen, 2006). However, studies of other populations have found that pregnant and lactating women who opt to fast for Ramadan are likely to not only eat fewer calories during this month but also are likely to eat a larger portion of their calories from grain and oil, leading to a less nutritionally dense diet with fewer micronutrients (Rakicioglu et al., 2006).

This problem is made more complex due to the fact that women around the world make choices during pregnancy based on preferences for smaller babies to help reduce difficulties during birthing (Nichter & Nichter, 1983). During my time as a Peace Corps volunteer in Morocco, pregnant women often cited this as a possible benefit of Ramadan fasting, allowing that babies might be smaller as a result. Given that medical care was not readily available, smaller newborns may make giving birth easier and less risky for mothers.

Summary of Birth Outcomes

Outcomes of Ramadan fasting during pregnancy may be predicted by gestational weight gain and trimester of exposure to Ramadan. Research from the Dutch Hunger Winter would lead to the prediction that in utero exposure to Ramadan may be more influential on birth size outcomes if it occurs in the third trimester, whereas other consequences would be predicted when fasting occurs earlier in gestation. If maternal gestational weight gain is reduced to less than 0.5 kg per week during fasting, more significant ramifications would be expected (Stein et al., 1995).

However, the results of studies on birth weight do not correspond precisely to what would be expected from other evidence from the Developmental Origins of Health and Disease (DOHaD) literature, which is expected given the wide variety of conditions and populations in which Ramadan fasting is practiced. The hypothesis that infant birth size would be most affected by maternal fasting in the third trimester is supported by the data from Yamauchi et al. (2009) and Awwad et al. (2012). However, Almond and Mazumder (2011) observed reduced birth weights when fasting occurred in the first or second trimester but not the third. Savitri et al. (2014) and Ziaee et al. (2010) found first-trimester fasting to be associated with a reduction in birth weight. Cross et al. (1990) and Arab and Nasrollahi (2001) also found an increased prevalence of low birth weight when Ramadan occurred in the second trimester, although not significant. Of course, other studies found no difference in birth weight by maternal fasting.

While birth weight is a valuable indicator of the intrauterine environment, it does not fully capture trade-offs made during fetal growth and development. This is demonstrated by studies of the Dutch Hunger Winter, in which exposure during the first trimester did not lead to reduced birth weight but did result in other consequences, including a higher risk of neurodevelopmental disorders (Susser, Hoek, & Brown, 1998). As would be predicted by this finding, evidence suggests there are also long-term effects on cognitive development of fetal exposure to Ramadan fasting, particularly when exposure was early in pregnancy (Almond & Mazumder, 2011; Almond et al., 2015; Oosterbeek & Van Der Klaauw, 2013). Early fetal exposure to the Dutch Hunger Winter was also associated with a higher risk of diabetes, obesity, coronary heart disease and reduced reproductive success in adulthood (Heijmans et al., 2008; Lumey & Van Poppel, 1994; Roseboom et al., 2000). Counter to this, fetal exposure to fasting was associated with reduced BMI in adulthood, but also with reduced stature in adulthood and reduced birth size of infants of mothers exposed to fasting in utero, demonstrating that additional long term consequences may result from fetal exposure to Ramadan (Alwasel et al., 2013; Van Ewijk et al., 2013). Given the tight direct correlation between maternal height and infant weight, it is possible that reduced infant birth size is suggesting in utero Ramadan exposure resulted in maternal stunting.

Ramadan Fasting: Impacts on Lactation

For exclusively breastfed infants, breast milk is the sole source of energy, nutrients, and hydration, but several other bioactive components of milk are transferred to the infant as well. These include immune factors, hormones, metabolites, and growth factors. Together, these components reflect the maternal phenotype and environment (Kuzawa & Quinn, 2009). In this section, I will explore research on the results of Ramadan fasting on breast milk composition, breast milk production, and infant feeding practices.

This discussion will begin with the effects of fasting on the nutritional composition of breast milk. Although nutritional changes to milk are not likely and have not been observed in studies of Ramadan fasting (Bener et al., 2001; Khoshdel et al., 2007; Rakicioglu et al., 2006), if the number of hours spent fasting are enough to induce altered endocrine activity associated with a physiological fasting state in mothers, it may also lead to physiological consequences that alter bioactive components of breast milk. Therefore, endocrine alterations in breast milk may be more likely compared to changes in nutritional composition. Recent research has linked to lactational programming in infant life history strategies due to maternal stress responses. In these studies, cortisol was implicated as mediating factor (Dantzer et al., 2013; Hinde et al., 2014), and will, therefore, be explored for its possible associations with maternal fasting and infant outcomes. Maternal fasting during Ramadan, which includes abstinence from water, may also have implications for milk production, which will also be addressed.

Effects of Ramadan Fasting on Nutritional Content of Breast milk

Results from research on the effects of Ramadan fasting on the nutritional composition of breast milk have not indicated significant alterations to milk that would influence infant growth or milk cortisol content. Milk fat and protein content are of particular interest because these macronutrients are positively correlated with glucocorticoid content and also mediate infant growth (Grunewald et al., 2014; Hinde et al., 2014; Nikniaz et al., 2009), but previous research has not found milk protein or fat content to be affected by Ramadan fasting. However, this may be due to the shorter duration of fasting hours in studies that have analyzed milk nutrient content. Changes in milk composition may be more perceptible when the number of hours spent fasting daily is higher.

In one study of Ramadan fasting when fasting was about 14 hours per day, Prentice et al. (1984) found a decrease in milk lactose concentration, along with other indicators of a disturbance in milk synthesis, though other macronutrients were not assessed. A study on a 24-hour fast detected an increase in milk protein and decrease in milk lactose (Zimmerman et al., 2009). However, two other studies that investigated milk macronutrient composition during Ramadan have not found significant changes in macronutrient composition. A study by Bener et al. (2001) took place when Ramadan fell during the winter when fasting time did not exceed 7-8 hours and therefore may not be representative of the effects when fasting time is longer. In a study by Rakicioglu et al. (2006) involved longer fasting periods, 10-11 hours, but milk samples were taken during Ramadan and compared to samples taken after Ramadan, and no samples were taken beforehand for comparison. Perhaps maternal fasting is more likely to influence macronutrient content when fasting hours are longer and/or in hotter climates, as seen in the study by Prentice et al. (1984).

Regarding milk micronutrient composition, the number of hours spent fasting daily may be less influential than dietary quality during non-fasting hours for some micronutrients. Because diet quality may change during Ramadan (Aoyama, 1999; Belgnaoui & Belahsen, 2006), maternal micronutrient intake may be affected. In Turkey, Rakicioglu et al. (2006) found that Ramadan fasting resulted in reduced maternal intake of almost all micronutrients along with a decline in breast milk micronutrient content, with significant declines in zinc, magnesium, and potassium. Breast milk-derived zinc, along with vitamins B12 and D as well as iodine, may also influence infant growth (Kovacs, 2012; Riordan, 2005; Semba & Delange, 2001; Stabler & Allen, 2004). Zinc deficiencies are one of the most common minerals attributed to infant morbidity and mortality, but breast milk concentrations are not thought to be significantly impacted by maternal diet (Black et al., 2008). Zinc levels also normally decline over the duration of breastfeeding (Riordan, 2005), which could be responsible for the finding of significantly reduced zinc concentrations after a month of Ramadan fasting, although this possibility was not discussed by the authors. In another study of breast milk during a 24-hour fast, fasting led to statistically significant biochemical changes in breast milk, increasing sodium and calcium levels while decreasing phosphorus levels (Zimmerman et al., 2009).

In a study by Prentice et al. (1984) which took place in the Gambia when fasting hours lasted about 14 hours per day, indications were found of a disturbance in milk synthesis in lactating women during Ramadan, including a 51% increase in milk sodium, which may have been more strongly impacted by dehydration than maternal nutrition and will be discussed further in the next section on milk production. Other than the findings regarding disturbances in milk synthesis and some micronutrient changes during longer fasts, overall these findings support the hypothesis that lactation helps to buffer infants against ecological variations in the food supply and that minimal changes to macronutrient and micronutrient composition of breast milk can be expected from fasting.

Ramadan and Milk Cortisol

Research on the effect of maternal fasting on milk hormonal composition, including cortisol, is currently lacking. Maternal fasting likely constitutes a stressor for numerous physiological systems, as suggested by evidence of elevated circulating maternal cortisol during fasting in pregnant women (Dikensoy et al., 2009) and when the typical overnight fast extends beyond 13 hours in pregnant women (Herrmann, 2001), but studies of lactating women are needed. Cortisol is responsive to maternal stress, an important hormone in regulating energy allocation and metabolism, and a bioactive component of breast milk that may influence infant growth, development and behavior (Hinde et al., 2014). Considering that fasting is expected to increase maternal cortisol if the number of hours spent fasting is long enough to trigger a physiological fasting response and considering that milk cortisol is strongly related to maternal circulating cortisol (Breakey, 2015), it is likely that milk cortisol is increased during maternal fasting. However, further research is needed to determine if this prediction is correct and if so, what consequences there may be to infant growth and development. If cortisol concentrations in breast milk are found to be increased during Ramadan fasting, it could have ramifications particularly for infant life history strategies and behavioral development.

Ramadan and Milk Production: Dehydration, and Infant Feeding

An important facet of Ramadan fasting is abstention from water, which may influence milk production, milk composition, perceptions of milk quantity and infant satiety, and infant feeding practices. Moreover, the ways in which lactation responds to water deprivation is not known (G. Bentley, 1998), so Ramadan may provide a unique context from which cross-population comparisons may be constructed. Studying changes in milk quality and quantity resulting from daily maternal fasting from food and water could increase our understanding of the evolutionary mechanisms that have developed in response to food and water scarcity.

Milk Production during Ramadan

In assessing the effect of water abstention on lactation, several milk constituents may be important indicators of disrupted milk production. In a Gambian study by Prentice et al. (1984), a disturbance in milk synthesis in lactating women during Ramadan was discovered by analyzing sodium potassium, and lactose, among other components. Increased sodium content in milk during maternal fasting may be significant; a study by Prentice et al. (1984) of Ramadan fasting (when fasting hours lasted about 14 hours) in lactating mothers found that sodium content of breast milk increased by 51%, even though maternal serums levels only increased by 7.5%. This also may have been linked to the 13% increase in lactose since the two components are inversely related. The Na:k ratio was disturbed, as the increase in milk sodium concentration was not accompanied by a proportional increase in potassium (the normal ratio is 1:2.3). This suggests a temporary partial loss of integrity of the mammary secretory epithelium, so small ions are able to pass between intercellular junctions (Prentice et al., 1984; Prentice, Prentice, & Lamb, 1983).

Although there did appear to be a decrease in milk production during Ramadan compared to prior to and after Ramadan, the evidence suggested that this was also affected by seasonal changes, so changes in milk quantity during Ramadan may have resulted from confounding factors (Prentice et al., 1984). Milk quantity is difficult to assess accurately but understanding maternal perceptions about milk quantity during fasting is also valuable. Abnormally high sodium content of breast milk can cause dehydration in the infant, (G. Bentley, 1998), so dehydration may be a risk for infants of fasting mothers even if milk quantity is maintained during fasting. In the Moroccan population being studies, other practices may exacerbate the risk of infants becoming dehydrated, such as swaddling. Swaddling practices in hot climates may exacerbate evaporative losses and increase dehydration risks (Fleming et al., 1990; Van Gestel, L'hoir, Ten Berge, Jansen, & Plötz, 2002).

Perception of Milk Production and Supplemental Feeding

Perception of a decrease in milk production may be as important as an actual decrease in its influence on infant feeding behaviors. Whether or not fasting reduces milk quantity, many women believe it does (Ertem, et al. 2001; Ozsoy, et al. 2014), and this perception may influence decisions about fasting and supplemental feeding behaviors. In Turkey, maternal fasting increased the likelihood of supplemental feeding of infants as young as two months old, and only a small fraction of those women supplemented with formula (Ertem, et al. 2001). In the pilot study for this research project, 17 of 21 women from the target population fasted during the previous Ramadan. Thirty-five percent of the fasting women felt they produced less milk during Ramadan, though only two felt they were producing an inadequate amount of milk due to Ramadan. Fifty-eight percent of the fasting women felt they were not producing enough milk, but eight of them felt they had never produced enough milk regardless of Ramadan All of these women supplemental fed during Ramadan, and no others did. The average age of supplementation was 3.76 months.

Increased supplemental feeding can reduce milk production (Powers, 2005). If milk quantity does not decline during Ramadan, the belief that it does may lead women to supplement the infant's diet, which may lead to an actual decline in milk production. Since supplemental feeding may cause different growth patterns for infants compared to exclusive breastfeeding, this is an important factor to consider. Formula feeding promotes excess weight gain in infancy (Dewey, Heinig, Nommsen, Peerson, & Lönnerdal, 1992) , and both formula feeding and rapid weight gain have been found to contribute to obesity and several metabolic diseases in adulthood. The risk is particularly high among individuals born at low birth and formula fed for later development of central adiposity, Type 2 diabetes, high cholesterol, and elevated blood pressure (Kuzawa & Quinn, 2009; Ong & Loos, 2006; Owen, Martin, Whincup, Smith, & Cook, 2005). Alternatively, suboptimal supplemental feeding, which includes non-exclusive breastfeeding for the first six months, early discontinuation of breastfeeding, and early introduction on non-milk liquids, is a clear cause of stunting (Black et al., 2008). If altered infant growth patterns are associated with maternal Ramadan fasting, it is possible that it is due to the relationship between maternal fasting and supplemental feeding. Supplementing with formula may cause increased infant weight gain whereas suboptimal supplemental feeding could cause decreased weight gain. Since women commonly report exclusive breastfeeding when further questioning reveals otherwise (Vitzthum 1994), this should be thoroughly investigated in the research of fasting and infant growth.

Due to the relationship between maternal perceptions of reduced milk quantity and increased supplemental feeding behaviors, the social and cultural context in which Ramadan takes place and the behaviors and norms of the population likely influence the impact of maternal fasting on maternal and infant health. While it is important to investigate the biological aspect of maternal fasting, including the effect on maternal physiology, lactation, and milk composition, the biological impact on mothers and infants are interwoven into the cultural context that underlies important factors such as reasons women choose to or not to fast and norms about supplemental feeding.

Summary

Ramadan fasting includes voluntary abstinence from food and water for a set period of time. This occurs in the absence of food and water insecurity and the accompanying psychological stress, and those who fast do not necessarily reduce daily energy intake. Findings on the outcomes of maternal fasting during Ramadan, therefore, may differ from other findings from situations of nutritional deprivation and stress.

The strongest evidence that fasting induces pregnancy loss is provided by studies that indicated reduced male to female sex ratios when Ramadan occurs during early pregnancy. Findings of reduced birth rates without assessing sex ratios may be explained by other cultural rationales for altered patterns of conception around Ramadan fasting, and studies limited to a short duration of time may be capturing other seasonal variations that would increase pregnancy loss.

However, given the multi-year data of some studies which also across a multitude of countries, evidence suggests that fasting constitutes a stressor strong enough to induce pregnancy loss in early pregnancy. There is some evidence to suggest that maternal fasting influences the length of gestation, as would be predicted, but research on this topic has had contradictory findings. However, research on this outcome is limited and has been more oriented toward rates of preterm birth rather than the length of gestation, per se. Taken together, it is clear that maternal fasting likely presents a great enough stressor to induce early pregnancy loss but might not trigger mechanisms that would calibrate a reduced length of gestation or induce earlier labor, though more research is needed.

Studies have been contradictory on the effects of fasting on birth weight. Although some studies have coincided with data from the Dutch Hunger winter and found reduced birth weight when fasting took place in the third trimester, other research suggests that fasting earlier in pregnancy may be more impactful on birth weight. As indicated by the literature on fetal programming, birth weight does not provide a complete picture of trade-offs made in utero to stressors, and findings on Ramadan fasting confirm this.

Studies have found other potential effects of maternal fasting, including consequences neurocognitive function and increased disability rates, reduced adult stature, and altered placental size. Altered placental size and function has been observed in other studies to provide short term benefits during reduced resource availability but may have long term impacts. Studies such as these indicate that in utero exposure to Ramadan fasting may have life-long impacts.

During lactation, the evidence does not suggest there is a decline in the nutritional quality of breast milk such that it would influence infant health, growth or development. Rather, evidence suggests that infants may be more susceptible to dehydration due to altered sodium content of the milk, which may be exacerbated in hot climates, and to increased supplemental feeding, with an increased likelihood of supplemental feeding being initiated earlier than recommended and which often involves suboptimal dietary items. These factors can influence infant health, growth rates, and development. There is not yet data to assess how other bioactive components of milk, such as cortisol, may be altered due to fasting and the effects that may have on infant growth, but evidence from animal studies, known hormone changes during fasting, and the correspondence between maternal circulating cortisol and milk cortisol suggest this is highly possible.

The purpose of this dissertation is to further contribute to this literature on fetal and lactational programming by researching the consequences of Ramadan fasting during late pregnancy on fetal growth and postpartum breast milk cortisol concentrations. In Chapter 4, I will detail the methodology used in this research to address the consequences of maternal fasting when daily fasting duration is at its longest, extending to approximately 16 hours per day.

Chapter 4: Research Setting and Methods

This dissertation broadly addresses the influence of maternal environment on infant life history strategies, using Ramadan as a natural experiment to explore the effects of over 16 hours without food and water for a month during pregnancy. This research will specifically assess the influence of maternal fasting on birth outcomes and the transmission of information on maternal environmental stressors via the hormonal milieu experienced by her offspring in postpartum breast milk.

The first topic this research will seek to address is determinants of fasting behavior, as this research is prefaced by the prediction that women who fast are different from women who do not in a number of ways. For example, many women do not fast while pregnant due to health concerns (Saleem, et al. 2010). Comparing outcomes for fasting and non-fasting women without considering determinants of fasting behaviors may mask genuine differences associated with fasting.

The next question regards birth outcomes in association with maternal fasting. As a physiological stressor, maternal fasting during third-trimester pregnancy is predicted to influence birth outcomes, including reduced fetal growth as measured by neonatal anthropometry and accelerated life history trajectory as indicated by gestational age at birth.

This study will also assess the amount of cortisol in breast milk at 48-72 hours post-partum to determine if it is higher in women who fasted in the days leading up to delivery compared to women who did not. Identifying ways in which the intrauterine environment and breast milk composition respond to maternal fasting is additionally important and can help better elucidate potential adaptations and trade-offs faced by the offspring. If maternal fasting contributes to fetal and lactational programming, identifying changes in the intrauterine environment and breast milk can further help understand mechanisms contributing to this programming. Cortisol has been identified as a potential mediator between maternal stressors and the fetus via the intrauterine environment and the infant via breast milk (Bolten et al., 2011; Hinde et al., 2014; Thayer &

Kuzawa, 2014). The interrelationship between maternal characteristics, fasting behaviors, fetal growth outcomes, and postpartum milk cortisol will be further explored to assess whether differences in milk cortisol gives insight into the effects of maternal fasting on birth outcomes and life history strategies.

In this chapter, I describe the study design and methodology used to answer these questions. I first describe the preliminary feasibility study that laid the framework for the present research. To provide additional context for the study design, I also summarize challenges and changes to the original study design and describe the hospital that housed the maternity ward where much of the study took place. I then detail the methodology employed in data collection, along with a brief overview of participants who took part in the study.

Preliminary Feasibility Study

To prepare for this research, I received funding from the Indiana University department of anthropology to conduct a feasibility study in Rabat in August of 2015. During that time, I administered a short survey to lactating women about their breastfeeding practices during the month of Ramadan. The preliminary feasibility study was focused on breastfeeding women rather than pregnant women, which reflects the initial study design for the present dissertation research prior to methodological changes that are discussed further below. Although the phase of maternal investment was altered, the data are still informative for the present study, since similar trends have been found among breastfeeding and pregnant women regarding variables that influence fasting decisions (Ertem et al., 2001; Kridli, 2011; Robinson & Raisler, 2005; Saleem et al., 2010; Van Bilsen et al., 2016).

Participants were recruited from two locations in Rabat: a private obstetrician's office and a public clinic that offers vaccinations and vitamins for infants. Women who brought their infants in for vaccinations were asked by the medical personnel if they had an infant that was under six months old during the month of Ramadan. If so, they were then asked if they were interested in participating in a survey about breastfeeding during Ramadan. Women who were interested in participating were then given an informed consent form, which was read to them by a doctor present if the woman could not read. I administered the survey orally to 21 women in Darija, the local dialect of Arabic. Although the doctors overseeing this project thought it may be difficult to find breastfeeding women who fasted, 81% of participants enrolled in the feasibility study chose to fast. About half of the women who fasted did so every day, while the other half missed 3-13 days due to illness, menstruation, or other cases of vaginal bleeding.

Through the survey, I also gained a better understanding of why women chose to fast or to opt out of fasting while lactating. Women who participated in this survey held different ideas about whether women should fast during lactation and under which circumstances it is acceptable to opt out. Overall, most women felt that if they were able to fast, they should. Reasons women gave that they thought would justify opting out of fasting included receiving medical advice against fasting, if a woman felt fasting was not the right choice for herself, if her family encouraged her to not to fast, or if scientific research demonstrated fasting during lactation would have negative consequences.

For three women, Ramadan occurred within 40 days after giving birth, a time frame during which women customarily do not fast. The other woman who did not fast because prior to Ramadan, she already felt that she was not producing enough milk, a problem exacerbated by working outside the home. She also did not intend to give her infant supplementary foods until six months of age and had educated herself on maternal and infant nutritional needs during breastfeeding.

Maternal fasting decisions are based on several factors, including work-related activities, perceived ability to fast during pregnancy or lactation, education about maternal and infant health, intentions and education about infant feeding practices, and, particularly for lactating women, perceived milk production and changes to milk production resulting from fasting. The aim of the ethnographic aspect of this research project was to further clarify what characteristics are associated with variations in maternal fasting behaviors.

During this feasibility study, I was able to affiliate with Pr. Asmaa Mdaghri Alaoui, who has published on breastfeeding behaviors in Rabat and oversaw this research project locally. She helped develop the connections within the maternity hospital where participant recruitment and most of the research took place for the present study. At that time, I also prepared and submitted the official paperwork to obtain approval for this research through the Centre Hospitalier Ibn Sina de Rabat (CHIS) and from their ethical review board.

Challenges and Changes to the Study Design

The initial study design for this project was altered from a longitudinal study of exclusively breastfeeding women with infants one to four months of age when Ramadan began in order to ascertain whether there were changes in milk hormones and infant growth patterns during Ramadan. This was altered to a primarily cross-sectional study of women who had recently given birth but for whom Ramadan had occurred during their eighth or ninth month of pregnancy. The resulting study assesses the results of fasting on birth anthropometry of the neonate and postpartum breast milk cortisol from approximately three days postpartum.

These alterations from the original study design were made due to several delays in beginning the study and restrictions set by the hospital in recruitment and research sites. There were changes in doctors affiliated with the research and therefore where I had access to recruitment and research sites, along with other administrative details that caused recruitment to be postponed. By the time permission to begin recruitment was granted, it was too late to recruit new mothers from the public maternity hospital, which was my only remaining recruitment site, as they would be recently post-partum at the beginning of Ramadan and still within the 40-day postpartum period in which it is customary not to fast. I, therefore, altered my study design to be suitable for mothers within the maternity ward with newborn infants and extended my recruitment period through Ramadan. These women would have fasted during their last month or second to last month of pregnancy. Therefore, I could retrospectively study the associations between fasting during the third trimester of pregnancy on birth outcomes and postpartum breast milk cortisol post-delivery. This change resulting in recruiting participants throughout the month of Ramadan and the month after and adding a cross-sectional element to the study design.

Although I attempted to retain a longitudinal component in the study design, having access only to patients at the maternity ward of the hospital and the requirement to complete infant anthropometry measurements at the hospital limited the feasibility of follow-up data collection. The patients served at this hospital tended to be of lower socioeconomic class, so many did not have access to phones or other means of contact and lived in more remote areas of the province. Few participants lived near enough to the hospital for it to be practical for them to return for follow-up measurements, which were required to be completed at the hospital. I was permitted to go to women's homes for the purpose of collecting milk samples. This was still exceptionally difficult to arrange, but I was able to visit a handful of participants' homes with guides. Some areas were not generally regarded as safe, and one of my assistant's husband asked male friends to accompany us to some of the locations. Participants' homes were often difficult to find and often did not have addresses. It was just as difficult to find our way back from homes that were deep within old medinas, which can feel like mazes if you are unfamiliar with the area. In both urban and rural areas of Morocco, navigation can be quite challenging, so it was not surprising when many participants said they were unable to explain how to get to their homes to people unfamiliar with the areas where they lived. Neither I nor my local contacts had knowledge of the areas so far removed from the city where many participants lived. The homes were often not accessible by vehicle or public transportation. For home visits that were able to be completed, we typically had to park near a specified landmark and walk for up to an hour. Individual visits usually took several hours. Therefore, very few follow-up appointments were able to be completed within the time frame of the study.

Additionally, the initial intention was to ship the milk samples to Indiana University for analysis. However, the milk samples were only permitted to be shipped to the United States if no lab in Morocco was able to do the analysis. Fortunately, Pr. Madghri Asmaa Alaoui was able to arrange a meeting with Pr. Chabraoui, the chief of service at a public laboratory, who agreed to run the analysis with another researcher, Dr. Nadia Safir. The supplies needed to analyze the cortisol in breast milk were not available within Morocco, and unfortunately, attempts to ship them failed due to difficulties with customs, even though the import permit for the lab kits was issued by the Ministry of Health. Therefore, I transported the kits to Morocco about six months after the data collection had been completed. At that time, the Moroccan lab released to me any samples that had more than one test tube to bring to the United States. This subset of samples was assayed at Indiana University. The lab results of the remaining samples are not yet available.

Description of the Field Site, Maternité Souissi Hospital

The hospital primarily serves lower socio-economic status communities within the larger Rabat-Sale-Kenitra region. This population has a low literacy rate, particularly among females ("CIA: The World Factbook: Morocco," 2014). Poverty is associated with increased average cortisol and cortisol reactivity in mothers and infants (Clearfield, et al. 2014; Thayer and Kuzawa 2014). It is also associated with increased risk of altered fetal and infant growth (Ball, et al. 2013; Karlberg 2006; Layte, et al. 2014), so the effects of maternal fasting in this population may not be generalizable to other populations.

The hospital itself is fairly resource-poor. Several areas smelled bad or looked unkempt and unsanitary. One of the elevators was usually not working, which was problematic when hospital personnel was trying to get hospital patients urgently to other areas of the hospital. Cats would occasionally be sleeping in or running along the hallways of the main floor.

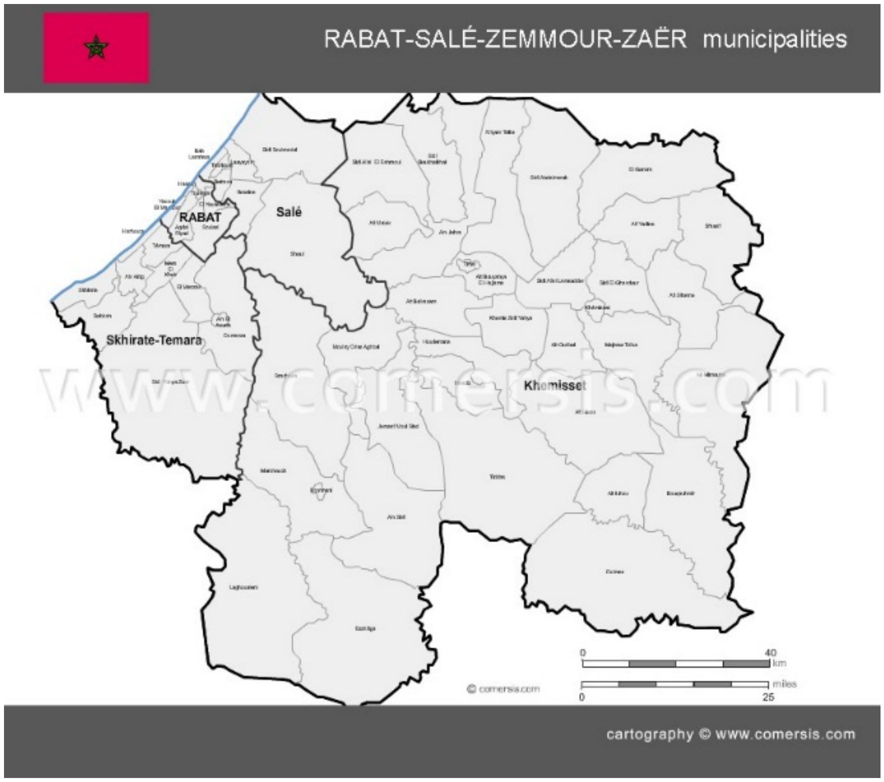

Figure 4.1: Rabat-Sale-Zemmour-Zaer municipalities map (Comersis)

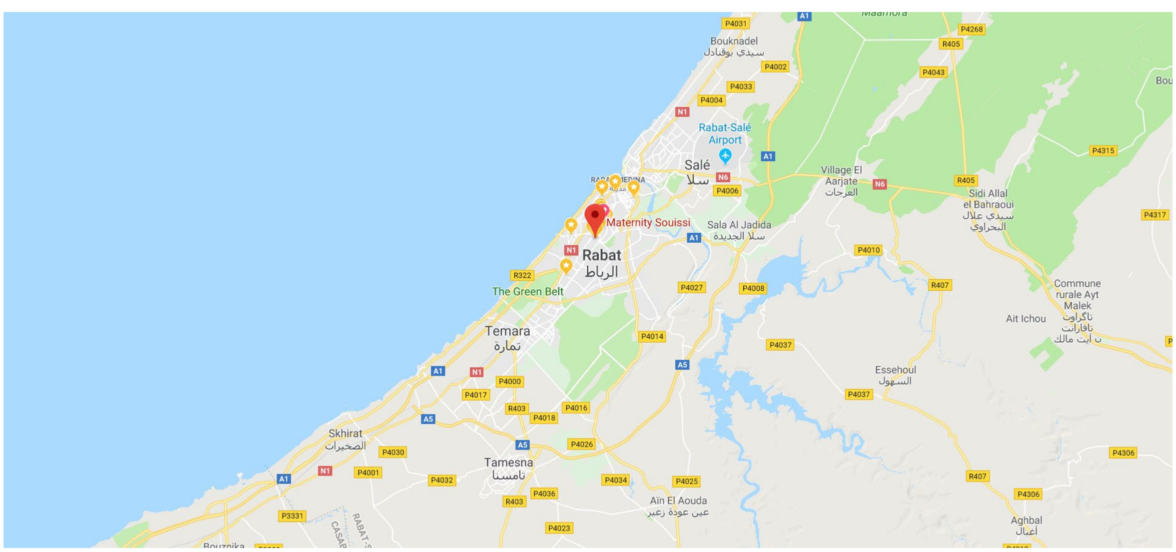

Figure 4.2: Map with Location of Maternite Souissi (Google Maps)

The population that is served by this hospital primarily speaks the Moroccan dialect of Arabic (Darija). Some patients also speak a dialect of the tribal language, locally called Tashlheet or Tamazight, and more widely known as Berber. Some also speak French. The hospital staff speak a mixture of Arabic and French and often switch mid-sentence between the two. Much of the medical training and terminology is in French, and most doctors are fluent in both languages. Some also speak English. Although the fact that doctors and patients generally speak Darija means that there is not an obvious language barrier between doctors and patients. However, with some patients being more comfortable in the tribal language and with the common use of French by the hospital staff, the language barrier may be greater than is readily apparent.

After giving birth, women and their infants were put into rooms with up to six other women. Infants roomed with their mothers and were usually in the beds with their mothers rather than in a cradle. Women whose babies had died during birth were put in the same rooms as women with their infants.

In some rooms, the hospital beds were high off the ground and, having just given birth vaginally or via c-section, patients found it very difficult to get down from them. These rooms had one stepstool per room, and it was too heavy to be carried around by women who had just had a c-section delivery, which is major abdominal surgery. When I entered these rooms to work, my first order of business was usually to move this footstool around several times for women in the room who had been waiting for someone to walk by so that they would be able to get up to get to the restroom.

The electrical outlets were scarce in the room as well, so women often asked for me to bring their phones to them or take them to one of the women whose cot had an outlet nearby. I was also often asked to open and close the window at the end of the room, though this tended to cause some tension between hospital patients. With five to seven women sharing a room, there was little consensus on whether the window should be open. Although some parts of the hospital had air conditioning, these rooms did not. During the hot summer, the rooms could get stifling hot. Even when the rooms were stifling hot, infants were often dressed in heavy clothing and blankets and were sweating. I do not know how regularly infants' temperatures were checked. Some of the rooms did not have trash cans and the rooms that did only had one tiny one at the end of the room. The cleaning staff cleaned the floors often, but a lot of trash and dirty diapers ended up on the floor between cleanings.

Figure 4.3: Courtyard of Children's Hospital, Connected to Maternity Hospital

There was little to no patient privacy in these rooms. No barriers were put up between other patients when one was being given an exam or when maternal or infant health concerns were discussed. Medical concerns did not appear to be considered a very private matter. For example, I remember one woman (not a participant) had been in the hospital longer than the usual time span for giving birth, and the other women in the room readily told me that she had to stay longer in the hospital due to having chlamydia.

Eating patterns after a c-section also impacted breastfeeding and consequently the collection of milk samples. Women said they were told by their doctors that they could not eat anything until after they had passed gas, in order to prevent surgery-related gas pain. They also often said they would not and could not breastfeed until they ate. This was often days after delivery. For reference, in the US, it is typical to recommend easily digestible, soft foods, and broths after a cesarean section. When I asked doctors at this hospital about the reason for the recommendation, they said that if women were not compliant when told to follow a restricted diet. When they tell them they can eat, they eat the heavy foods that are culturally prescribed during the postpartum period. Since these traditional postpartum foods tend to make surgery-related gas pains worse, doctors tell women that they cannot consume anything but water.

I observed several instances that led me to believe that the hospital puts a low priority on keeping women together with their infants and a low priority on breastfeeding in general, especially when the infant is sick. Women whose infants had to be in the neonatal care unit rather than with their mothers were on another floor, in another area of the hospital, so visiting infants was difficult. Women were also not given much information about how to see their infants if they were separated from them. When I inquired for one woman about whether or not she could pump and have her family bring the breast milk to the infant, only then did the medical personnel tell her she could go see her infant if her family would take her during visiting hours.

One woman in the study who only took the questionnaire did not continue with the study due to not having been reunited with the infant. The infant was born at 36 weeks and was kept in the clinic for breathing complications. They were separated the whole time.

A representative from a formula company was given access to the mothers in their rooms. She always shut the door behind her and would tell women why they should buy powdered formula. Participants reported on this during interviews, and I saw one representative several times but was not certain that was what she was doing until participants told me (as the representative would not tell me when I asked). I'm also not certain if there were multiple representatives or only the one I saw repeatedly. The doctors and staff in the hospital were aware of this and would often complain that these representatives would write fake prescriptions for infant formula. They would sometimes rip these up and tell the mothers that they didn't need formula, but they did not stop the representative from entering. Upon discussing this situation with the chief of service of one of the floors, she expressed interest in trying to work with the World Health Organization and their International Code of Marketing Breast-milk Substitutes.

Several women in the hospital had breast pumps with them, but the only pumps I saw were bulb-style pumps, a.k.a. bicycle horn breast pumps. These pumps are inexpensive, but they can cause trauma to the nipple and breast (observed in one participant), can easily become contaminated due to difficulties cleaning and are not efficient to use (WHO, 2009). Their inefficiency is particularly important if women are relying on pumping for the majority of breastfeeding, such as might be the case when infants were separated from their mothers.

Over the course of the study, I employed the assistance of translators and research assistants, particularly during the informed consent process, interviews, and follow-up calls. Occasionally doctors and nurses assisted with the neonatal anthropometry as well. During follow-up calls, one of my translators and I learned that one participant in the study had to take her infant back to the hospital for a fever when the infant was six days old. The infant had to stay in the hospital for four nights. Up until that time, the infant was breastfeeding well and exclusively, and the mother had intended to continue to breastfeed exclusively for four to six months. The hospital must give formula to the infants during their stay because they limit the mother's visiting hours so much that exclusive breastfeeding is not practical. The hospital rules keep visiting hours of mothers to four or five hours in the afternoon, but at the beginning of the infant's hospital stay, the rules were not enforced, and they allowed mothers to go see the infants starting at 10:00 or 11:00 AM and stay until about 8:00 PM. Even then, with over 14-hour breaks in breastfeeding, exclusive breastfeeding would be nearly impossible to maintain in the absence of proper pumping equipment, milk storage equipment, and motivated medical staff.

Unfortunately, during the course of this infant's stay, another infant was taken from the neonatal unit without the hospital's consent, though it was believed that the infant was taken by its mother. Due to this, this unit of the hospital began strictly enforcing the visitation rules. One morning after the rules were enforced, I found the infant's mother waiting with a group of other mothers sitting on an uncomfortable bench down the hall from the neonatal care unit. They had all arrived at 10:00 AM to see their sick neonates, only to find they would have to wait several hours before they were allowed in. It was heartbreaking. During a follow-up with the mother four days after the infant was out of the hospital, she was struggling to breastfeed and found she had to give a lot of formula.

Breastfeeding support was lacking on the floors I was able to work on, although one floor of the hospital had more support regarding educating patients of the importance of breastfeeding and providing breastfeeding assistance. I had completed a lactation consultation certification course prior to beginning fieldwork for multiple reasons. It helped me prepare to implement my methodology for this research, but the certification and credentials also allowed me more credibility with expertise from a program related to nursing. I also recognized that the training might allow me the skills to provide a service to study participants if they struggled with breastfeeding, which did occur during the study. I was able to provide several participants with breastfeeding support throughout the course of the study. For example, I remember one young participant had been waiting for her mother to visit before she began breastfeeding. She did not feel confident about trying it herself. Since she had not initiated breastfeeding by two days postpartum, she did not intend to give a sample. However, my research assistant and I helped her initiate breastfeeding. We also were able to help a woman who had been struggling with getting her infant to latch due to inverted nipples, another who had damaged her nipples with a bicycle breast pump, women who were having problems with engorgement, and others who were struggling to position the infants due to pain from their c-section incisions. Based on these observations of infants and mothers being separated and in the difficulties patients at this hospital had in breastfeeding, increased importance placed on keeping mothers and infants together and on breastfeeding support would clearly benefit patients at this hospital.

When I explained my research to doctors prior to implementing the study, they consistently told me that I would not find participants because they did not believe women would be fasting if they were pregnant or breastfeeding. However, given that my feasibility study, the current study, and various other studies have tended to find that women often chose to fast in these circumstances. Given how closely the doctors work with this population, it is unclear why the medical personnel do not recognize what a large proportion of women fast during pregnancy and breastfeeding. It is possible that fasting decisions are largely shaped by socioeconomic class in this region since the doctors at this hospital are typically from a higher socioeconomic class than the population they serve.

In the feasibility study, some women said that they felt they should fast unless told otherwise by a doctor. However, in discussing this with doctors, they made it clear that they did not feel it was their place to say, barring a medical condition. I was told by more than one doctor that women who thought they were required to fast do not understand the religion.

Methods

Population and Participant Recruitment: This study took place in Rabat, the capital of Morocco, at the public maternity hospital that serves the Rabat-Sale-Kenitra region. Morocco is an ideal location for this research, as it is a Muslim country, In addition, due to the latitude of the country and the fact that Ramadan overlapped with the summer solstice at the time of the study, daily duration of fasting extended to over 16 hours during the time of the study. As it would be predicted that more pronounced outcomes of fasting during pregnancy would be observed when fasting duration is longer, it is an ideal time to conduct this research in this region of the world. I further chose to do this research in Morocco due to my familiarity with the country after having served as a Peace Corps volunteer there from 2009-2011. This research also required a setting in which maternal fasting is common. My experience living and working in the country led me to believe that a large percentage of pregnant and nursing women fast during Ramadan, an observation that is supported by studies of other Muslim countries in the MENA region and in other areas of the world (Ertem et al., 2001; Joosoph et al., 2004; Mubeen et al., 2012; Ozsoy et al., 2014; Robinson & Raisler, 2005; Saleem et al., 2010). The nature of this researched required it to be set in a large city with a research hospital that had a high patient capacity. Although I worked in a rural area in the Middle Atlas Mountains, Peace Corps headquarters is located in Rabat, so I was well-acquainted with the city. Rabat was also an ideal location due to the large size of the city with hospitals with well-established processes for research. The hospital in which this work was conducted is associated with a university where research is regularly carried out.

This study was conducted from May to July of 2017 when Ramadan fasting lasted about 16 hours each day. Women who gave birth in the maternity hospital between May 30th and July 21st were recruited one to three days after delivery. Women were recruited from two areas of the hospital that were primarily devoted to mothers and infants without serious health concerns. There were some patients in these areas with common maternal health conditions, including gestational diabetes and hypertension. If infants needed observation or treatment, mothers stayed in this area and infants were kept in the neonatal unit.

Since many patients at the hospital were not literate, all recruitment was completed with a translator to ensure complete understanding of the informed consent documents. All mothers who agreed to participate in the study signed two informed consent documents, one approved by the

IRB at Indiana University and another from the ethical review board for research at the hospital, which was through Université Mohammed V and Faculté de Médecine et de Pharmacie in Rabat.

Both women who had fasted and who had not fasted during the month of Ramadan were included in the study. Women with twins were excluded from the full study, but during the initial phase when only questionnaires were administered, this exclusionary criterion was suspended. Initially, the study sought only participants who were exclusively breastfeeding while in the hospital. However, due to the high rate of supplemental feeding while in the hospital, this requirement constrained the potential sample size and was dropped early in the study. One woman with twins was enrolled during this time.

Participation was limited to women who would be at the hospital for at least 48 hours after delivery, which was primarily women who had given birth by cesarean section (c-section). The reason for this inclusion criteria was due to the amount of milk requested for the donation compared to typical postpartum breast milk production. Mothers were asked to donate 2-4 mL of breast milk if they felt they were able. Milk production averages about 30 mL within the first 24 hours post-partum and increases thereafter. In order to take a negligible percentage of total milk production, milk samples were not taken until at least 48 hours after birth. Due to hospital regulations, most women who give birth vaginally are released after 24 hours. Women giving birth by c-section are required to stay for at least 72 hours, and therefore, most women eligible for participation were those that gave birth by c-section. The first seven participants enrolled in the study were only asked to take part in the questionnaire while the approval from the Indiana University IRB was pending for changes to other parts of the study design. These seven women had given birth vaginally. Otherwise, only one participant gave birth vaginally and she completed all portions of the study. Scheduled c-section deliveries have been associated with reduced maternal cortisol, but this is likely due to labor not being initiated naturally since the natural initiation of labor is characterized by a dramatic rise in cortisol (Stjernholm, Nyberg, Cardell, & Höybye, 2016).

It was not assessed whether labor had been initiated at the time of the c-section, but most c-sections were not scheduled. Therefore, it is likely that labor had been initiated naturally in most cases.

As previously noted, women often shared rooms with up to six other women, although there were some rooms with fewer patients. The number of women in a room affected participation. Often, if the first woman in the room decided not to participate in the study, the rest of the women also declined. However, if the first woman agreed to participate, other women were more likely to agree as well. If one woman changed her mind, many others in the room also changed their mind. Some women changed their minds about participation after seeing that infants were partially undressed when taking the neonatal anthropometry measurements since many women were opposed to removing any of the infant's clothing. Literacy was also important. If one woman in the room was literate and the rest were not, typically she was the deciding person for the whole room. Other times, families made the decision. A woman might enroll in the study but after her husband or mother had visited, they would decide she should not participate. Sometimes, this trend reduced participation rates. At other times, there was an advantage in having several women in a room for increased enrollment. If some women in the room were not sure about participating in the study, after they observed what other participants were asked to do, they also wanted to participate.

As I was not able to predict who might be most receptive to participation, it was difficult to strategize how to best approach the participants. The only note I can make is that it was best if my translator and I talked to the women about participation first when no medical personnel was present. If the medical staff asked women, they almost always said yes initially but often changed their minds when I discussed it with them later. Being asked by a doctor or having a doctor present may have made them feel compelled to participate, which may have made them feel less comfortable with the study. Alternatively, they may have been under the impression that it was part of the hospital procedure because a doctor was present. When they realized it was not being done by a doctor, perhaps they were not interested. Of course, there are several possible reasons for this trend that could be speculated, given the position of power doctors are often in and given my position as a foreign researcher.

Ramadan was ongoing during the first half of the recruitment period, so women who gave birth before Ramadan was over would not have had the opportunity to fast the full 29 days. Women who did fast but gave birth between June 26-July 23rd had the opportunity to fast for the whole month of Ramadan and had a number of days of non-fasting between the end of Ramadan and delivery. This was accounted for in the data analysis and is discussed later.

Data Collection

Data was collected from various sources. Methods of data collection will be detailed in the following sections. Within 72 hours postpartum, data collected at the maternity ward included a questionnaire administered at the time of enrollment, maternal anthropometric measurements, neonatal anthropometric measurements, and a sample of postpartum breast milk. Some of this data was obtained from the participants' medical charts, including maternal height, the infant's weight at the time of birth, and estimated gestational age. I took all the other anthropometry measurements. Within six weeks after giving birth, participants who were available for follow-up calls or appointments also participated in follow-up questionnaires. Some additionally participated in follow-up neonatal anthropometric measurements and gave an additional maternal milk sample. If participants were not available for follow-up appointments but had a weight taken at a clinic, this was recorded. Additionally, within the day to day context of my research, I had several informal conversations and interactions with doctors and other hospital staff. I drew on information gleaned from these discussions at times when it provided relevant context and background information.

Table 4.1 lists the number of participants completing each portion of the data collection. All participants completed the questionnaire, which included 92 participants, although some did not participate in other aspects of the study for various reasons. The first seven study participants were only asked to complete the questionnaire while modifications to the rest of the study design were pending approval. Some participants also changed their minds about participating after completing the questionnaire. Data from medical charts may be missing if the participant changed their mind about participation after taking the questionnaire but before data from the chart was recorded.

Maternal anthropometric measurements were taken for 73 participants and neonatal anthropometric measures were taken for 75 infants, and 72 mother-infant pairs have maternal and neonatal measurements. Maternal anthropometry was not available for some participants because some did not want to stand, as they were often only a few days post c-section surgery and some were experiencing pain and/or dizziness. Most were able to get up and walk around and agreed to participate but were always encouraged to opt out if they felt unable to stand.

Some infant anthropometric measurements were also missing. Mothers often did not want their infants to have their clothes off, regardless of the temperature of the room. Newborn infants have a difficult time regulating their own body temperature, and cultural practices in Morocco have developed around keeping a newborn warm. However, many infants were wrapped in multiple heavy layers, even in the intense heat of summer, and infants were often perspiring. One of my research assistants also refused to ask women if their infant could be undressed for the measurements and often told me she would not allow me to take any infants clothing off for measurements. However, when working with doctors and nurses at the hospital or with other research assistants, no others took issue with asking. When the mothers declined, this was respected and as many measurements as possible were taken given the constraint of the clothing. Most mothers consented to have enough clothing removed to complete some or all measurements, but arm circumference and skinfold measurements were not possible to take in some cases. Also, one woman decided after completing the questionnaire that the only additional part of the study she wanted to complete was the infant weight, so all other data are missing for that participant. Due to the clothing that remained on the infants during the measurements, neonatal weight was likely overestimated. The estimated weight of the clothing is adjusted for in the analysis and is discussed below.

Some women did not give a milk sample for various reasons. Some tried but could not. Some had not initiated breastfeeding, which was common for women who had not eaten in the days since the delivery per doctors' orders. Some were experiencing breast pain or did not know how to position their infants so as not to aggravate their c-section stitches. Different participants were able to complete different portions of the study, so the number of participants who completed all parts was reduced.

Additionally, there were four infants born preterm and one set of twins enrolled in the study. One participant had twins (a male and female), but this participant only completed the questionnaire portion of the study. Four mothers, including the mother with twins, gave birth prior to 37 weeks gestation. Of these participants, three only completed the questionnaire, and one woman, who gave birth at 36 weeks gestation, also completed maternal and neonatal anthropometric measurements but was unable to provide a milk sample. For one mother that gave birth at 35 weeks, maternal height was recorded but no other maternal anthropometric measurements. These participants are removed from some analyses when appropriate.

Table 4.1: Number of Participants Completing Each Portion of the Study

Total Participants	**N**
Questionnaire	92
Neonatal Anthropometry	75
Maternal Anthropometry	73
Gave Initial Milk Sample	63
Follow up questionnaire	39
Second infant anthropometry	16
Second infant anthropometry by the researcher	8
Gave a second milk sample	9

Questionnaires and Medical Chart

Enrollment Questionnaire: Upon enrolling in the study, participants were given an enrollment questionnaire, which was administered orally 24 to 72 hours after giving birth and is available in the Appendix. This included information regarding the mother, including health during pregnancy, fasting behavior during Ramadan, number of previous children, and supplemental feeding practices in the hospital, along with intended feeding behaviors in the first six months. There were also questions to help assess maternal vitamin D status through questions about dress and vitamin supplementation. The questionnaire also included questions about the infant, including date and time of birth, sex, estimated gestational age at birth, and health status.

Ninety-two mothers completed this questionnaire, which was administered orally upon enrollment. Some information for the questionnaire was obtained from patient medical charts, including date and time of birth, gestational age if available, infant weight at birth, maternal height, and maternal reproductive history. Infant birth weight was available for 87 singleton infants and for the one set of twins. An estimate for gestational age was available for 60 newborns; for other infants, the doctors recorded whether they believed the infant was born at term or preterm but did not make an estimate on gestational weeks at birth.

Follow-Up Questionnaires: When possible, contact information of the mother was recorded if she agreed to be contacted to answer follow-up questions over the phone. Questionnaires were orally administered during a follow-up session on the phone or in person. Women were asked whether they were still breastfeeding if they were supplemental feeding and if so, with what, how their experience of breastfeeding has been going, if she and the infant had been healthy since leaving the hospital, and if they had any additional infant measurements from doctor visits. The follow-up questionnaire is available in the appendix. Thirty-nine women participated in a follow-up questionnaire.

Maternal Age and Anthropometry

The Tanita Ironman Body Composition scale was used approximately 72 hours postpartum to measure maternal weight, body fat percentage, and lean body mass, along with other measurements via bioelectric impedance. Age and height were manually entered to set up the Tanita scale for each participant. Age was reported by the participant. Maternal height was typically measured by the hospital upon check in to the hospital, but when this was not available, I took this measurement. It was taken from the record whenever possible to reduce the burden on participants who had recently given birth. Seventy-three women participated in this portion of the study. Of those that did not participate, four additionally provided their age and seven provided their height.

Neonatal Anthropometry

Anthropometric measurements were taken for each newborn, within 48-72 hours postpartum. Measurements included weight, length, head circumference, mid-arm circumference, and triceps and subscapular skinfolds. Weight was measured using a portable scale. Length was measured with an infant measuring mat. Head and arm circumference were measured with a retractable tape measure for body measurements. Skinfold measurements were taken using high-quality body fat calipers. All measurements were taken at least twice when possible, although some measurements were taken only once if mothers were anxious to redress the infant or if medical personnel required the mother or infant. Seventy-five infants participated in neonatal measurements, but some measurements are missing for six of these infants. Additionally, eight participants participated in follow-up anthropometry within six weeks postpartum, following the same methodology. Given the small sub-sample of follow-up participants, this data will not be used.

As discussed previously, neonatal weight measurements were usually taken with clothing on the infant as many mothers were opposed to taking off infant's clothing for the anthropometric measurements. Most women allowed the outer layers to be removed and allowed the hat and socks to be removed for the length measurement. Due to this, there is a degree of error to be expected for the infant weight measurements and, for some infants, certain measurements are missing. Almost all infants were wearing diapers, which weigh approximately 16 g, and a short-sleeved or long-sleeved onesie, which weight approximately 37 g. One newborn sleeper was tested to weight 82 g, but it was uncommon that the sleeper was not allowed to be removed, so this was not included in the adjustment. A onesie and diaper are predicted to increase an infant's weight by about 53 g. This was adjusted for in calculating z-scores and the ponderal index, but not when using the raw data, with the assumption that the margin of error would be evenly distributed.

Both birth weight, as recorded by a doctor at the time of birth, and the neonatal weight, which I collected 48-72 hours postpartum, were used in calculated ponderal indexes and weight z-scores. Ponderal Index is calculated as weight divided by length cubed and is a measure of infant leanness. Z-scores for birth weight, neonatal weight, length, and head circumference were calculated based on averages and standard deviations previously published from the same maternity hospital for infants born at 37-42 weeks gestational age, which includes different equations by infant sex. Gestational age was to calculate z-scores for full-term infants for the subset of infants with that information available based on the total average and standard deviations for each sex by gestational age provided by Radouani et al. (2015).

Milk Samples

Milk Collection: Initial postpartum breast milk samples were given at the maternity ward with the intention of collecting the sample when the infant was approximately 48 to 72 hours postpartum, although in three cases the first sample was collected after 72 hours (see Table 4.2). Follow-up samples were collected either at the hospital if the mother was able to return, or at the woman's home, when I was able to travel to visit her there.). Breast milk transitions from postpartum breast milk to transitional milk around five days postpartum and to mature milk approximately 15 days postpartum (Sala-Vila, Castellote, Rodriguez-Palmero, Campoy, & López-Sabater, 2005). Although most initial milk samples would be considered colostrum and most follow-up samples were within the mature milk stage, some milk samples were taken within the possible transitional stage both for the initial sample and for the follow-up sample. Therefore, the first sample will be referred to as initial samples or postpartum breast milk to distinguish it from the follow-up breast milk samples.

For all initial and follow-up samples, milk was collected by mid-feed manual expression in the morning between the hours of 8:00-11:00 AM (Miller et al., 2013). To note, Morocco suspends daylight savings time shift for Ramadan, so a time shift occurred in the middle of the study, and hospital schedules were adjusted accordingly. When possible, women were asked to give the sample when two hours or more had passed since the last time they breastfed from the sample breast. The sample breast was identified as the opposite side as the woman's dominant hand, unless there was another reason to use one breast or the other, including nipple pain. For the follow-up sample, the same breast was always used as the sample breast as had been used for the initial sample. Women were asked to breastfeed the infant for 2.5 minutes prior to beginning the milk collection to ensure letdown. If milk flow stopped, the infant was put back to the breast for 30-60 seconds before beginning to collect milk again. Women who were able to donate milk were asked for 2-4 mL for the initial sample and 4-7 mL for the follow-up sample. When the sample was taken, I recorded the time the sample was taken, which breast it was taken from, the time of the last breastfeeding session from each breast, the time the mother woke, the milk volume collected, and whether the infant was offered the breast again after the collection.

Seventy-four women tried to give an initial milk sample, but 11 were unable to for various reasons, including being unable to manually express milk and struggling with infant latch, resulting in sixty-three participants who were able to give milk samples. Forty percent of women were able to produce 4 mL for the sample, 29% donated 0.75-1 mL, and the remainder of the women donated at least 2 mL of milk. Nine women were able to provide a second milk sample, one of whom gave samples on two separate occasions. Details about the samples are summarized in Table 4.2.

Breast Milk Cortisol Analysis: Samples were frozen and stored at -80 °C at the Ibn Sina Laboratory in Rabat, a public laboratory associated with the maternity hospital. In March 2018, I returned to Rabat and, for all samples that were large enough milk sample to fill two test tubes (>1.5 mL), I transported the second test tube to the Primate Environmental Endocrinology Lab at Indiana University. This included forty-three initial samples and ten follow-up samples. These samples were transported in a cooler packed with ice via plane as checked luggage and then by car. Some samples did begin to thaw but no samples thawed completely during transit. At the Primate Environmental Endocrinology Lab, samples were stored here samples were stored a -20 °C until analyzed for cortisol content.

Cortisol concentration was measured using Enzo's Cortisol ELISA kit, which had been used to assay breast milk cortisol in a previous study (O'rourke et al., 2018). After an initial test at the lab at Indiana University, it was determined that neither extraction nor dilution of the samples was necessary since the concentrations were within the appropriate range for the kit and there was not a discernable matrix effect. Samples were clarified (or defatted) to prepare them for analysis by centrifuging them at 10,000 rcf for 15 minutes, pipetting the middle aqueous layer into another centrifuge test tube, discarding the top layer of fat and the bottom protein pellet. This was repeated twice, and the samples were centrifuged a third time. If there remained a top fatty layer, the aqueous layer was again pipetted out for use in the assay. If there was no remaining fatty layer, the sample was used directly in the assay. After preparing the samples, the Enzo kit instructions were followed. Samples were run in triplicate. Some samples were very high in cortisol and were too high to be read given the standard curve. These samples were diluted in a 1:5 ratio and assayed again. Cortisol concentrations of samples analyzed at the Primate Environmental Endocrinology Lab are summarized in Table 4.2, which included 43 initial samples and 10 follow-up samples. As one woman gave two follow-up breast milk samples, the samples from the other eight women were summarized once with her first follow-up sample and once with her second follow-up sample.

Table 4.2: Summary of Breast Milk Samples, Initial and Follow-Up

Initial Postpartum Breast Milk Sample Donated in Hospital	**N**	**Mean ± St Dev. (Range)**
Amount of Milk Donated (mL)	63	2.7 ± 1.3 mL (0.75-4.5 mL)
Days Postpartum	63	3.0 ± 1.0 (2 - 9*)
Follow-Up Breast Milk Sample (First or Only)		
Amount of Milk Donated (mL)	9	5.9 ± 2.2 (3-10)
Days Postpartum	9	24.2 ± 8.5 (10 - 36)
Follow-Up Breast Milk Sample (Last or Only)		
Amount of Milk Donated (mL)	9	5.9 ± 2.2 (3-10)
Days Postpartum	9	26.6 ± 8.8 (10 - 37)

*Three initial milk samples were given by participants after 3 days post-partum. These were taken at 5, 6 and 9 days postpartum.

Overview of Data Analysis

Data Analysis: In Chapter 5, the determinants of maternal fasting behaviors are assessed. Chapter 6 includes an analysis of neonatal anthropometry in relation to maternal fasting behavior.

Chapter 7 includes an analysis of postpartum breast milk cortisol for its relationship to maternal fasting. A detailed discussion of specific data analysis methods is available in each results chapter. Data analysis was completed using StatalC10 and StataSE15.

Sharing of Data Analysis with Study Participants, Individuals Involved in the Research and Research Site: Preliminary results were shared with researchers at the hospital and laboratory, and a full analysis of the results will be shared upon completion. Research assistants were provided with an overview of the results of the study. Results of the study were hoped to be shared with participants as well. However, many participants did not have phone numbers to contact them of those that did, only a few were still in service when attempting to call them. Therefore, only a handful of participants were informed of the study results.

Chapter 5: Determinants of Maternal Fasting Behaviors

One objective of the present study was to investigate the determinants of maternal fasting behavior. This is critical before making analyses of pregnancy and birth outcomes associated with maternal fasting, as observed pregnancy outcomes may be due to differences in maternal characteristics rather than effects of fasting per se. In this chapter, I analyze various biological, cultural, and environmental characteristics as potential determinants of maternal fasting behaviors.

Several variables have been associated with maternal fasting behavior in previous studies, including familial support (especially the opinion of the husband), maternal anthropometry, health concerns, and parity (Ertem et al., 2001; Joosoph et al., 2004; Mubeen et al., 2012; Saleem et al., 2010; Van Bilsen et al., 2016). The effect of medical advice on fasting behavior is unclear. In Iran, about 85% of pregnant women report that they take medical advice about fasting seriously (Firouzbakht et al., 2013), but a study in the United States, medical advice against fasting was not often taken, and participants discussed being unconvinced of risks associated with fasting (Robinson & Raisler, 2005). In the US, doctors often did not share the patients' religious and cultural backgrounds, and this divide between patient and doctor may have also played a role in patient perception of medical advice. In the general population in the United Arab Emirates, the role of medical advice in fasting has not been found to be predictive of abstaining from fasting (Bachar et al., 2017). I have not seen previous studies including vitamin intake as a predictor of fasting. However, it was included here as it may indicate variation in education or awareness about the importance of micronutrients during pregnancy, attention to prenatal health and engagement in risk reduction strategies, access to medical advice, and access to financial resources considering the cost (Cheng, Mistry, Wang, Zuckerman, & Wang, 2018; Gonzalez-Casanova et al., 2017; Nisar, Dibley, & Mir, 2014). Infant feeding intentions may also be related to maternal perceptions of energetic resources and therefore were considered as well.

Data Analysis

Data collection methods were detailed previously in Chapter 4. Fasting behavior was the outcome of interest in the present data analysis and was quantified in three ways: the number of days fasted, non-fasting versus any fasting, and some or no fasting versus daily fasting as outcome variables. Several maternal characteristics were considered for their predictive value for each fasting outcome variables. These independent variables were divided into two categories: biological characteristics and cultural and environmental characteristics.

For each fasting variable, univariate analyses were run with each independent variable, and then all variables found to be significant were added to multivariate regression. In the univariate analysis of the number of days fasted, maternal characteristics were assessed for their predictive value using pairwise correlations for continuous variables and student t-tests for binomial variables. Two-tailed p-values were used in the tables unless previous research suggested a one-tailed t-test was appropriate, and if so, this was noted. For non-fasting versus any fasting and some or no fasting versus daily fasting, univariate logistic regressions were used to identify associated maternal characteristics. Maternal anthropometric measurements were expected to be interrelated, so all anthropometry variables were collectively added to a stepwise multivariate model for each outcome variable, except for BMI so as not to include BMI and weight together in the model.

Variables significantly associated with fasting in univariate analyses were then added to stepwise multivariate regression. Linear regression was used for the number of days fasted and logistic regression for the categorical outcome variables. Significance level was set at $p<0.05$; however, for the purpose of identifying potentially confounding variables, any variable that was significant at the 0.10 level in the univariate analysis was included into the stepwise multivariate analyses. The stepwise model significance level was set to 0.2, with variables that have over a 0.2 p-value removed from the analysis.

Although the original intention for the study was to omit participants with health conditions that may confound the results, including diabetic women, this recruitment plan omitted a significant portion of the population. The prevalence of both Type 2 and gestational diabetes in this population is believed to be around 12% (Utz et al., 2017). In this population, it was evident that pregnant women with this condition must navigate a cultural environment in which maternal fasting during pregnancy is the norm, so the experience of Ramadan for this portion of the population deserves attention. Therefore, women with common health conditions were included in the study. A risk of including diabetic women in this data analysis was that diabetes could overshadow other variables that influence fasting decisions. To account for this challenge, the analyses were run on the subsample of non-diabetic women. Variables that became significant were discussed and included in the multivariate models.

Participant Overview

In this chapter, I analyzed potential biological determinants of maternal fasting, including reproductive history, age, anthropometry, and maternal health, and potential cultural and environmental determinants, including advice received from family about fasting, medical advice about fasting, vitamin intake, style of dress, infant feeding intentions, and reported experience of stressors during pregnancy. Infant sex was also considered with cultural variables, although it was not assessed whether women knew the sex of their infant before birth. These participant characteristics are summarized in Table 5.1 and Table 5.2.

Table 5.1: Overview of Participants

Overview of Maternal Characteristics (N=92)		
Reproductive History	**N**	**%**
Primiparous	35	38%
Multiparous	57	61%
Primigravida	32	36%

Multigravida	58	64%
History of Miscarriage	19	21%
Maternal Health		
Reported one or more complication during birth (including breech and premature membrane rupture)	9	10%
Reported one or more health concerns during pregnancy	51	55%
Diabetes	6	7%
Hypertension	8	9%
Diabetes and/or hypertension	11	12%
Anemia	22	24%
Other (such as exhaustion, fainting, hypotension, bleeding)	29	32%
Family Advice About Fasting		
No Advice or Neutral Advice	57	63%
Advised to Fast	3	3%
Advised Not to Fast (Not Resulting from Advice from Doctor)	25	28%
Advised Not to Fast (Family Advice Attributed to Advice of Doctor)	5	6%
Medical Advice About Fasting		
Doctor Advised Against Fasting	9	10%
Vitamin intake		
Any Vitamin	78	85%
Other (including vitamin D, multivitamin, folic acid, and/or magnesium)	18	20%
Style of Dress/ Sun Exposure		
More Traditional Conservative, Less Sun Exposure	74	82%
Less Conservative, More Sun Exposure	16	18%
Infant Feeding Intentions		
Intended to Exclusively Breastfeed	50	64%
Intended to Breastfeed and Give Water and/or Vervain Tea	16	21%
Intended to Give Formula	12	15%
Reported Stressors During Pregnancy		
Yes	8	9%
Infant Sex		
Male	48	54%

Maternal Biological Characteristics

Maternal biological characteristics assessed for their relationship to maternal fasting included reproductive history, age, anthropometry, and health. Reproductive history and health characteristics are summarized in Table 5.1. Sixty-one percent of the sample was multiparous and 64% was multigravida. Twenty-one percent of the sample had one or more previous miscarriages.

Fifty-one participants (55%) reported any maternal health concern during pregnancy. Anemia, hypertension, and diabetes were the most commonly reported health conditions. Due to the low incidence of any other health condition being reported, all others were combined into one category for analysis.

One woman had Type 1 diabetes, another woman had Type 2 diabetes, and four women developed gestational diabetes. Three diabetic women fasted (one of whom also had hypertension) and three did not. One woman only found out about her diabetic status in the last week of her pregnancy, after Ramadan had completed; she fasted all 29 days of Ramadan. She may not have had gestational diabetes at the time, and since her knowledge of her diabetic status did not play into her decision-making regarding fasting, she was excluded the group of women who had diabetes for this analysis. The women who did not fast all cited their diabetic status as the reason for not fasting. Of the three who did fast, one woman fasted for three days and stopped due to medical advice. The other two women did not fast the whole time, one fasting for 27 days and skipping two days and the other fasting for 22 days and skipping seven days, but on these days, they only drank water and did not eat during fasting hours.

Of the eight women with hypertension, five fasted and three did not. The three who did not fast said that their decision was due to having hypertension, and one of these women said that her decision was due to the need to take medication for hypertension, rather than the condition itself. Of those who fasted, three fasted every day of Ramadan that passed prior to going into labor, which was only two days for two of the women, who went into labor at the beginning of Ramadan, and the other woman gave birth after Ramadan and fasted the full 29 days. One woman fasted for 17 days and stopped for the last six days prior to labor. The other woman also had diabetes and fasted for 29 days from food, but for seven of the days, she fasted she did consume water.

There was some overlap between women with diabetes and hypertensive disorders, which is not surprising considering that diabetes and hypertension have similar risk factors. Of the six women who were diabetic and eight women who had hypertension, three had both. Eleven women, therefore, made up the group that had either or both diagnoses. Due to the overlap and similar risk factors for both, these groups were combined when appropriate.

Iron-deficiency anemia was the most prevalent health concern among participants, as 24% of participants reported being anemic when asked during enrollment. Of the 22 women who had anemia, four did not engage in any fasting. Of the women who did not fast, none cited anemia as their reason for not fasting. Being anemic was given as a reason for not fasting every day of Ramadan that passed before going into labor, but anemia was not used as a reason not to fast at all. Of the 18 women who fasted, fasting ranged from 2 to 29 days and averaged 22.8 days. Ten anemic women fasted every day of Ramadan that passed before going into labor, which was two days for one woman who gave birth at the beginning of Ramadan, and 28-29 days for other 9 women who gave birth at the end of or after Ramadan.

Thirty percent of participants noted a health problem other than hypertension, diabetes, or anemia. These health concerns included hypotension, exhaustion, fatigue, bleeding, and, for one participant, being a smoker. Due to the small sample size and the low number of participants reporting other conditions, these were grouped into an “other” category.

Age and anthropometric variables were collected for a smaller subset of participants. Maternal age, height, weight, BMI, and body fat measures were collected 48-72 hours postpartum and are summarized in Table 5.2. Age and anthropometry ranged widely in this sample.

Table 5.2: Overview of Maternal Anthropometry

Maternal Anthropometry	N	Mean (Range)
Age	77	30.6 (18-45)
Height (cm)	79	159.1 (147-175)
Weight (kg)	73	69.1 (45.5-109.6)
BMI	73	27.2 (17.9-42.4)
Body Fat (%)	72	33.3 (13.1-50.1)

Cultural and Environmental Characteristics

Cultural and environmental characteristics that were considered for their relationship to the number of days spent fasting included family advice, medical advice, vitamin intake, style of dress, infant feeding intentions, and reported stressors (Table 5.1). Family advice on fasting was predicted to influence maternal fasting behaviors. When asked if participant's families gave advice on whether to fast, not to fast, or no specific advice, most (63%) participants said that their families did not give them specific advice about fasting or told them to do what they felt was best. Few reported that their families advised them to fast (3%); being advised to opt out of fasting was more common (34%).

Nine (10%) participants were ordered by a doctor not to participate in fasting, one due to her hypertension medication, one due to her diabetic status, one due to being told not to fast while in labor for 6 days, two due to hypotension, two due to dizziness, fainting and vomiting, and two due to a negative effect fasting was having on the fetus after fasting 20-21 days. Two of these women were advised not to fast prior to the start of Ramadan and never fasted. The other women fasted but stopped when they were medically advised to do so. Women who reported being medically advised not to fast discontinued fasting upon being advised against it.

Seventy-eight participants (85%) in this study took vitamins, and all but one of those women was taking iron. Eighteen women (20%) took vitamins other than or in addition to iron. Vitamin intake was assessed due to its potential role in infant growth, although vitamin intake during pregnancy may have other implications about the maternal environment. Due to their cost, not all families have access to vitamin supplements, so vitamin supplementation may indicate some variation in access to financial or health care resources. Hypothetically, vitamin intake may be a proxy for increased education or awareness about the importance of micronutrients during pregnancy, increased attention to prenatal health and risk reduction strategies, and/or increased access to medical advice.

For analysis of dress in relation to fasting behavior and outcomes, women were categorized as either wearing more conservative or less conservative dress. The category of more conservative dress was comprised of women who wore the hijab (only hands and face exposed to sun) or niqab (only eyes exposed). The less conservative, more modern dress category included women who wore clothing that would have more skin exposed to the sun than if wearing the hijab (including at least face and neck, forearms or feet, and possibly arms and calves). Analysis of clothing style is considered due to both biological and cultural implications. Biologically, more conservative dress is associated with lower vitamin D levels (Alagol et al., 2000; Fadoua et al., 2009), which has physiological consequences for both mother and infant (Brannon, 2012; Dror & Allen, 2010; Javaid et al., 2006; Kovacs, 2012). From a cultural perspective, style of dress may indicate more exposure to western culture and a greater likelihood of living in a less conservative or more urban area where cultural norms around maternal fasting may differ from more conservative or rural areas. In Morocco, clothing choice likely indicates social norms of friends, family, and neighbors and generational trends, and local cultural norms may also influence fasting behaviors and other choices that influence maternal health and fetal growth and development. A study from Morocco found that age, education, marital status, and friends' opinions were stronger predictors of the style of dress than religiosity (Hamelin, Benachour, & Bachleda, 2014), but relationships between the style of dress and fasting have not been explored in this population to the best of my knowledge.

Women were categorized by their infant feeding intentions for 3-6 months post-partum. Breastfeeding is a large demand for maternal energetic resources and hydration, so infant feeding intentions may influence fasting behavior or vice versa since fasting poses an energetic and hydration stress for mothers. Women who intended to breastfeed exclusively were compared with women who intended to give any supplements, and women who intended to give formula were compared with women who did not intend to give formula but intended to exclusively breastfeed or give infants water or Vervain tea. Vervain tea is brewed from the herb Vervain, sometimes with sugar and sometimes without, and it a cultural norm in some areas of Morocco to feed this to neonates and infants. It might be given if the baby is fussy, for an upset stomach, or simply because the mother or another caretaker wanted to give it to the baby. Women who intended to exclusively breastfeed were also compared to women who intended to give formula, those who intended to give Vervain tea, and those who intended to give water.

Participants were not directly asked about stressful circumstances or life events that occurred during pregnancy. However, when asked about health during pregnancy, some participants indicated that they experienced stressful circumstances during pregnancy, such as family deaths and financial challenges. Therefore, participants who reported these stressors were compared to women who did not.

Infant sex was also included as a potential cultural predictor of fasting since son preference has been reported in this region (Obermeyer & Cárdenas, 1997). Although sex is assessed as a predictor, whether women were aware of the sex of the infant prior to birth was not assessed. Some women said they did know the sex during the interviews, but the doctors at the hospital estimate about half of the participants would have had access to that information prior to giving birth.

Fasting Behaviors

For the present analysis, maternal fasting behavior was quantified in three ways: the number of days fasted, no fasting versus any fasting, and fasting daily versus occasional fasting (summarized in Table 5.3). Most mothers opted to fast, with only 12% of the sample opting out of any fasting. The number of days fasted ranged from zero to 29 days.

Because study participants were giving birth during and after the month of Ramadan, the number of days fasted may not reveal as much about the biological and cultural differences between mothers who chose to fast, skip days, or not fast at all, because mothers given birth early in the study period may have been able and willing to fast for the entire month had they not gone into labor. Therefore, mothers who opted not to fast were compared to women who engaged in any fasting, and mothers who fasted every day of Ramadan possible before going into labor were compared to women who skipped days or did not fast.

Table 5.3: Summary of Maternal Fasting Behavior

Maternal Fasting Behavior Overview	**N**	**%**
Did Not Fast	11	12%
Fasted, But Not Every Day	29	31.5%
Fasted Every Day of Ramadan that Passed Prior to Labor	52	56.5%
Number of Days Spent Fasting by Group:		**Mean (Range)**
Did Not Fast	11	0
Fasted, But Not Every Day	29	17.1 (1-28)
Fasted Every Day of Ramadan that Passed Prior to Labor	52	20.8 (1-29)
Summary of Days Fasted and Days between Fasting and Labor:		
Number of Days Spent Fasting (All Participants)	92	17 (0-29)
Number of Days Between Last Day Fasting and Labor (All fasting participants)	81	10 (0-43)
Number of Days Spent Fasting by Groups for Analysis:		
No Fasting Group versus Any Fasting Group		
No Fasting	11	0
Any Fasting	81	19.5 (1-29)
No and Some Fasting Group versus Daily Fasting Group		
No or Some Fasting	40	12.4 (0-28)
Fasted Daily	52	20.8 (1-29)

Determinants of Days Fasted

The number of days fasted during pregnancy was expected to capture the degree to which study participants felt capable of fasting during late pregnancy, whether the reason was due to their personal experience of the difficulty of fasting, their perceived risk of fasting, including risk in relation to health concerns and medical advice, social pressure and support, societal norms, and the occurrence of stressful circumstances during pregnancy. Because this study included women who gave birth during Ramadan, some variation in the number of days fasted is due to the timing of labor. For women who enrolled early in the study, fewer days of Ramadan had passed during their pregnancies. This obstacle is addressed with the following fasting outcome variables, any fasting, and daily fasting. To assess the relationship between the number of days fasted and maternal characteristics, linear regressions were used for continuous variables, age and anthropometry, and t-tests for binomial variables. Significant variables were then added to a stepwise multivariate linear regression.

Maternal Biological Characteristics

Women may make different decisions about fasting due to biological factors, including reproductive history, age, body composition, and health. Age and body composition may influence how difficult fasting during pregnancy is, along with the risk of health conditions that additionally impact fasting decisions, medical advice about fasting, and fasting difficulty. Health conditions have been previously reported as a reason that pregnant and nursing women opt not to fast (Ertem et al., 2001; Joosoph et al., 2004; Mubeen et al., 2012; Saleem et al., 2010; Van Bilsen et al., 2016), so health conditions in relation to days fasted were also explored in relation to number of days fasted.

Maternal Reproductive History Reproductive history was analyzed for its relationship to the number of days fasted. It is predicted that multiparous women fast more than primiparous women based on previous research (Joosoph et al., 2004). Multiparous mothers fasted longer on average than primiparous mothers (Table 5.4). When removing diabetic individuals from the analysis, multiparous women did fast significantly longer than primiparous women (19.6 ± 1.4 days compared to 15.0 ± 2.1 days, $p<0.029$).

Table 5.4: T-Tests for Maternal Reproductive History and Days Fasted

Maternal Reproductive History	N	Average Number of Days Fasted	p-value
Primiparous	35	15.0 ± 2.1	NS* (p<0.08)
Multiparous	57	18.5 ± 1.4	
Primigravida	32	15.4 ± 2.1	NS
Multigravida	58	17.7 ± 1.4	
No Previous Miscarriages	72	16.5 ± 1.3	NS
One or More Previous Miscarriages	19	19.0 ± 2.7	

*NS= Not significant

Maternal Age and Anthropometry In univariate analyses, the number of days fasting was negatively associated with maternal weight but no other age or anthropometric measures (Table 5.5). A stepwise multivariate linear regression model for days fasted included maternal age, height, weight, and body fat percentage. BMI was excluded in favor of weight since maternal weight was significant in the univariate analysis. Decreased weight and increased body fat percentage were retained as predictive of more days fasting, but only weight reached significance (Table 5.5). When diabetic women were excluded from the analysis, days fasted was positively correlated with maternal age (p<0.040) and remained negatively correlated with weight (0.045)

Table 5.5: Pairwise Correlation of Maternal Anthropometry and Number of Days Fasted and Stepwise Multivariate Regression of Number of Days Fasted with Maternal Age and Anthropometry Variables (Excluding BMI)

	Maternal Anthropometry and Number of Days Fasted	Pearson's Correlation	p-value
Pairwise Correlations	Age (years)		NS
	BMI	-0.22	NS (0.06)
	Weight (kg)	-0.25	0.036
	Height (cm)		NS
	Body Fat (%)		NS
Variables retained in Stepwise Multivariate Linear Regression		**Coefficient (β)**	
	Weight (kg)	-0.35	0.006
	Body Fat (%)	0.47	0.057

Maternal Health Previous studies suggest that maternal health concerns reduce the likelihood of fasting (Ertem et al., 2001; Saleem et al., 2010). Variability in days fasted by reported health conditions during pregnancy was analyzed with t-tests (Table 5.6). Reporting any health condition was not predictive of the number of days a woman fasted. Participants with diabetes, those with hypertension, or both fasted for nine fewer days on average. Neither anemia nor other health conditions were predictive of the number of days fasted.

Table 5.6: T-Tests Comparing Days Fasted by Maternal Health Concerns

Maternal Health Concern	N	Average Number of Days Fasted	p-value
Reported one or more health conditions	51	16.6 ± 1.7	
No health condition reported	41	17.8 ± 1.6	NS
Diabetic and/or Hypertensive	11	9.3 ± 3.6	
Not Diabetic or Hypertensive	81	18.0 ± 1.2	0.007
Hypertensive	8	9.0 ± 4.2	
Not Hypertensive	84	17.9 ± 1.2	0.017
Diabetic	6	8.7 ± 5.1	0.029
Not Diabetic	86	17.7 ± 1.2	
Anemic	22	18.6 ± 2.6	
Not Anemic	70	16.4 ± 1.3	NS
Other (exhaustion, fatigue, hypotension, bleeding)	29	19.2 ± 1.9	
No Other Concern Reported	63	16.2 ± 1.5	NS

Days Fasted: Multivariate Analyses with Significant Biological Variables

A stepwise multivariate linear regression of days fasted with variables that were previously found to be significant in univariate linear regressions and t-tests included multiparous, BMI, weight, diabetes, and hypertension (both separately and combined) as independent variables. Age and anemia were also added since they were significant if diabetic participants were excluded. Weight and height were used in the analysis instead of weight and BMI. Reduced fasting was associated with increased weight and having diabetes and/or hypertensive disorders (Table 5.7).

Table 5.7: Stepwise Multivariate Linear Regression of Days Fasted with Biological Variables That Had Significant Correlations with Days Fasted in Univariate Regressions and That Varied by Category in T-Tests

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
Weight (kg)	-0.2	0.053
Maternal Age (years)	0.3	0.070
Diabetes and/or Hypertension	-8.6	0.021

Maternal Cultural and Environmental Characteristics

Cultural and environmental characteristics may influence fasting decisions. T-tests were used to analyze differences in numbers of days fasted by groups with different cultural and environmental characteristics, including differences in family advice and medical advice, vitamin intake, style of dress, intentions about infant feeding, and stressors experienced during pregnancy.

Family Advice All participants were asked during interviews if their husbands or families told them that they should or shouldn't fast or gave no advice. Advice against fasting was predicted to decrease days fasted, based on previous research (Van Bilsen et al., 2016). Women who were encouraged to fast fasted an average of 20.7 ± 6.4 days, and a t-test showed that this was not significantly different from women who were given neutral or no advice from family (19.2 ± 1.4 days), so women who were given advice against fasting were compared to women given neutral advice or were advised to fast. Five women who responded to this question did not specifically indicate that their families advised against fasting, rather the doctor advised against fasting and their families were supportive of complying with the doctor's orders. The following t-test was run with and without those included in the sample of women who were advised against fasting by their families.

Table 5.8: T-Tests Comparing Days Fasted by Women Who Received Advice from Family Against Fasting Versus Women Who Did Not Receive Specific Advice or Were Encouraged to Fast

Family Advice Regarding Fasting	N	Average Number of Days Fasted	p-value
Family Advised to Fast or Did Not Give Specific Advice	60	19.5 ± 1.3	
Family Advised Against Fasting	30	13.4 ± 2.3	p<0.007
Family Advised to Fast or Did Not Give Specific Advice	60	19.5 ± 1.3	
Family Advised Against Fasting (Excluding Women Who Said Family Supported Doctor's Advice Against Fasting)	25	15.2 ± 2.5	p<0.050

Women whose families encouraged them not to fast, including women who were encouraged not to fast by families resulting from medical advice, fasted for an average of 6 fewer days (p<0.007) than women who were given no advice at all and women who were encouraged to fast. If women whose families advised against fasting due to medical advice are excluded from the analysis, the p-value increased to 0.05 (Table 5.8).

Several participants elaborated on their answer to the question of whether family members advised them to fast or not. Many participants who said nobody told them what to do either way added that their families said something to the effect of, "fast if you can and want to, don't fast if you can't or don't want to" so their initial answer implies that they understood that their families supported either decision but did not advise them to try either. Women who elaborated on being encouraged not to fast by family often said something similar, such as "you shouldn't fast if fasting makes you feel tired/feint/sick." Five women whose families advised against fasting followed up their answer with "but I felt like I could, so I did." Very few women reported being told by their families to fast, but of those who did, they said that their families were trying to be encouraging rather than telling them what to do. Some of the women who had been told by a doctor not to fast said that their families told them not to fast, but some said more specifically that their family told them to listen to the doctor. One woman said nobody gave her advice, but if they had told her not to, she wouldn't have listened because she is "a good Muslim". One woman said that her 13-year-old son asked her not to fast, and he had been very concerned, saying "don't kill my brother" (which he evidently believed may be an outcome of fasting).

Medical Advice Being medically advised not to fast was associated with a shorter duration of fasting, averaging 9 fewer days than the rest of the sample (18.0 ± 1.2 compared to 9.2 ± 3.2, $p<0.014$).

Vitamin Intake Although any vitamin supplementation was not associated with fasting behaviors, women who supplemented with vitamins other than iron fasted an average of 5.5 days less than women who did not take supplements or who took only iron (Table 5.9).

Table 5.9: T-Tests Comparing Number of Days Fasted by Maternal Vitamin Intake

Maternal Vitamin Intake	N	Average Number of Days Fasted	p-value
No Vitamins	14	16.9 ± 3.0	NS
Any Vitamins	78	17.2 ± 1.3	
No Vitamins or Iron Only	74	18.2 ± 1.3	p<0.066
Takes Multivitamin, Magnesium, Vitamin D, and/or Folic Acid	18	12.7 ± 2.9	

Style of Dress I predicted that less conservative and more modern dress be indicative of more European influence on behaviors and of living in less conservative, more urban areas. Attitudes about maternal fasting may also be impacted by foreign influence, which is more common in urban areas. However, there was no association between more conservative dress and the number of days women fasted, so this was not the case in this sample.

Intentions for Infant Feeding There were no significant differences in fasting behavior by intentions to exclusively breastfeed or give formula in this sample. When using a subset of the sample to compare women who intended to exclusively breastfeed to those that intended to give water, Vervain tea, or formula, only women who intended to give water were significantly different from women who intended to exclusively breastfeed (Table 5.10). When comparing women who intended to give water to all other women in the sample, the difference in days fasted between the groups remained.

To note, earlier in the study, more women who intended to breastfeed and give water enrolled early in the study period, so that may account for this observation. This was not related to average temperatures, as temperatures rose over the course of the study. The intention to give water does not seem to be related to other maternal variables, so the reason for this may just be chance. The other possible explanation for the decrease in women with the intention to breastfeed later in the study is that I told the doctors water supplementation was not recommended by the World Health Organization, even in hotter climates. Therefore, the medical personnel may have stopped recommending giving water if mothers asked. If this was the case, I do not believe that my advice per se was recommended. Rather, the World Health Organization recommendation was an authoritative source, and they either trusted that I knew their recommendations or looked the information up for themselves after I suggested it. Still, infant feeding intentions are often formed before birth, and I was not aware of changes in recommendations while doing research at the facility, though there may have been.

Table 5.10: T-Test Comparing Days Fasted by Intended Infant Feeding Practices

Infant Feeding Intentions	N	Average Number of Days Fasted	p-value
All Participants			
Did Not Intended to Exclusively Breastfeed	28	14.1 ± 2.1	
Intended to Exclusively Breastfeed	50	18.4 ± 1.6	NS
Intended to Give Formula	12	15.1 ± 3.3	
Did Not Intend to Give Formula (Exclusive Breastfeeding, or Intended to Give Water or Vervain Tea)	66	17.2 ± 1.4	NS
Subgroups			
Intended to Give Formula	12	15.1 ± 3.3	
Intended to Exclusively Breastfeed	50	18.4 ± 1.6	NS
Intended to Breastfeed and Give Vervain Tea	6	19.5 ± 4.3	
Intended to Exclusively Breastfeed	50	18.4 ± 1.6	NS
Intended to Breastfeed and Give Water	14	11.1 ± 2.7	
Intended to Exclusively Breastfeed	50	18.4 ± 1.6	p<0.032

Stressors During Pregnancy Women who reported stress during pregnancy fasted for more days than those that did not, but this was not significant.

Infant Sex Women who gave birth to males versus females did not vary in fasting duration.

Days Fasted: Multivariate Analyses with All Cultural and Environmental Variables

All cultural and environmental variables that were previously found to be significant (family advice, medical advice, and taking vitamins other than iron) were added to a stepwise multivariate linear model as predictors of days fasted. Exclusive breastfeeding versus giving water was excluded since that did not contain other supplemental feeding participants and therefore decreased the sample size substantially. Decreased fasting was significantly related to having received medical advice and family support for not fasting (Table 5.11), so the advice from medical professionals and family was the strongest cultural predictor of reduced fasting.

Table 5.11: Stepwise Multivariate Linear Regression of Days Fasted with Cultural and Environmental Variables That Had Significant Correlations with Days Fasted Varied by Category In T-Tests

Independent Variables Retained in Model	Coefficient (β)	p-value
Family Advice	-5.7	0.019
Medical Advice	-8.5	0.026

Multivariate Linear Regression

All biological cultural and environmental variables that were previously found to be significant in previous analyses (multiparous, maternal weight, BMI, body fat, age, having diabetes, hypertension or anemia, family advice, medical advice, and taking vitamins other than iron) were added to a stepwise multivariate linear model as predictors of days fasted. Weight and height were added instead of weight and BMI. Diabetes and hypertension categories were added both separately and combined. Exclusive breastfeeding versus giving water was excluded since that did not include other supplemental feeding participants and decreased the sample size substantially.

The model retained weight, body fat, diabetes, medical advice, and family advice as predictors of days fasted. Family advice, diabetes, and weight were significant (Table 5.12). Being encouraged not to fast by family members was related to reduced fasting. Whether women received this advice because they had chosen not to fast and their families were expressing support for their choice or if women were less likely to fast after their family members have advised them against it is not clear from this study, though both may be true.

Having diabetes was also associated with reduced fasting. Having hypertension was not retained as predictive, in contrast to the model of only biological variables. Higher weight was associated with reduced fasting.

Table 5.12: Stepwise Multivariate Linear Regression of Days Fasted with Variables That Had Significant Correlations with Days Fasted in Univariate Regressions and That Varied by Category In T-Tests

Independent Variables Retained in Model	Coefficient (β)	p-value
Family Advice	-5.1	0.036
Medical Advice	-6.0	0.153
Age (years)	0.3	0.099
Weight (kg)	-0.3	0.030
Body Fat (%)	0.3	0.188
Diabetes	-10.7	0.027

Determinants of Any Fasting Versus No Fasting

Eleven of the 92 participants opted not to fast at all during Ramadan. Biological, cultural, and environmental differences between women were considered for their predictive value in pregnant women's decisions about whether to engage in any religious fasting during the third trimester, using logistic regression for binomial variables and t-tests for continuous variables, which include age and anthropometry. Multivariate logistic regression was then used to assess the relationship between any significant predictors of any fasting in univariate analyses.

Reasons Women Gave for Not Fasting

Table 5.13: Reasons Participants in The Non-Fasting Group Said They Never Fasted

Reason Participants Did Not Fast Some or All Days (N=11)	
Did not feel she could (due to thirst, fatigue, or simply "could not")	(N=4) 36%
Medical reason: Maternal health (gestation, Type 1 or Type 2 diabetes, hypertension, hypotension, anemia, illness, fainting)	(N=5) 45%
Medical reason related to the pregnancy	(N=1) 9%
No reason provided	(N=1) 9%

Of the 11 women who opted not to engage in any fasting, the reason given was most commonly related to medical concerns, mostly related to maternal health concerns (54%). Otherwise, the other reason women said that they did not fast was that they did not feel they could, which some participants attributed to thirst or fatigue (Table 5.13).

To assess if reasons for not fasting varied by maternal anthropometry, stepwise multivariate logistic regression of maternal weight, height, body fat, and age was used to compare women who participated in any fasting to women who did not fast for medical reasons and then for women who did not feel able to fast. To compare if reasons for not fasting varied by health status, medical advice, family advice, or infant sex, chi-squared tests were used to compare across groups (any fasting, non-fasting for medical reasons, and non-fasting due to feeling unable). Women who did not fast for medical reasons were heavier (81.3 kg compared to 68.5 kg, $p<0.018$), more likely to have any medical condition ($p<0.012$) and particularly diabetes and/or hypertension ($p<0.000$), and more likely to report having received advice from family not to fast ($p<0.045$). Women who felt unable to fast did not vary from women who fasted in any analysis. These groups did not vary by medical advice or infant sex.

Maternal Biological Characteristics

Maternal Reproductive History Reproductive history was not predictive of women's decisions to fast or opt out of any fasting based on logistic regression.

Maternal Age and Anthropometry Univariate analyses did not reveal significant differences between non-fasting and fasting women by their age or anthropometry. With age and anthropometry variables, excluding BMI, included in a stepwise multivariate logistic regression, decreased weight and increased body fat together were significant predictors of non-fasting (Table 5.14).

Table 5.14: Stepwise Multivariate Logistic Regression of Fasting versus Non-Fasting with Age and Anthropometry Variables

Independent Variables Retained in Model	Odds Ratio	p-value
Body Fat (%)	1.2	0.044
Weight (kg)	0.9	0.034

Maternal Health Having any maternal health concern was associated with a higher frequency of non-fasting (p<0.04). Women who had either diabetes (p<0.011) or hypertension (p<0.038), or both (p<0.015) were more likely to opt out of any fasting than other women. Anemia and other health concerns were not predictive of fasting versus non-fasting (Table 5.15). When excluding women with diabetes from the analysis, having anemia increased the likelihood of being in the non-fasting group (OR=0.28, p<0.092).

Table 5.15: Determining the Role of Maternal Health Concerns in Non-Fasting Versus Any Fasting with Logistic Regression

Maternal Health	**Non-Fasting**	**Fasting**		
	N	**N**	**Odds Ratio**	**p-value**
No health concerns	1	39		
Reported one or more health concerns	10	42	0.11	0.038
Not Diabetic	8	78		
Diabetic	3	3	0.10	0.011
Not Hypertensive	8	76		
Hypertensive	3	5	0.18	0.034
Not Diabetic or Hypertensive	7	74		
Diabetic and/or Hypertensive	4	7	0.17	0.015
Not Anemic	7	63		
Anemic	4	18	0.50	NS
No health concerns in "Other" category	8	55		
Reported health concerns in "Other" category	3	26	1.5	NS

No Fasting vs. Any Fasting: Multivariate Logistic Regression of Biological Variables

The biological variables that were found to be significant in the previous analyses were maternal weight, BMI, body fat, reporting any maternal health concern, having anemia, having diabetes, having hypertension, or being in the group of women who had diabetes and/or hypertension. Weight was used rather than both weight and BMI. The stepwise multivariate model retained increased weight, increased height, reduced body fat, and having anemia or diabetes as predictors being in the non-fasting group. Of these, the significant variables that predicted non-fasting were having diabetes, having anemia, and higher body fat. Weight and height were retained in the model but were not significant (Table 5.16).

In a region where fasting during pregnancy appears to be the norm, these participants did not attempt to fast, so their decision not to fast was not likely based on attempting to fast and finding it too difficult unless they had tried during previous pregnancies. The relationship between certain health concerns and non-fasting may indicate a higher perceived risk of fasting during pregnancy if certain health conditions were present.

Table 5.16: Stepwise Multivariate Logistic Regression of Fasting Versus Non-Fasting with Biological Variables That Had Significant Correlations with Any Fasting in Univariate Logistic Regressions

Independent Variables Retained in Model	**Odds Ratio**	**p-value**
Diabetes	0.1	0.047
Anemia	0.1	0.037
Weight (kg)	0.9	0.154
Height (cm)	0.9	0.183
Body Fat (%)	1.2	0.041

Maternal Cultural and Environmental Characteristics

Cultural and environmental characteristics that were considered for their relationship to whether women participated in any fasting included family advice, medical advice, vitamin intake, style of dress, infant feeding intentions, and reported stressors.

Family Advice Women whose families advised them not to fast were more likely to opt out of fasting entirely ($p<0.017$). When removing the participants who cited medical advice as the reason for family advice against fasting, this correlation was no longer significant (Table 5.17).

Table 5.17: Determining the Role of Family Advice in Non-Fasting Versus Any Fasting with Logistic Regression

	Non-Fasting	**Fasting**		
Family Advice	**N**	**N**	**Odds Ratio**	**p-value**
Family Advised to Fast or Did Not Give Specific Advice	3	57		
Family Advised Against Fasting	7	23	0.17	0.017
Family Advised to Fast or Did Not Give Specific Advice	3	57		
Family Advised Against Fasting (Excluding Women Who Said Family Supported Doctor's Advice Against Fasting)	4	21	0.28	NS

Medical Advice Medical advice was not indicative of women's decisions to entirely opt out of fasting. In most cases, participants received medical advice against fasting due to the experiences they were having during fasting, so this is unsurprising.

Vitamin Intake Women who took vitamins other than iron were less likely to fast than women who took no vitamin supplements or only iron ($p<0.03$). All but one participant who took any vitamin took iron, and neither any vitamin supplementation or supplementing with iron was not predictive of whether a participant fasted (Table 5.18).

Table 5.18: Logistic Regression Comparing Vitamin Supplementation Status as a Determinant of Fasting Versus Non-Fasting

	Non-Fasting	**Fasting**		
Maternal Vitamin Intake	**N**	**N**	**Odds Ratio**	**p-value**
No Vitamins	2	12		
Any Vitamins	9	69	1.28	NS
No Vitamins or Iron Only	6	68		
Takes Multivitamin, Magnesium, Vitamin D, and/or Folic Acid	5	13	0.23	0.030

Style of Dress Style of dress was not indicative of women's decisions to entirely opt out of fasting.

Intentions Regarding Infant Feeding Infant feeding intentions were not predictive of whether women engaged in any fasting.

Stressors during Pregnancy All women who reported experiencing stressful circumstances during pregnancy were in the group of women who fasted. Since a logistic regression analysis is not possible when no participants fall into one category, this analysis could not be run. A Fisher's exact chi2 did not find the relationship significant.

Infant Sex Women who gave birth to males versus females did not vary by any versus no fasting.

No Fasting versus Any Fasting: Multivariate Analyses of Cultural and Environmental Variables

Family advice and taking vitamins other than iron were predictive of fasting versus non-fasting in univariate analyses. Both were retained in a stepwise multivariate logistic regression, but only family advice was significant (Table 5.19), which was also a significant predictor of days fasted. The advice between non-fasting and family advice against fasting may be influenced to some degree by maternal health concerns, but it may also indicate the importance of family advice in fasting decisions.

Table 5.19: Stepwise Multivariate Logistic Regression of Fasting Versus Non-Fasting Participants with Variables That Had Significant Correlations with Any Fasting in Univariate Logistic Regressions

Independent Variables Retained in Model	Odds Ratio	p-value
Family Advice	0.2	0.026
Taking vitamins other than iron	0.4	0.166

Multivariate Logistic Regression

All biological, cultural, and environmental characteristics that were found significant predictors of fasting versus non-fasting in the previous analyses were considered for addition to a stepwise multivariate analysis (Table 5.20). Decreased likelihood of fasting was related to increased weight, increased height, decreased body fat, having any maternal health concerns, having diabetes or hypertension, having anemia, receiving family advice against fasting, and taking vitamins other than iron.

The stepwise multivariate logistic regression retained weight, body fat, family advice, anemia and diabetes as predictive of fasting, with reduced weight and having diabetes each reaching significance. Having diabetes and reduced weight were also predictors of fewer days fasted. As previously suggested, having diabetes may be associated with a perceived increased risk of fasting. Although a causal link between increased weight and non-fasting was not possible to determine given the cross-sectional nature of this study, hypotheses for this relationship were explored in the discussion.

Table 5.20: Stepwise Multivariate Logistic Regression of Fasting Versus Non-Fasting with Biological, Cultural, and Environmental Variables Found to be Significant in Univariate Analysis

Independent Variables Retained in Model	**Odds Ratio**	**p-value**
Weight (kg)	0.9	0.049
Body Fat (%)	1.2	0.094
Diabetes	0.1	0.046
Anemia	0.2	0.092
Family Advice	0.1	0.054

Determinants of Daily Fasting Versus Some or No Fasting

Forty of the 92 participants opted not to fast all or some of Ramadan and the remaining 52 participants fasted every day of Ramadan that passed before going into labor. Biological, cultural, and environmental differences between women were considered for their predictive value in pregnant women's decisions about whether to engage in religious fasting daily during the third trimester using logistic regression. Multivariate logistic regression was then used to assess the relationship between any variables found to be significant predictors of daily fasting in univariate analyses.

Reasons Women Gave for Opting Out of Fasting Some or All of Ramadan

Women who fasted commonly said they did so because they felt they were able to do so. The most common reason given for not fasting for at least one day (45%) was that she did not feel capable of fasting, commonly attributed to thirst, high summer temperatures, exhaustion, fatigue, or dizziness. Forty-three percent cited medical concerns, with 35% reporting that they opted not fast due to a maternal health concern, and another 8% reporting that it was due to a problem with the pregnancy or with the fetus (Table 5.21). Additionally, 8% opted out due to reasons unrelated to health or pregnancy, such as travel.

To assess if reasons for not fasting daily varied by maternal anthropometry, a stepwise multivariate logistic regression was used to compare women who participated in daily fasting to women who did not fast for medical reasons and then for women who did not feel able to fast. Variables that were compared included maternal weight, height, body fat, and age. To compare if reasons for not fasting varied by health status, medical advice, family advice, or infant sex, chi-squared tests were used to compare across groups (daily fasting, non-fasting for medical reasons, non-fasting due to feeling unable, and non-fasting for other reasons).

There were no differences by age or anthropometry. Women who did not fast for medical reasons were more likely to report having received medical advice against fasting ($p<0.000$) and having diabetes and/ or hypertension than women who fasted daily ($p<0.008$). Women who did not fast for medical reasons were also more likely to have a male infant ($p<0.010$). Women who felt they could not fast were more likely to have any medical condition during pregnancy than women who fasted daily ($p<0.029$), even though they did not list a medical concern as a reason they did not fast. No other differences were found for this group.

Table 5.21: Reported Reasons for Not Fasting Daily for Women Who Did Not Fast or Did Not Fast Every Day Before Labor

Reason Participants Did Not Fast Some or All Days (N=40)	
Did not feel she could (due to thirst, heat, weakness, exhaustion, fatigue, dizziness)	45%
Medical reason: Maternal health (gestational, Type 1 or Type 2 diabetes, hypertension, hypotension, anemia, illness, fainting)	35%
Medical reason: related to the pregnancy or the baby	7.5%
Reason not directly related to pregnancy or health (travel, work, emotional distress)	7.5%
Reason not provided	5%

Maternal Biological Characteristics

Table 5.21 shows that the most commonly cited reason for not fasting daily was due to feeling unable to do so for reasons other than medical concerns. Medical reasons were the next most commonly cited reason. The high percentage of women who cited medical reasons indicate that health concerns would likely be a significant predictor of not participating in daily fasting but feeling physically less capable of fasting may also indicate biological differences between these groups of women. Differences in reproductive history, age, anthropometry and health concerns were compared between women who did and did not fast daily.

Maternal Reproductive History Reproductive history was not predictive of whether women fasted every day of Ramadan that passed prior to labor based on logistic regressions.

Maternal Age and Anthropometry In univariate and multivariate logistic regression analyses, maternal age and anthropometry were not predictive of whether women fasted every day of Ramadan that passed prior to labor. Anthropometry itself is not, therefore, a strong predictor of daily fasting.

Maternal Health Fifty-four percent of mothers reported at least one health condition. Reduced frequency of daily fasting was seen amongst women with one or more health condition, but this did not reach significance. No diabetic participants fasted daily, so this variable cannot be added to a logistic regression. Based on a Fisher's exact chi2, the relationship was significant ($p<0.005$), so having diabetes was a strong determinant of not engaging in daily fasting in this sample (Table 5.22).

Table 5.22: Logistic Regression to Determine the Role of Maternal Health Concerns in Daily Fasting Versus No or Some Fasting

Maternal Health	**No or Occasional Fasting**	**Fasted Daily**		
	N	**N**	**Odds Ratio**	**p-value**
No health concerns	14	26		
Reported one or more health concerns	26	26	0.50	NS
Not Diabetic	34	52		
Diabetic	6	0		
Not Hypertensive	35	49		
Hypertensive	5	3	0.43	NS
Not Diabetic or Hypertensive	32	49		
Diabetic and/or Hypertensive	8	3	0.24	0.049
Not Anemic	28	42		
Anemic	12	10	0.56	NS
No health concerns in "Other" category	26	37		
Reported health concerns in "Other" category	14	15	0.75	NS

Women in the group of participants who had diabetes and/or hypertension were less likely to fast every day of Ramadan that passed prior to labor ($p<0.04$). However, no diabetic women fasted every day and having hypertension was not predictive of daily fasting, so the reduced frequency of daily fasting is largely accounted for by diabetic women.

No or Some Fasting vs. Daily Fasting: Multivariate Logistic Regression of Biological Variables

The variables found to be potential predictors of daily fasting included height, weight, BMI, and being in the group of women with diabetes and/or hypertension. No woman with diabetes fasted daily so this variable could not be included in a logistic regression. Only having diabetes and/

or hypertension was predictive of not fasting daily (OR=0.2, p<0.044), and this relationship are likely driven by women with diabetes. Therefore, the biological variables assessed within this study, other than diabetes, were not strong predictors of daily fasting.

Maternal Cultural and Environmental Characteristics

Cultural and environmental characteristics that were considered for their relationship to daily fasting versus no or some fasting included family advice, medical advice, vitamin intake, style of dress, infant feeding intentions, and reported stressors.

Family Advice Although family advice was found to be predictive of other fasting behavior outcome variables, women who received advice from family against fasting were not less likely to fast daily than women who received advice to fast or that did not receive specific advice.

Medical Advice Women who reported that a doctor advised against fasting unanimously stopped fasting immediately, so as would be expected, of women who were advised not to fast by a doctor, none fasted daily. As such, this variable cannot be added to a logistic regression. The relationship was significant (p<0.000) based on a Fisher's exact chi2, so medical advice was a strong determinant of not engaging in daily fasting in this sample.

Vitamin Intake Taking vitamins other than iron was associated with a reduced likelihood of daily fasting (OR=0.22, p<0.009). Taking any vitamin was not predictive of daily fasting.

Other Cultural and Environmental Variables Maternal style of dress, intentions regarding infant feeding, stressors pregnancy, and infant sex were not predictive of whether women engaged in daily fasting.

<u>*No or Some Fasting vs. Daily Fasting: Multivariate Logistic Regression of Cultural Variables*</u>

No participant that received medical advice against fasting was in the group of women who fasted daily, so this variable cannot be added to the multivariate logistic regression. There was only one other cultural or environmental factor that was found in a univariate analysis to be a significant predictor of daily fasting, which was taking vitamins other than iron, and therefore a multivariate logistic regression of significant predictors cannot be completed.

Multivariate Logistic Regression

Variables found significant in predicting daily fasting and included in the multivariate logistic regression included taking a vitamin other than iron, height, weight, BMI, and having diabetes and/or hypertension. No women who had diabetes or who received medical advice against fasting were in the group of women who fasted daily. BMI was excluded due to its relationship with weight. Taking any vitamin other than iron and having diabetes and/or hypertension were retained in the model but were not significant (Table 5.23).

In the univariate analysis, reduced likelihood of daily fasting was predicted by having diabetes and medical advice against fasting, so although those variables could not be added to the multivariate model, they remain important predictors. Medical concerns may indicate higher risk pregnancies or a perceived higher risk of fasting to maternal and fetal health. From the present analysis, it is unclear what characteristics other than medical concerns differentiate women who fast daily and those who skip days or do not fast.

Table 5.23 Multivariate Logistic Regression of No Or Some Fasting Versus Daily Fasting with Biological Variables That Had Significant Correlations with Days Fasted in Univariate Logistic Regressions

Independent Variables Retained in Model	Odds Ratio	p-value
Vitamin Other than Iron	0.4	0.143
Diabetes and/or hypertension	0.2	0.060

Interactions between Independent Variables

Several variables that were associated with fasting behaviors may be interrelated. These interactions were explored with the aim of better understanding the correlations found between these variables and fasting and how they relate to fasting decisions.

Study Day

As this study began as Ramadan began and continued enrollment throughout the duration of and after Ramadan, fewer days of Ramadan passed for those that enrolled early in the study and therefore, early enrollees had fewer days that they could have participated in fasting compared to those that enrolled later. Some trends that appear to be related to fasting could be related to the random distribution of participants in study enrollment, given the small sample size.

In a linear regression, study day was positively correlated with maternal age ($p<0.035$). T-tests found that anemic participants were more likely to enroll later in the study (36 ± 3.5 days into the study period compared to 22.3 ± 1.8 days for non-anemic participants, $p<0.000$). Women who intended to exclusively breastfeed enrolled later than women who did not intend to do so (29.5 ± 2.4 days compared to 18.3 ± 2.6 days, $p<0.004$). Women who planned to give water to their infants enrolled much earlier than women who planned to exclusively breastfeed (14.9 ± 3.0 days compared to 29.5 ± 2.4 days, $p<0.001$).

Reproductive History

History of miscarriage was related to having diabetes and/or hypertension (OR=6.2, $p<0.007$), and hypertension individually (OR=4.5, $p<0.047$), but not diabetes. Maternal age predicted parity (OR=1.1, $p<0.002$).

Interaction Between Maternal Anthropometry and Maternal Health

Both maternal health and anthropometry were related to fasting behavior, but maternal anthropometry and health risks for reported health conditions are related to each other, so those relationships were analyzed. Higher maternal anthropometry measurements may be associated with maternal fasting behaviors due to their relationship with maternal health conditions. Maternal health conditions were analyzed for their relationship to maternal age and anthropometry with univariate logistic regression and stepwise multivariate logistic regression.

All Health Conditions Combined

All health conditions combined were not found to be related to maternal anthropometry in univariate or multivariate logistic regression analyses.

Diabetes

A stepwise multivariate logistic regression of diabetes prevalence using all maternal age and anthropometry excluding BMI as predictors. In the full model, increased age, body fat, and weight were retained as predictors of having diabetes, but only age was significant ($p<0.022$).

Hypertension

A stepwise multivariate logistic regression of hypertension risk with maternal age and anthropometry variables, not including BMI, retained increased weight as predictive of hypertension risk (OR=1.1, $p<0.016$); decreased body fat percentage was also retained but not significant (OR=0.86, $p<0.052$)).

Diabetes and Hypertension

Age and anthropometry did not vary by diabetic and/or hypertensive status in t-tests. A stepwise multivariate logistic regression showed that, when all maternal anthropometry variables were added to the full model, higher weight was predictive of diabetes and hypertension prevalence in this sample ($p<0.041$). Body fat percentage was also retained.

Anemia

In univariate logistic regression analyses, no maternal age and anthropometry indicators were significantly related to anemia. In a multivariate logistic regression including all maternal age and anthropometry indicators as independent variables, shorter stature was retained in the output but not significant (0.087), and no other variables were retained in the model.

Other

No maternal anthropometry measurement was related to other health conditions, and these health conditions were not related to maternal fasting behaviors.

Cultural and Environmental Variables

Family Advice

Advice from family members against fasting was predictive of reduced numbers of days fasting and of non-fasting. Family advice was not related to maternal reproductive history.

Medical Advice

In logistic regression analyses with health conditions, medical advice was associated with having diabetes and/or hypertension but was not significant ($p<0.053$). Six out of seven of the women who had been given medical advice against fasting gave birth to male infants, but this was not significant in a logistic regression.

Vitamin Intake

The relationship between taking vitamins other than iron and reduced fasting was assessed for its potential relationship to medical concerns. Based on logistic regression analyses, there was not a significant relationship between vitamin intake and medical advice against fasting. Anemia was the only health condition associated with taking a vitamin other than iron ($p<0.03$), but anemia was not associated with reduced fasting. No health conditions were associated with taking any vitamin or taking iron. Based on a logistic regression with women who did not opt out of any days fasted as the index group, women who opted out of fasting for medical reasons were more likely to take a vitamin other than iron (0.006), but women who opted out of fasting because they did not feel they could fast or for non-health related reasons were not significantly different from the index group.

Style of Dress

Dress was also considered for its relationship to family advice, as dress and advice may both indicate the norms of people in the women's environment, but there was not a relationship between family advice and dress. In a stepwise logistic regression with maternal age and anthropometry, less conservative dress was associated with younger maternal age (OR=0.82, p<0.006) and increased BMI (OR=1.21p<0.029). Given that less conservative dress was associated with decreased age, parity was also tested in a logistic regression. Primiparous mothers were more likely to dress less conservatively (OR=0.22, p<0.010).

Intentions for Infant Feeding

Infant feeding intentions did not vary by gestational age at birth or for women who reported an infant health concern. Intention to give water (but not formula) versus exclusively breastfeeding was increased in women who reported any health condition (logistic regression: OR= 3.8, p<0.045), but no individual health condition was significantly related to intention to give water.

Discussion

In order to make meaningful conclusions about the effects of maternal religious fasting on maternal and infant biology, the differences between women who opt to fast and those that do not or that skip days must be addressed. Maternal characteristics, such as anthropometry and health concerns, may confound or mask effects of fasting. The variables that were predictive of fasting behaviors in this sample included maternal biological characteristics, including maternal anthropometry and health concerns, and cultural and environmental characteristics, including advice from family members against fasting, medical advice against fasting, and vitamin intake. These variables will be discussed in more depth below as to how they related to fasting behaviors, with suggestions as to their potential significance as predictors of fasting behaviors.

Maternal Biological Characteristics and Fasting Behaviors

Maternal health and anthropometry were consistently predictive of fasting behaviors, with a specific emphasis on diabetes, hypertension, anemia, and weight. Having diabetes and hypertension was associated with reduced fasting, and women who had these health concerns cited them as the reason they did not fast or that they were advised not to fast.

Having diabetes was associated with a reduced number of days fasting, non-fasting, and not fasting daily. Half of the women with diabetes did not fast at all, which was likely due to a perceived risk of fasting with diabetes and medical advice against fasting. This condition may be perceived as a sign of a high-risk pregnancy, causing more women to opt out of any fasting. The other half of women with diabetes fasted but did not fast the whole time. Fasting may also be more difficult with a condition that is related to glucose metabolism, and fasting with diabetes may potentiate medical complications. Evidence suggests that blood glucose levels may increase during Ramadan in participants with diabetes. This may be associated with increased sugar consumption during non-fasting hours, but this may make fasting with diabetes during pregnancy particularly difficult and risky (Alnasir, 1996).

Hypertension was associated with non-fasting and reduced number of days fasted. Women with this condition may opt out of fasting due to having higher risk pregnancies or in order to take medicine. However, hypertension was not predictive of reduced daily fasting, so women with hypertension may not experience increased difficulty fasting or increased risks associated with fasting. Although research on pregnant women with hypertension is lacking, research on hypertensive non-pregnant individuals has generally found that blood pressure and risk of adverse consequences may be improved during Ramadan fasting (Dewanti, Watanabe, Sulistiawati, & Ohtsuka, 2006; Salahuddin, Sayed Ashfak, Syed, & Badaam, 2014; Samad et al., 2015; Turin et al., 2016). Fasting may reduce blood pressure because it results in the depression of the sympathetic nervous system (Koppeschaar, Meinders, & Schwarz, 1983; Samad et al., 2015). In rats, fasting was found to result in sympathetic nervous system depression, and in hypertensive rats specifically, fasting additionally triggered an opiate-mediated vasodepressor response (Einhorn, Young, & Landsberg, 1982). Weight loss during fasting is another hypothesized reason for the resulting reduced blood pressure (Dewanti et al., 2006).

Having iron-deficiency anemia was also related to a reduced likelihood of fasting when considering biological variables (OR=0.1, p<0.037). However, participants who did not fast due to medical reasons did not cite anemia as the reason. Since having anemia was not given as a reason to opt out of any fasting, it may not be viewed as a high-risk health condition by participants. However, given the present data, anemia may be an underlying reason for opting out of fasting. Symptoms of anemia include dizziness and fatigue, which were common reasons women listed for feeling like they could not fast. Anemia is also associated with increased risk of other health complications that would cause women to opt out of fasting, such as infectious diseases including the flu (He et al., 2017) and pneumonia (Graves, 2010). Anemia may make fasting more difficult. In a study of non-pregnant individuals, fasting also exacerbated the anemic condition (Dewanti et al., 2006), so it may worsen symptoms when pregnant women attempt to fast. Although anemia from iron sequestering is known to be an adaptive defense against infectious diseases, particularly malaria (Wander, Shell-Duncan, & Mcdade, 2009), a protective benefit of anemia in Morocco is unclear as the prevalence of malaria is low (Faraj et al., 2009).

Maternal weight and body fat were repeatedly associated with fasting behaviors, with increased weight and reduced body fat predicting reduced fasting. This relationship may be primarily due to the association between higher weight and an increased risk for other health concerns, including diabetes and hypertension. In this sample, increased weight and reduced body fat predicted both reduced fasting and having diabetes and/or hypertension, so the relationship between fasting and anthropometry may be due to the interceding factor of maternal health. Obesity is also associated with increased risk of other maternal health concerns during pregnancy that might cause women to reduce fasting, such as infectious diseases like the flu (He et al., 2017). Women who cited medical reasons for not fasting were heavier than women who fasted, but women who said they felt unable to fast for non-medical reasons were not significantly different in anthropometry or age from women who fasted. This suggests the relationship between weight and fasting may be mediated by maternal health.

Although weight and health conditions are interrelated, weight was retained as a significant predictor of fasting even when health conditions were included in multivariate analyses, suggesting increased weight was associated with reduced fasting beyond the contributions of health concerns. Although religious fasting is not directly comparable to dieting for health and weight loss, some studies have found that increased BMI and waist circumference is associated with reduced adherence to dietary restrictions and weight loss plans (Bautista-Castano, Molina-Cabrillana, Montoya-Alonso, & Serra-Majem, 2004; Downer et al., 2016). Reasons for decreased adherence in these groups are unclear, but it is possible that being heavier is independently associated with decreased ability to adhere to dietary restriction.

Alternatively, since the anthropometric measures were taken after Ramadan fasting, the difference in fasting by anthropometry may be a result of fasting rather than a determinant of it. Pregnant women who fast may be more likely to gain less weight or lose weight during fasting and therefore weigh less post-Ramadan than they would have had they not fasted. This was observed in a population in the Gambia, where Ramadan fasting led to weight loss in pregnant and lactating women. Fasting during late pregnancy in particular led to difficulty maintaining glucose homeostasis and susceptibility to 'accelerated starvation", a state characterized by hypoglycemia, and reduced circulating amino acids, and elevated free circulating fatty acids, circulating plasma and urinary ketones, and urinary nitrogen excretion (Prentice, Prentice, Lamb, et al., 1983).

Muscle and bone mass were also estimated by the Tanita scale, and higher bone and muscle mass predicted reduced maternal fasting. The scale has not, to the best of my knowledge, been validated for post-partum women and the numbers obtained were outside of an expected range, so these variables were excluded from the analysis. When included in the multivariate analyses of fasting, the output was relatively similar except that increased muscle mass tended to be a better predictor of reduced maternal fasting than other maternal anthropometry variables. This does not change the previous interpretation on maternal anthropometry; it is possible that maternal body composition, including weight, muscle mass and/or bone mass, cause reduced fasting in women, likely because they were also predictive of health conditions. However, another possibility is increased fasting results in decreased weight, bone mass, and muscle mass. A previous study on non-pregnant individuals observed a decrease in weight, body fat and bone mass but not muscle mass as measured via a bioimpedance scale (Fahrial Syam, Suryani Sobur, Abdullah, & Makmun, 2016), but pregnant women may experience different changes in body composition when fasting compared to non-pregnant individuals. If fasting causes maternal weight loss, the results of this study allude to the loss of muscle mass more than the loss of fat mass when fasting occurs in late pregnancy. Since fat mass is a large portion of maternal weight gain during healthy pregnancies and may be mobilized to meet energetic needs during lactation (Butte & Hopkinson, 1998; Møller, Við Streym, Mosekilde, & Rejnmark, 2012), fat mass may be preferentially maintained. Suboptimal weight gain during pregnancy can have negative consequences for fetal growth and development, so this possibility should be addressed with further research.

These data show that women who did not fast were different from women who did fast in ways that can confound the results of fasting on outcome variables like neonatal anthropometry. When pregnant women were overweight, diabetic or hypertensive, these biological characteristics may be relevant to outcomes of fasting on infant birth size and health. Infants of mothers should not be compared based on fasting behavior without controlling for maternal weight and diabetes or hypertension status.

Cultural and Environmental Characteristics and Fasting Behaviors

Only 11% of women in this sample opted out of fasting completely and 58% fasted every day of Ramadan that passed before labor, so fasting during pregnancy appears to be the norm.

There may be some sense of social pressure around maternal fasting, and previous research suggests there is a general sense of an obligation to fast if able (Mubeen et al., 2012). Some women in this study expressed a sense of internal pressure to fast, rather than external pressure. This sentiment is illustrated in the participant who said she would not listen to anybody who tried to tell her not to fast because she is a "good Muslim". As the main social predictors of reduced fasting were being advised not to fast by medical professionals or family members, this may indicate that the advice reduces social expectations of fasting during pregnancy.

Regardless of whether women said that they were encouraged by family members to fast, given neutral advice, or encouraged not to fast, most participants said that their families said something fairly similar: fast if she felt like she could and don't fast if she felt that she couldn't or shouldn't. Therefore, women who were fasting may have taken these similar words of advice as an encouragement to fast if they felt able, while women who decided not to fast may have taken the same advice as support for not fasting, or as neutral advice that did not try to influence them one way or the other. Overall, it can be interpreted that most women felt they had autonomy in making their own decisions about fasting.

When a participant reported that her family members advised her not to fast, participants were less likely to fast and fasted fewer days. Social support may have caused a decrease in fasting; if a woman's family advised her not to fast, she was less likely to do so. I observed this trend in people outside of the study sample in this region that were pregnant. For example, one of my research assistants was pregnant during Ramadan and said that she had not thought of not fasting until her husband advised her not to fast. Alternatively, it is also possible that participants said that they were advised not to fast because they had decided not to, and family members were expressing their support for the decision they had already made. The option not to fast appeared to be an accessible decision to most of the participants. Being advised by others against fasting or having that decision supported by family members may allow women to feel more comfortable with the option that is less often taken within the population.

About 10% of participants were advised not to fast by a medical professional, and, since all participants who reported having been medically advised not to fast stopped fasting immediately, it can be inferred that medical advice was taken seriously in this population. No woman who reported being medically advised not to fast was in the group of women who fasted daily. Medical advice against fasting was also predictive of fewer days spent fasting. However, this may not be generalizable to a larger population. In places where doctors are less likely to be Muslim, women have reportedly been less open about discussing their fasting decisions with their doctors and less inclined to take doctors' advice against fasting seriously without a persuasive rationale (Bachar et al., 2017; Robinson & Raisler, 2005). Medical advice against fasting was always due to a medical concern in this sample, but if more recommendations against fasting were given without a rationale, perhaps this advice would not have been as strongly heeded. In other words, medical advice may be so highly respected due to the fact that it is given with explanations and consideration for personal circumstances but not given as a blanket statement against maternal fasting. Doctors at this hospital often expressed the belief that women would not be fasting during pregnancy but, they also repeatedly stated that it is not their place to make recommendations about fasting unless they had reason to believe fasting would be harmful.

Taking vitamins other than iron was a predictor of fewer days fasted and reduced likelihood of any fasting and of fasting daily. This may be related to medical concerns and access to healthcare, increased education about prenatal health, and financial resources. Women who were taking vitamins were more likely to cite medical concerns as the reason they did not fast all or some of the month, and increased exposure to healthcare has been linked to increased prenatal vitamin supplementation in other populations (Gonzalez-Casanova et al., 2017; Nisar et al., 2014). It is also possible that increased awareness about maternal health and fetal health is related increased prenatal vitamin supplementation, as seen in other populations (Nguyen et al., 2017; Nisar et al., 2014). Mothers with increased awareness of prenatal health may have fasted less and been more likely to take vitamins. Purchasing vitamins is also not an insignificant cost to women of low socioeconomic status, so taking vitamins may be related to financial resources and family support (Cheng et al., 2018; Gonzalez-Casanova et al., 2017; Nguyen et al., 2017; Nisar et al., 2014). The hospital largely serves women from lower socioeconomic status communities, but vitamin intake may indicate that more financial resources and family support were available to a participant.

Maternal dress was not found to be a significant predictor of maternal fasting in this sample, but since sun exposure and vitamin D status may have implications for neonatal anthropometry and growth, future studies on maternal fasting and infant growth should consider maternal dress in the local population. This may be particularly relevant in less homogeneous populations, such as immigrant populations. For example, in permanent residents of a Muslim population in Colorado, Kopp (2002) found a direct relationship between religious practice and modest dress, and in the United States, the importance of religious practice has been found to also be predictive of fasting behavior (Fahmy & Mohamed, 2018).

Infant sex may additionally be relevant to maternal fasting behaviors. Although it was not overall predictive of fasting behavior, women who opted out of fasting daily for medical concerns were more likely to give birth to males. Because participants were not asked if they knew the sex of the infant prior to birth, the reason for the association between infant sex and reduced fasting is difficult to identify. If mothers or doctors knew the infant sex, this finding may be a product of cultural norms, such as son preference, which has been documented in this country (Obermeyer & Cárdenas, 1997). However, if infant sex was not known, this may reflect a biological phenomenon demonstrating sexually dimorphic maternal and fetal responses to the nutritional stress of fasting. The doctors at the hospital said that many patients live in remote areas without access to prenatal care and believe that only about half of the women who deliver at the hospital have an opportunity to learn the sex of the fetus. Given that the group of women who opted out of fasting did so due to medical advice and medical concerns, they more likely had access to medical and prenatal care. Therefore, the participants in this group were the most likely to have an opportunity to learn the sex of the infant. If infant sex is only predictive if mothers or doctors have knowledge of the infant's sex, infant sex may have been a stronger predictor of fasting behavior if more participants knew the sex of the infant. If women with medical concerns were more likely to opt out of fasting if they have male infants compared to female infants, male and female infants may be differentially exposed to fasting and any associated risks. Female infants of mothers with higher risk pregnancies may be more exposed to the compounded stress of the maternal health condition and consequences of food and water deprivation in utero.

Conclusion

Given the high prevalence of fasting in this sample, fasting during pregnancy appears to be the norm among the study population. Of the maternal characteristics that were investigated, the main predictors of reduced fasting during late pregnancy included having diabetes, hypertension, or anemia, having higher body weight and lower body fat, being advised not to fast by medical personnel or family members, and taking vitamins. Many of these maternal characteristics have implications for fetal growth. For example, infants of diabetic women are often larger (Brydon et al., 2000; Catalano, Kirwan, Haugel-De Mouzon, & King, 2003; Persson, Norman, & Hanson, 2009), infants of anemic women are often smaller (Scholl & Hediger, 1994), and maternal anthropometry is predictive of infant birth size (Kramer, 2003; Voigt et al., 2010). Having elucidated these potential confounding factors, Chapter 6 explores the effects of fasting on infant birth size in this sample.

Chapter 6: Results: Maternal Fasting and Outcomes: Neonatal Anthropometry

Maternal fasting during the month of Ramadan constitutes a physiological stressor that may influence fetal growth and birth outcomes, but research findings on the relationship between fasting during pregnancy and infant birth size have been inconsistent. This chapter aims to elucidate the associations between maternal fasting during late pregnancy and several infant anthropometric measurements as indicators of fetal growth. Prior to assessing the relationship between fasting and fetal growth, it is important to address the differences between women who fast and women who do not fast. Maternal characteristics, such as anthropometry and health status, were found in Chapter 5 to be associated with fasting behaviors, and these characteristics are also associated with variation in fetal growth. Therefore, relationships between neonatal anthropometry and non-fasting variables that may influence fetal growth were explored and controlled for in the analysis of neonatal anthropometry and fasting variables. These variables included those identified in Chapter 5 that varied between women who engaged in different fasting behaviors in this sample.

Studies on Ramadan fasting have had inconsistent findings on the relationship between in utero exposure to fasting in different trimesters and infant birth size. Few studies have used outcome variables other than birth weight and many have been based on population-level data without assessing actual fasting behavior. Fasting has been associated with a reduction in birth weight in Iranian, Lebanese, American and Indonesian populations (Almond & Mazumder, 2011; Awwad et al., 2012; Yamauchi et al., 2009; Ziaee et al., 2010). One study included birth weight, length, and head circumference. The researchers found fasting during the first trimester to be associated with an increased relative risk of 1.5 of having a low birth weight infant but no other relationships between fasting during any trimester and anthropometry (Ziaee et al., 2010). In a study by Almond and Mazumder (2011) fasting was significantly associated with reduced birth weight when Ramadan occurred during the first and second trimesters, whereas in the study by

Yamauchi et al. (2009), the reduction in birth weight was seen in infants born shortly after the month of Ramadan. Several studies have also not found birth weight to be related to Ramadan fasting. Two studies that spanned several years found non-significant increases in low birth weight infants when Ramadan occurred during the second trimester but no other indications that fasting may reduce birth weight (Arab & Nasrollahi, 2001; Cross et al., 1990). Kavehmanesh and Abolghasemi (2004) did not find fasting to be associated with reduced gestational age at birth or with infant birth weight after controlling for maternal arthrometry. None of these studies stated if gestational age was controlled for in the analysis, though it may have been. Also, one study Ramadan fasting demonstrated that fasting during the second trimester was associated with reduced gestational length (Tith et al., 2019), but three other studies have not found evidence of reduced gestational length (Awwad et al., 2012; Hefni, 1993; Kavehmanesh & Abolghasemi, 2004)

Analyses of infant anthropometric variables other than birth weight in relationship with maternal fasting are lacking, but other variables associated with growth and development have been considered. Alwasel et al. (2010) found reduced placental weight and reduced placental to birth weight ratio in infants of mothers who had fasted in the second and third trimesters but not the first trimester. Birth weight was not significantly different, but their results suggest that fasting may result in reduced uterine blood flow. The study by Almond and Mazumder (2011) demonstrated a higher risk of disabilities when in utero exposure to Ramadan occurred very early in the gestational period in populations in Iran and Uganda, although birth weight data were not analyzed in that portion of the study. Taken together, these studies should convey the importance of considering outcome variables beyond birth weight. Moreover, the lack of associations between fasting and birth weight should not lead to the conclusion that fetal growth and development are not otherwise affected by maternal fasting, as birth weight does not adequate indicator of intrauterine environmental stress (Lumey & Van Poppel, 1994; Parsons, Power, & Manor, 2001; Aryeh D Stein et al., 2004).

Inconsistent results in outcomes associated with fasting are not surprising given the high variability in the practice of Ramadan fasting, as discussed in Chapter 2. Outcomes of fasting likely vary by population, location, and year, as the number of fasting hours per day can be fewer than seven or more than 16 depending on the year and location. Climate patterns, physical activity, and duration of fasting may make the risk of spending a long duration of the fasting hours in a dehydrated state more extreme for some populations and in some year. Physical activity levels, sleep patterns, and dietary changes during non-fasting hours are also variable. Ramadan fasting requires several hours per day of abstinence from food and water but does not necessarily result in reduced caloric intake (Bakhotmah, 2011), so the effects of Ramadan fasting on fetal growth may not be well-captured by studies of food scarcity, caloric restriction, or malnutrition during pregnancy. Rather, it may be better modeled by research on dehydration (Mulyani, Hardinsyah, Briawan, & Santoso, 2018) and hormonal changes involved in the fasting state, including cortisol (Bolten et al., 2011; Christian, 2012; Li et al., 2012), although not likely associated with the psychological stress that accompanies situations of food or water insecurity (Wutich & Ragsdale, 2008). In women in late pregnancy who are already energetically stressed, Ramadan fasting has also been shown to induce a state of accelerated starvation, even with dietary supplements (Prentice, Prentice, Lamb, et al., 1983), which indicates that Ramadan's impact on physiology is beyond what would be expected by daily caloric restriction alone.

The present analysis tested the hypothesis that maternal fasting in late pregnancy is associated with reduced birth size, with the prediction that reduced infant size at birth would follow trends that are comparable to other findings of acute nutritional stress during late pregnancy. This includes reduced ponderal index, arm circumference, and skinfold measurements as evidence of increased leanness at birth (Villar, Altobelli, Kestler, & Beliźan, 1986), and reduced weight, length, head circumference, and ponderal index, as was seen in late pregnancy exposure to the Dutch Hunger Winter (Aryeh D Stein et al., 2004). Additionally, based on evidence from the

Dutch Hunger Winter, which demonstrated that reductions in birth size rebounded within weeks of the discontinuation of exposure to the famine (Aryeh D Stein et al., 2004), in utero catch-up growth was expected with an increased duration between the last day of fasting and birth.

In this analysis, infant anthropometry outcomes included birth weight, as recorded by the hospital staff at the time of birth, and neonatal weight, length, head circumference, arm circumference, triceps skinfold, and subscapular skinfold measurements, which I took three days postpartum on average. Outcome variables also included the sum of triceps and subscapular skinfold measurements and ponderal index, a weight to length ratio that indicates infant leanness and was calculated based on both birth weight and neonatal weight. For infants with known gestational age at birth, z-scores for birth weight, neonatal weight, length, and head circumference were also calculated based on reference data from the hospital (Radouani et al., 2015). Gestational age based on the first day of the last menstrual cycle was also included as an outcome variable, as a reduction in gestational age at birth would be predicted if maternal fasting accelerates the offspring life history trajectory. However, even with precise records of last menstrual period or access to refined measurements of gestational age such as can be attained with ultrasound, detecting shifts in gestational age requires a large sample size and therefore is not likely to be perceptible in this study.

Participant Overview

Of the 92 mother-infant pairs in this study, infant anthropometry and gestational age were available for a subset of the sample. Most infants (87) had birth weight data, recorded by a doctor at the time of birth and documented during the enrollment questionnaire. Seventy-five infants were available for additional anthropometric measurements at approximately 48-72 hours after birth. To differentiate the two weight measurements, the weight taken by the doctor at the time of birth is referred to as birth weight, and the weight at 48-72 hours postpartum is referred to as neonatal weight. Of the infants with birth weight data and with neonatal weight, gestational age was known for 60 infants and 46 infants, respectively. Therefore, the participants included in this study were divided into subsamples of those with birth weight, birth weight, and gestational age, neonatal weight, and neonatal weight and gestational age. Before summarizing infant anthropometry, I provided an overview of the participants comprising each subsample, summarizing infant sex and maternal characteristics including anthropometry, reproductive history, health concerns, style of dress, and vitamin intake. These variables were also considered for their potential confounding effects in the analysis of maternal fasting during pregnancy and birth outcomes.

Infant Sex

The number of male and female infants in the study was close to fifty percent in all subsets (Table 6.1).

Table 6.1: Summary of Infant Sex by Participant Subsample

	Participants with Infant Birth Weight		**Participants with Birth Weight and Gestational Age**		**Participants with Neonatal Weight**		**Participants with Neonatal Weight and Gestational Age**	
Infant Sex	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Male	46	53%	30	51%	40	53%	23	50%
Female	41	47%	29	49%	35	47%	23	50%

Maternal Anthropometry

Postpartum maternal anthropometry was detailed in Chapter 5 for all women who participated in this portion of the study. Maternal anthropometry was similar across subsets, but among the subsets with known gestational ages, the average age was slightly lower and anthropometric measurements were slightly higher (Table 6.2).

Table 6.2: Summary of Maternal Anthropometry per Participant Subsample

	Participants with Infant Birth Weight		**Participants with Birth Weight and Gestational Age**	
Maternal Anthropometry	**N**	**Mean ± St Dev (Range)**	**N**	**Mean ± St Dev (Range)**
Age	76	30.7 ± 6.7 (18-45)	49	29.6 ± 6.4 (18-45)
Height	79	159.1 ± 6.1 (147-175)	51	160.6 ± 5.9 (147-175)
Weight	72	69.1 ± 14.6 (45.5-109.6)	45	71.5 ± 14.9 (45.5-109.6)
BMI	72	27.3 ± 5.1 (17.9-42.4)	45	27.7 ± 4.9 (17.9-42.1)
Body Fat	71	33.3 ± 7.4 (13.1-50.1)	44	33.8 ± 7.7 (13.1-50.1)
	Participants with Neonatal Weight		**Participants with Neonatal Weight and Gestational Age**	
Age	73	30.9 ± 6.5 (18-45)	45	29.9 ± 6.1 (18-45)
Height	75	159.3 ± 6.0 (148-175)	46	161.0 ± 5.6 (149-175)
Weight	72	69.3 ± 14.5 (45.5-109.6)	44	71.9 ± 14.8 (45.5-109.6)
BMI	72	27.3 ± 5.1 (17.9-42.4)	44	27.7 ± 5.0 (17.9-42.1)
Body Fat	71	33.4 ± 7.3 (13.1-50.1)	43	34.0 ± 7.7 (13.1-50.1)

Other Maternal Characteristics

Table 6.3: Summary of Maternal Characteristics per Participant Subsample

	Infant Birth Weight		**Birth Weight and Gestational Age**		**Neonatal Weight**		**Neonatal Weight and Gestational Age**	
Reproductive History	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Primiparous	30	34%	25	42%	23	31%	17	37%
Primigravida	28	33%	23	39%	21	28%	15	32%
History of Miscarriage	19	22%	12	20%	18	24%	11	24%
Maternal Health								
Any Maternal Health Concern	49	56%	34	58%	41	55'%	26	43%
Diabetic	6	7%	3	5%	5	7%	2	4%
Hypertensive	8	9%	5	8%	6	8%	3	7%
Diabetic and/or Hypertensive	11	13%	7	12%	9	12%	5	11%
Anemic	21	24%	13	22%	18	24%	10	22%
Other Health Conditions	28	32%	21	36%	24	32%	17	37%
Maternal Style of Dress								
More Conservative Dress	71	84%	49	84%	61	84%	38	84%
Maternal Vitamin Intake								
Took Any Vitamin	74	85%	52	88%	64	85%	41	89%
Took Any Vitamin Other than Iron	16	18%	14	24%	16	21%	13	28%

Table 6.3 summarizes maternal reproductive history, health, style of dress, and vitamin intake by subsample. All subsets of women had similar percentages of participants in each category. There was some variability between groups in the percentage of women who were primiparous, ranging from 31-42% and primigravida, ranging from 28-39%.

Differences in percentages in participants with maternal health concerns were minimal, but in the category of participants with neonatal anthropometry and known gestational ages, less than half of women reported any health condition (43%), whereas in the other subsample, the percentage of women reporting health conditions was between 55-58%. Anemia had the highest prevalence of reported health conditions in this sample, followed by hypertension and diabetes.

Three individuals had both hypertension and diabetes, but the conditions were considered separately in this analysis as their effects on fetal growth are different. Several other health conditions were reported but by two or fewer women, so these conditions were combined into the other health conditions category. These conditions included hypotension, hypoglycemia, back pain, exhaustion, and being a smoker, among other things.

There were no evident differences in style of dress across subsample. Maternal dress style was categorized as either more conservative/ traditional or less conservative/ more modern. More conservative and traditional dress included women who wore the hijab (only hands and face exposed to sun) or niqab (only eyes exposed). Less conservative and more modern dress included women who had increased sun exposure than if wearing the hijab, including at least face and neck, forearms or feet, and possibly arms and calves.

Variation in vitamin intake was minimal across subsamples. All but one woman who reported taking any vitamin was taking iron. Some women took vitamins other than iron, which included multivitamins, folate, magnesium, and vitamin D, and sometimes women did not know what vitamins they were taking. There was some variability in women taking vitamins other than iron, ranging from 18% of participants in the largest group based on just birth weights to 28% when restricting the sample to only participants with neonatal weight and known gestational age.

Overview of Outcome Variables: Infant Gestational Age and Anthropometry

Weight was recorded at the time of birth for eighty-seven infants, and seventy-five infants were available for neonatal measurements 48-72 hours after birth. Neonatal measurements included weight, length, head circumference, arm circumference, triceps skinfolds, and subscapular skinfolds. Due to constraints of infant clothing, as discussed in Chapter 4, not all measurements were taken for all infants. Ponderal index and the sum of the triceps and subscapular skinfold measurements were included in this analysis. Additionally, gestational age estimates were available for about two-thirds of the participants. Z-scores were calculated based on gestational age for birth weight, neonatal weight, length, and head circumference based on reference data from the hospital (Radouani et al., 2015). Z-scores were calculated only for full-term infants (37 weeks or older) with known gestational ages.

The following tables summarize each infant anthropometric variable that was assessed for a relationship to maternal fasting variables, divided by the subsets relevant to the following analysis. Table 6.4 provides an overview of birth weight data, categorized by those all infants and infants with additional gestational age data. Table 6.5 describes infants with neonatal anthropometric measurements, categorized by all infants with neonatal measurements and those with additional gestational age data. One participant with neonatal measurements did not have a recorded birth weight. Gestational age and birth weight for infants with neonatal measurements were also summarized for this subset. Averages z-scores for birth weight, length, and head circumference in this sample were significantly higher than zero ($p<0.022$, 0.000, and 0.000 respectively). Enrollment in this study was limited to women who would spend 48-72 hours in the maternity ward after giving birth, which limited participation to predominantly women who had given birth by cesarean section. This might be a reason for higher z-scores. Additionally, the doctors commented frequently that rates of cesarean deliveries were highest during the summertime, so it is also possible that this observation was driven by seasonal trends in fetal growth.

Table 6.4: Overview of Birth Weight Data, Categorized by All Infants with Recorded Birth Weight and Infants with Additional Gestational Age Data

	Participants with Birth Weight Measurement		**Participants with Birth Weight and Gestational Age**	
Infant Anthropometry	**N**	**Mean ± St Dev (Range)**	**N**	**Mean ± St Dev (Range)**
Gestational Age			60	39.1 ± 2.5 (27-42)
Birth Weight (g)	87	3,453 ± 636 (1,500-5,370)	59	3,439 ± 643 (1,500-4,910)
Birth Weight z-scores			56	0.34 ± 1.09 (-1.80-3.60)

Table 6.5: Overview of Infant Anthropometry, Categorized by All Infants with Neonatal Measurements and Infants with Additional Gestational Age Data

	Participants with Neonatal Weight		**Participants with Neonatal Weight and Gestational Age**	
	N	**Mean ± St Dev (Range)**	**N**	**Mean ± St Dev (Range)**
Infant Anthropometry				
Gestational Age			46	39.6 ± 1.4 (36-42)
Birth Weight (g)	74	3,512 ± 603 (2280-5370)	46	3,530 ± 591 (2400-4910)
Birth Weight z-score			45	0.40 ± 1.11 (-1.73-3.60)
Neonatal weight (g)	75	3,394 ± 589 (2,260-5,400)	46	3,422 ± 553 (2,320-4940)
Neonatal Weight z-scores			45	0.06 ± 1.00 (-2.03-2.99)
Length (cm)	74	51.0 ± 2.4 (44-57)	46	51.2 ± 2.3 (47.5-55)
Length z-scores			45	0.93 ± 0.70 (-0.20-2.60)
Ponderal Index based on birth weight	73	2.65 ± 0.27 (2.04-3.51)	46	2.62 ± 0.27 (2.08-3.04)
Ponderal Index based on neonatal weight	74	2.51 ± 0.26 (1.88-3.49)	46	2.50 ± 0.24 (2.12-3.02)
Head Circumference (cm)	70	35.6 ± 1.3 (33-38.3)	43	35.7 ± 1.3 (33.5-38.3)
Head Circumference z-scores			42	1.21 ± 0.78 (-0.10-3.16)
Arm Circumference	70	11.1 ± 1.3 (8.5-14)	43	11.1 ± 1.3 (8.5-14)
Sum of Triceps and Subscapular Skinfold	69	8.7 ± 2.4 (4-15)	42	8.9 ± 2.2 (4-14)
Triceps Skinfold (mm)	70	4.4 ± 1.1 (2-7)	43	4.4 ± 1.1 (2-7)
Subscapular Skinfold (mm)	69	4.4 ± 1.3 (2-8)	42	4.5 ± 1.3 (2-8)

Analysis of the Association between Fasting Behaviors and Neonatal Anthropometry

As discussed in chapter 5, maternal fasting behaviors were related to several maternal characteristics that may also be related to fetal growth and infant birth size, including maternal anthropometry and health. These differences may confound associations between fasting and neonatal anthropometry. Linear regressions and t-tests were used to identify maternal biological, environmental and cultural characteristics that were related to neonatal anthropometry. Variables relevant to infant anthropometry were then added to multivariate analyses with fasting variables to clarify the relationship between maternal fasting and infant anthropometry.

Fasting was quantified in four ways: any fasting versus no fasting, fasting every day of Ramadan that passed prior to labor versus no or some fasting, the number of days fasted, and the number of days between fasting and labor. Fasting behaviors were summarized in Chapter 5, Table 5.3. Each neonatal anthropometry outcome variable was assessed for its relationship to each fasting variable in univariate analysis, with t-tests used for the two categorical variables and pairwise correlations used for the two continuous variables. Stepwise multivariate analysis was then used to determine if fasting was correlated with neonatal anthropometry after controlling for the other previously identified variables, with the significance level set to 0.20. Infant sex, maternal height, BMI, and body fat were included in the model, regardless of whether they were significant in the univariate analysis. Maternal weight was not be included since BMI was added to the model.

Gestational age was included as a dependent variable but is expected to be related to other infant anthropometric variables. Gestational age was recorded by the medical staff for 60 infants total and 46 infants who also had neonatal anthropometric measurements. Adding gestational age to the multivariate analyses reduced the sample size, but, since this variable was associated with infant anthropometric variables, the multivariate analyses were run with and without gestational age.

It would be hypothesized that any association between fasting duration and infant birth size would be attenuated by an increased number of days between fasting and labor. Therefore, the multivariate analyses of these two independent variables were combined and both were added. Infant birth size could have varied over the course of the study, so to control for this possibility, the study duration was included in multivariate analyses with days fasted and days between fasting and labor and discussed if significant.

Infant Anthropometry and Potentially Confounding Variables

Before analyzing the associations between maternal fasting and infant birth size, I explored potentially confounding variables. These variables included gestational age at birth for infants with this data, infant sex, maternal reproductive history, maternal anthropometry, health, style of dress, and vitamin intake. Study duration was also summarized to address changes in anthropometry through the course of the study. Any variables with a p-value of less than 0.10 were considered possible confounding factors and were included in the following multivariate analyses with fasting variables, and infant anthropometry variables that were not associated with the independent variable of interest at this significance level were not shown in the following tables.

Gestational Age

Gestational age is expected to be relevant to neonatal size. Table 6.6 provides a summary of pairwise correlations of gestational age with infant anthropometry. Infants with later gestational ages had higher birth weights, were longer, and had larger head circumferences. They also had lower ponderal indexes and were, therefore, thinner at higher gestational ages. Although z-scores account for gestational age, infants had higher average length and head circumference z-scores at later gestational ages.

Table 6.6: Pairwise Correlations Between Gestational Age and Infant Anthropometry

Infant Anthropometry	**Gestational Age**
Birth Weight	R=0.46**
Length (cm)	R=0.42**
Length Z-score	R=0.44**
Ponderal Index at Birth	R= -0.25^
Head Circumference (cm)	R=0.33*
Head Circumference Z-scores	R=0.41**
Legend:	**=p<.01 *=p<0.05 ^= NS but meets inclusion criteria for multivariate analysis (p<0.1)

Infant Sex

Neonatal anthropometry differed by sex (Table 6.7). Male infants had higher average weight, length, head circumference, and arm circumference compared to female infants. There were no significant differences in skinfold measurements or gestational age at birth by infant sex. To note, univariate analyses did not show a relationship between infant sex and maternal fasting variables, and maternal health concerns did not vary by infant sex. However, based on a chi-squared test with categorized reasons for opting out of fasting, women with male infants were more likely to opt out of fasting for medical reasons ($p<0.043$) and in all but one of the seven cases in which a woman was ordered not to fast by a doctor and infant sex was known, the infant was male. Although reasons for these differences in maternal fasting and medical advice may be cultural or biological, they do suggest that infant sex may play a role in fasting decisions and therefore may be a confounding variable in this analysis beyond the expected difference in infant size at birth by sex.

Table 6.7: Infant Anthropometry by Infant Sex (T-Tests)

	Male Infants		Female Infants		p-value (one-tailed)
	N	Mean ± St. Err	N	Mean ± St. Err	
Birth Weight (g)	46	3,614 ± 93	41	3,273 ± 94	0.006
Birth Weight z-score	28	0.69 ± 0.20	28	-0.01 ± 0.19	0.008
Neonatal Weight (g)	40	3,555 ± 89	35	3,221 ± 97	0.006
Neonatal Weight z-scores	22	0.38 ± 0.21	23	-0.24 ± 0.19	0.018
Length (cm)	40	51.7 ± 0.4	34	50.1 ± 0.4	0.002
Length z-score	22	1.14 ± 0.15	23	0.72 ± 0.14	0.022
Head Circumference (cm)	40	36.0 ± 0.2	30	35.1 ± 0.2	0.002
Head Circumference z-scores	22	1.44 ± 0.16	20	0.95 ± 0.16	0.020
Arm Circumference	40	11.4 ± 0.2	30	10.7 ± 0.2	0.007

Reproductive History

First-time mothers have been found to have a higher risk of low birth weight and small for gestational age infants (Shah, 2010). In this sample, birth weight, birth weight z-scores, and length z-scores were lower in primiparous mothers (Table 6.8). Trends were similar primigravida mothers (Table 8), as infants had lower average birth weight, birth weight z-scores, and length z-scores, and gestational age was also about one week shorter in primigravida mothers.

Table 6.8: Infant Anthropometry by Primiparous Versus Multiparous and Primigravid versus Multigravida Mothers (T-Tests)

	Primiparous		**Multiparous**		**p-value (one-tailed)**
	N	**Mean ± St. Err**	**N**	**Mean ± St. Err**	
Gestational Age	25	38.5 ± 0.65	34	39.5 ± 0.3	0.057
Birth Weight (g)	30	3,208 ± 108	57	3,582 ± 83	0.004
Birth Weight z-score	23	-0.01 ± 0.17	33	0.59 ± 0.21	0.020
Length z-score	17	0.67 ± 0.12	28	1.08 ± 0.14	0.027
	Primigravid		**Multigravida**		
Gestational Age	24	38.4 ± 0.7	36	39.5 ± 0.3	0.045
Birth Weight (g)	28	3,196 ± 114	58	3,562 ± 81	0.005
Birth Weight z-score	21	-0.35 ± 0.19	35	0.56 ± 0.20	0.022

Neonatal Anthropometry and Maternal Anthropometry

As discussed in Chapter 5, maternal anthropometry was associated with fasting behavior in this sample. Therefore, it is important to acknowledge how maternal anthropometry and neonatal anthropometry were related before comparing infants of women with different fasting behaviors. Several infant anthropometric measurements were positively correlated with maternal anthropometry (Table 6.9). Maternal weight was correlated with birth weight, and maternal BMI was correlated with neonatal weight z-scores. Maternal weight, BMI, and body fat percentage were correlated with arm circumference, triceps skinfold, and subscapular skinfolds. Maternal height was correlated with neonatal length and head circumference. Gestational age and ponderal index were not associated with any maternal anthropometric variables in univariate analysis.

Table 6.9: Pairwise Correlations Between Maternal Anthropometry And Infant Anthropometry

	Maternal Anthropometry				
Infant Anthropometry	Age	BMI	Weight	Height	Body Fat
Gestational Age at Birth					
Length (cm)			R=0.22^	R=0.29*	
Length Z-scores					
Birth Weight		R=0.21^	R=0.24*		
Birth weight Z-score	R=0.28^	R=0.29^	R=0.27^		
Weight at 48-72 hours (g)			R=0.23^	R=0.23^	
Neonatal Weight Z-scores	R=0.27^	R=0.31*	R=0.28^		
Ponderal Index at Birth					
Ponderal Index at 48-72 hours					
Head Circumference (cm)				R=0.25*	
Head Circumference Z-scores					
Arm Circumference		R=0.26*	R=0.27*		
Triceps skinfold		R=0.27*	R=0.27*		R=0.25*
Subscapular skinfold		R=0.32**	R=0.32**		R=0.31*
Sum of Triceps and Subscapular Skinfold		R=0.32**	R=0.32**		R=0.30*
Legend:	**=p<.01 *=p<0.05 ^= NS but meets inclusion criteria for multivariate analysis (p<0.1)				

Maternal health

Maternal health conditions can have varied effects on fetal growth. Some reported conditions have been associated with increased fetal growth, such as diabetes, while others have been associated with reduced fetal growth, such as being a smoker (only one participant in the sample reported smoking). In this sample, reporting any health concern was not significantly associated with differences in neonatal anthropometry. Any maternal health concern met the inclusion criteria for the multivariate model for z-scores for birth weight and neonatal weight (Table 6.10).

Table 6.10: Infant Anthropometry by Any Health Concern (T-tests)

	No Health Concerns		**Any Health Concern**		**p-value (two-tailed)**
	N	**Mean ± St. Err**	**N**	**Mean ± St. Err**	
Birth Weight z-scores	24	0.05 ± 0.22	32	0.56 ± 0.18	0.084
Neonatal Weight z-scores	19	-0.26 ± 0.23	26	0.29 ± 0.19	0.063

Specific health conditions reported among participants include diabetes, hypertension, anemia, and any other condition. Infant anthropometry did not vary by mothers who have hypertension or that were in the other health conditions category.

Of the six diabetic participants, one had Type 1 diabetes, one had Type 2 diabetes, and four had gestational diabetes. As increased fetal growth may result from maternal diabetes during pregnancy (Brydon et al., 2000; Catalano et al., 2003; Persson et al., 2009), infants of diabetic women were hypothesized to be larger than infants of non-diabetic women. Diabetes was associated with increased measurements for several neonatal anthropometry variables (Table 6.11). Average neonatal ponderal index, weight at birth and at three days, arm circumference, and length were higher in infants of mothers with diabetes.

Table 6.7: Infant Anthropometry by Diabetic Status (T-tests)

	Not Diabetic		**Diabetic**		**p-value (one-tailed)**
	N	**Mean ± St. Err**	**N**	**Mean ± St. Err**	
Birth Weight (g)	81	3,400 ± 67	6	4,162 ± 339	0.002
Birth Weight z-scores	53	0.25 ± 0.14	3	1.96 ± 0.91	0.003
Neonatal weight (g)	70	3,348 ± 64	5	4,116 ± 399	0.002
Neonatal Weight z-scores	43	-0.03 ± 0.14	2	1.95 ± 0.61	0.003
Length (cm)	69	50.1 ± 0.3	5	52.8 ± 0.7	0.035
Length z-scores	43	0.88 ± 0.10	2	1.98 ± 0.61	0.013
Ponderal Index based on birth weight	68	2.63 ± 0.03	5	2.94 ± 0.16	0.006
Ponderal Index based on neonatal weight	69	2.50 ± 0.03	5	2.74 ± 0.21	0.019
Arm Circumference	66	11.0 ± 0.2	4	12.4 ± 0.4	0.020
Subscapular Skinfold (mm)	65	4.3 ± 0.2	4	5.3 ± 0.9	0.091

Although some research suggests that iron deficiency and anemia increases the risk for low birth weight infants (Scholl & Hediger, 1994), in this sample, infants of anemic mothers had higher birth weight z-scores and lower gestational age at birth (Table 6.12).

Table 6.8: Infant Anthropometry by Anemic Status (T-tests)

	Non-Anemic		**Anemic**		**p-value (two-tailed)**
	N	**Mean ± St. Err**	**N**	**Mean ± St. Err**	
Gestational Age	46	39.4 ± 0.2	14	38.1 ± 1.2	0.083
Birth Weight z-scores	45	0.22 ± 0.16	11	0.82 ± 0.3	0.100

Style of dress

More conservative dress has been associated with reduced sun exposure, hypovitaminosis D, and poor infant growth outcomes (Leffelaar, Vrijkotte, & Van Eijsden, 2010; Nabulsi et al., 2008), so infant anthropometry is hypothesized to be lower among infants of more conservatively dressed mothers. In this sample, arm circumference and triceps skinfold measurements were reduced in infants of more conservatively dressed mothers. Gestational age was significantly lower when including pre-term infants (Table 6.13).

Table 6.93: Infant Anthropometry by Maternal Style of Dress (T-tests)

	More Conservative Dress		**Less Conservative Dress**		**p-value (one-tailed)**
	N	**Mean ± St. Err**	**N**	**Mean ± St. Err**	
Gestational Age	50	38.4 ± 03	9	37.7 ± 1.5	0.031
Arm Circumference	56	11.0 ± 0.2	12	11.8 ± 0.3	0.025
Sum of Triceps and Subscapular Skinfold	56	8.5 ± 0.3	11	9.5 ± 0.9	0.097
Triceps Skinfold (mm)	56	4.2 ± 0.1	12	4.9 ± 0.24	0.025

Maternal dress may indicate differences in urban versus rural living and therefore different subsistence strategies, differential access to health care, and different health and nutritional risks. The relationship between maternal dress, maternal anthropometry, and reproductive history was assessed. Using two-tailed t-tests, only maternal age was associated with the style of dress; women who dressed more conservatively averaged about five years older than less conservatively dressed women (31.4 ± .8 years old compared to 26.7 ± 1.6 years old, $p<0.02$). Maternal age was not associated with any neonatal anthropometric measurements, so this is not likely a confounding factor in this sample.

More conservatively dressed mothers were also more likely to be multiparous and multigravida than less conservatively dressed women ($p<0.007$). More conservative dress was associated with a greater likelihood of having had one or more miscarriages (Fisher's exact chisquare p<0.019), which could be related to the relationship between higher maternal age and both higher likelihood of having had a miscarriage and more conservative dress.

Vitamin intake

Taking iron and other vitamins can have a significant impact on fetal growth (Cogswell, Parvanta, Ickes, Yip, & Brittenham, 2003; Preziosi et al., 1997; Ribot et al., 2013), so infants of mothers who took vitamins were predicted to be larger. In this sample, mothers who took any vitamin and that took iron specifically had infants with higher length z-scores and these variables met the inclusion criteria for the multivariate analysis for several other infant anthropometric measurements (Table 6.14).

Table 6.10: Infant Anthropometry by Supplementation with Any Vitamin and Any Vitamin Other Than Iron (T-tests)

	No Vitamin		**Any Vitamin**		**p-value (1-tailed)**
	N	**Mean ± St. Err**	**N**	**Mean ± St. Err**	
Gestational Age (weeks)	7	37.9 ± 0.7	53	39.2 ± 0.34	0.084
Birth Weight z-scores	5	-0.35 ± 0.26	51	0.41 ± 0.15	0.068
Neonatal Weight z-scores	4	-0.56 ± 0.31	41	0.25 ± 0.16	0.068
Length z-scores	4	0.26 ± 0.16	41	0.99 ± 0.11	0.024
Sum of Triceps and Subscapular Skinfold (mm)	10	7.8 ± 0.84	59	8.9 ± 0.30	0.099
Subscapular Skinfold (mm)	10	3.8 ± 0.50	59	4.5 ± 0.17	0.072
	No Vitamin or Iron Only		**Any Vitamin Other Than Iron**		
	N	Mean ± St. Err	N	Mean ± St. Err	
Birth Weight z-scores	43	0.22 ± 0.15	43	0.75 ± 0.36	0.062
Neonatal Weight z-scores	32	-0.08 ± 0.16	13	0.40 ± 0.34	0.076
Length z-scores	32	0.81 ± 0.11	13	1.20 ± 0.23	0.045

Fasting and Infant Anthropometry

Maternal fasting behavior is quantified in 4 ways: no fasting versus any fasting, fasting daily versus occasional fasting, the number of days fasted, and days between fasting and labor. These variables were summarized in Chapter 5, Table 5.3. If fasting influences fetal growth, infants of fasting mothers were hypothesized to be smaller than infants of non-fasting mothers. However, women who fast were different from women who do not fast in various ways, as discussed in Chapter 5, so differences between their infants may be due to factors other than fasting.

Some women in this study felt they could fast every day of Ramadan that passed prior to labor whereas others did not, often for health reasons, medical advice, or feeling unable to due to non-medical reasons such as thirst or dizziness. Women who did not feel they could fast daily may have made different fasting decisions due to an increased sense of risk associated with fasting with a medical concern or they may be different in other ways that made the experience of fasting more difficult. The daily fasting variable could, therefore, be more indicative of differences between women than differences in fasting behaviors. Women who fasted daily did fast about 8 days longer than women who did not fast daily, which was significant in a t-test (20.8 days versus 12.4 days, $p<0.000$), so if daily fasting is significantly associated with infant anthropometry after controlling for other possible contributors, it may be due to the difference in average fasting duration between groups, although it is also possible that a confounding variable was not accounted for in the analysis. Any fasting versus non-fasting and number of days fasted were expected to capture the relationship between maternal fasting and birth outcomes, and days between fasting and labor was included to identify whether fetal growth trajectories varied after maternal fasting was discontinued, given the possibility of in utero catch-up growth.

Fasting Versus Non-Fasting

Fasting during pregnancy was predicted to reduce fetal growth, so infants of women who participated in any fasting were hypothesized to be smaller than infants of non-fasting women. Before adjusting for other variables, an analysis of these data supports this hypothesis. T-tests indicated that any fasting was associated with reduced birth weight and neonatal weight z-scores, length and length z-scores, and head circumference and head circumference z-scores (Table 6.15). All infant anthropometric variables were analyzed in multivariate regressions to assess if any fasting remained or became associated with infant anthropometry after controlling for other variables.

Table 6.11: T-tests: Gestational Age and Infant Anthropometry by Non-Fasting Versus Fasting (T-Tests)

	Non-fasting		Fasting		p-value (one-tailed)
	N	**Mean ± St. Err**	**N**	**Mean ± St. Err**	
Gestational Age	10	38.2 ± 1.3	50	39.3 ± 0.3	NS
Birth Weight (g)	11	3,505 ± 241	76	3,385.6 ± 124.06	NS
Birth Weight z-scores	9	0.96 ± 0.35	47	0.22 ± 0.15	0.031
Neonatal weight (g)	8	3,588 ± 165	67	3,377 ± 73	NS
Neonatal Weight z-scores	7	0.64 ± 0.35	38	-0.05 ± 0.16	0.050
Length (cm)	8	52.7 ± 0.8	66	50.8 ± 0.3	0.013
Length z-scores	7	1.52 ± 0.28	38	0.82 ± 0.10	0.006
Ponderal Index based on birth weight	8	2.59 ± 0.07	65	2.65 ± 0.03	NS
Ponderal Index based on neonatal weight	8	2.41 ± 0.03	66	2.53 ± 0.06	NS
Head Circumference (cm)	7	36.5 ± 0.5	63	35.5 ± 0.2	0.031
Head Circumference z-scores	6	2.02 ± 0.27	36	1.07 ± 0.12	0.002
Arm Circumference	7	11.2 ± 0.4	63	11.1 ± 0.2	NS
Sum of Triceps and Subscapular Skinfold	7	9.9 ± 0.8	62	8.7 ± 0.3	NS
Triceps Skinfold (mm)	7	4.4 ± 0.2	63	4.3 ± 0.2	NS
Subscapular Skinfold (mm)	7	4.6 ± 0.6	62	4.3 ± 0.2	NS

Gestational age

Variables identified in the univariate analyses for inclusion in the multivariate analysis of gestational age include style of dress, parity, gravida, any vitamin supplementation during pregnancy, and anemia. Any fasting was not associated with gestational age in univariate or multivariate analyses. In the multivariate analysis, the only significant predictive variable related to later gestational age was taking any vitamin.

Birth Weight

Neither birth weight nor neonatal weight varied by any fasting versus no fasting in univariate analysis. Neonatal weight was positively correlated with maternal weight and height, was higher in male infants and in mothers with diabetes; any fasting remained unpredictive of neonatal weight controlling for these variables in the multivariate analysis. Birth weight was also positively correlated with maternal weight, and maternal BMI was higher in male infants and in mothers who were multiparous, multigravida, or diabetic. In the multivariate model without gestational age, any fasting was not significantly associated with birth weight. When adding gestational age to the model, fasting was retained as a significant predictor of birth weight (Table 6.16). However, gestational age was not retained in the model as a covariate, so the change may have resulted from restricting the sample size to the population with gestational age measurements rather than due to controlling for gestational age.

Table 6.16: Multivariate Linear Regression of Any Fasting with Other Predictors (Including Gestational Age) of Birth Weight

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
Infant Sex (Female)	-620	0.000
BMI	20	0.161
Diabetes	823	0.012
Multiparous	239	0.110
Any Fasting	-413	0.034

Z-scores

Both birth weight z-scores and neonatal weight z-scores were positively correlated with maternal weight, BMI, and age. They were higher for male infants and for infants of mothers who took any vitamin, took any vitamin other than iron, reported any maternal health concern, had anemia and had diabetes. They were higher in infants of non-fasting women than women who engaged in any fasting. Birth weight z-scores were also higher in mothers who were multiparous or multigravida. In multivariate analysis, any fasting was retained as a significant variable in predicting reduced birth weight z-scores, along with being female, lower maternal BMI, not having diabetes, and not taking any vitamin (Table 6.17). Any fasting was retained as a predictor of neonatal weight z-scores but not significant (p<0.059).

Table 6.17: Multivariate Linear Regression of Any Fasting with Other Predictors of Birth Weight Z-Scores

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
Infant Sex (Female)	-0.6	0.050
BMI	0.1	0.015
Diabetes	1.7	0.010
Multiparous	1.0	0.128
Multigravida	-0.9	0.183
Taking any vitamin	1.2	0.025
Any Fasting	-1.1	0.006

Neonatal Length

Infant length was positively correlated with maternal weight and BMI. It was higher in male infants and in infants of mothers who had diabetes. It was higher in infants of non-fasting women than women who engaged in any fasting. It was also positively correlated with gestational age. In a multivariate analysis of infant length with height, BMI, infant sex, diabetes, and any fasting was retained but not significant. When adding gestational age, any fasting was a significant predictor of reduced length (Table 6.18).

Table 6.18: Multivariate Linear Regression of Any Fasting with Other Predictors (Including Gestational Age) of Infant Length

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
BMI	0.1	0.040
Gestational Age	0.7	0.001
Infant Sex	-1.9	0.001
Diabetes	1.9	0.139
Any Fasting	-1.6	0.049

Z-scores

Infant length z-scores were higher in male infants and in infants of mothers who were multiparous, multigravida, took any vitamin, that took any vitamin other than iron and had diabetes. They were positively correlated with gestational age and maternal height. They were higher in infants of non-fasting women than women who engaged in any fasting. In a multivariate analysis of infant length with these variables, the significant predictors of increased neonatal length z-scores were increased gestational age and non-fasting (Table 6.19).

Table 6.19: Multivariate Linear Regression of Any Fasting with Other Predictors of Infant Length Z-scores

Independent Variables Retained in Model	Coefficient (β)	p-value
Any Vitamin	0.5	0.105
BMI	0.0	0.158
Gestational Age	0.2	0.018
Infant Sex	-0.3	0.088
Diabetes	0.6	0.136
Multiparous	0.3	0.148
Any Fasting	-0.6	0.014

Head Circumference

Head Circumference

Head circumference was positively correlated with maternal height and gestational age at birth. It was higher in male infants. It was higher in infants of non-fasting women than women who engaged in any fasting. Prior to controlling for gestational age in a multivariate analysis, height and infant sex were retained as significant predictors of head circumference but any fasting was not. When controlling for gestational age, any fasting was a significant predictor of head circumference (Table 6.20).

Table 6.20: Multivariate Linear Regression of Any Fasting with Other Predictors (including Gestational Age) of Head Circumference

Independent Variables Retained in Model	Coefficient (β)	p-value
Maternal BMI	0.05	0.138
Gestational Age	0.29	0.020
Infant Sex (female)	-1.03	0.002
Any Fasting	-1.10	0.030

Z-scores

Head circumference z-scores were positively correlated with increased maternal height and gestational age and were higher for male infants. They were higher in infants of mothers who did not fast compared to mothers who participated in any fasting. Fasting was retained as predictive of reduced head circumference z-scores, as well as reduced gestational age and the infant being female (Table 6.21). Maternal anthropometry and style of dress were not significant.

Table 6.21: Multivariate Linear Regression of Any Fasting with Other Predictors of Head Circumference Z-scores

Independent Variables Retained in Model	Coefficient (β)	p-value
Gestational Age	0.21	0.018
Infant Sex (female)	-0.48	0.027
Maternal Body Fat	0.02	0.191
Any Fasting	-0.68	0.033

Measures of Fatness: Ponderal Index, Arm circumference and Skinfolds

Ponderal Index

Ponderal index at birth and at time of neonatal measurements was greater in mothers with diabetes and inversely related to gestational age, but no other independent variables were associated with ponderal index. Any fasting was not retained as a predictor of ponderal index at birth or about three days after birth in multivariate regression with diabetes, gestational age, and maternal anthropometric variables.

Arm Circumference

Arm circumference was higher in male infants and in infants of women who dressed less conservatively, who had diabetes, and who had anemia and was positively correlated with maternal weight and BMI. It did not differ by any fasting versus no fasting. In a stepwise multivariate analysis, arm circumference was predicted by maternal anthropometry and infant sex but not predicted by any fasting compared to no fasting.

Triceps Skinfold

Triceps skinfolds were larger in infants of women who dressed less conservatively and who were multigravida and were positively correlated with maternal weight, BMI and body fat. They did not differ by any fasting versus no fasting in univariate or multivariate analyses.

Subscapular Skinfold

Subscapular skinfolds were larger in infants of woman that took any vitamin and women who had diabetes and were positively correlated with maternal weight, BMI and body fat. They did not differ by any fasting versus no fasting in univariate or multivariate analyses.

Sum of Triceps and Subscapular Skinfolds

The sum of triceps skinfolds and subscapular skinfolds were larger in infants of woman that took any vitamin and that dressed less conservatively and were positively correlated with maternal weight, BMI and body fat. They did not differ by any fasting versus no fasting in univariate or multivariate analysis, with or without gestational age.

Summary: Any Fasting and Infant Anthropometry

Women who participated in any fasting had infants with reduced head circumference and length measurements compared to women who did not fast when controlling for gestational age. Any fasting was also predictive of reduced z-scores for birth weight, length, and head circumference. These data suggest that any maternal fasting during late pregnancy is associated with reduced neonatal weight, length and head circumference for gestational age. This sample size was small, so these results need to be replicated in larger studies, but these results should emphasize the necessity of controlling for gestational age when assessing the relationship between maternal fasting and neonatal anthropometry.

Fasted Daily versus No or Some Fasting

Some women in this study felt they could fast every day of Ramadan that passed prior to labor whereas others did not, often due to health reasons, medical advice against fasting, or feeling unable to due to non-medical reasons such as thirst or dizziness. Women who did not feel they could fast daily may have made different fasting decisions due to an increased sense of risk associated with fasting with a medical concern or they may be different in other ways that made the experience of fasting more difficult.

Due to the nature of the study design, women who fasted every day of Ramadan that passed prior to going into labor and gave birth earlier in the study fasted for very few days, while there were women in the category of women who did not fast daily that fasted for almost the entire month but skipped one or two days. Therefore, the range for the number of days fasted is similar for both groups. However, since the group that fasted daily still fasted significantly longer than the group that did not fast daily based on a t-test, averaging 20.8 ± 11 days of fasting compared to 12.4 ± 11 days ($p<0.000$), there remains the possibility that some of the differences seen between groups would be associated with fasting.

In initial t-tests, infants of mothers who fasted every day of Ramadan that passed prior to delivery had lower neonatal weight and birth weight, neonatal weight, length, and head circumference z-scores (Table 6.22). All anthropometric variables were analyzed in multivariate regressions to assess if any fasting remains predictive after controlling for other variables.

Table 6.22: Gestational Age and Infant Anthropometry by No/Some Fasting versus Fasted Daily (T-Tests)

	No fasting or occasional fasting		**Fasted Daily**		**p-value (one-tailed)**
	N	**Mean ± St. Err**	**N**	**Mean ± St. Err**	
Gestational Age	28	39.1 ± 0.6	32	39.1 ± 0.4	NS
Birth Weight (g)	38	3,545 ± 755	49	3,386 ± 124	NS
Birth Weight z-scores	25	0.68 ± 0.25	31	0.07 ± 0.16	0.018
Neonatal weight (g)	34	3,549 ± 116	41	3,282 ± 76	0.027
Neonatal Weight z-scores	23	0.36 ± 0.24	22	-0.25 ± 0.16	0.021
Length (cm)	34	51.4 ± 0.4	40	50.6 ± 0.4	NS (0.0639)
Length z-scores	23	1.12 ± 0.16	22	0.72 ± 0.12	0.0258
Ponderal Index based on birth weight	34	2.66 ± 0.05	39	2.64 ± 0.04	NS
Ponderal Index based on neonatal weight	34	2.54 ± 0.05	40	2.49 ± 0.04	NS
Head Circumference (cm)	32	35.8 ± 0.2	38	35.4 ± 0.2	NS
Head Circumference z-scores	22	1.40 ± 0.16	20	0.99 ± 0.17	0.0459
Arm Circumference	32	11.3 ± 0.3	38	10.9 ± 0.2	NS
Sum of Triceps and Subscapular Skinfold	31	9.1 ± 0.4	38	8.3 ± 0.4	NS (0.0829)
Triceps Skinfold (mm)	32	4.6 ± 0.2	38	4.2 ± 0.2	NS (0.0953)
Subscapular Skinfold (mm)	31	4.7 ± 0.3	38	4.2 ± 0.2	NS (0.0675)

Gestational age

Gestational age did not differ by women who fasted every day prior to childbirth compared to women who did not fast or skipped days in univariate or multivariate regression. In the multivariate analysis, the only significant predictive variable related to later gestational age was taking any vitamin.

Infant Weight

Birth weight did not differ by women who fasted every day prior to childbirth compared to women who did not fast or skipped days in univariate or multivariate analysis. Birth weight z-scores, neonatal weight, and neonatal weight z-scores were lower in those whose mothers fasted every day prior to childbirth compared to women who did not fast or skipped days in the univariate analysis, but after controlling for maternal anthropometry, parity, vitamin intake, and health conditions in the multivariate analysis, daily fasting was not retained as a predictive variable.

Infant Length

Infant length and length z-scores were lower in infants of women who fasted every day prior to childbirth compared to women who did not fast or skipped days in univariate analyses Fasting daily was insignificant when controlling for other variables in the multivariate analyses.

Head Circumference

Head circumference did not differ by women who fasted every day prior to childbirth compared to women who did not fast or skipped days in univariate or multivariate analyses, including when controlling for gestational age. Head circumference z-scores were lower in infants of women who fasted every day prior to childbirth compared to women who did not fast or skipped days in univariate analysis but did not remain significant in the multivariate analysis; maternal anthropometry, gestational age at birth, and infant sex were retained as significant predictors of head circumference z-scores.

Measures of Fatness: Pondera Index, Arm Circumference and Skinfolds

Ponderal index did not differ by women who fasted every day prior to childbirth compared to women who did not fast or skipped days in univariate or multivariate analyses. Arm circumference did not differ by infants of women who fasted every day prior to childbirth compared to women who did not fast or skipped days in univariate or multivariate analyses, with or without gestational age included. In univariate analysis, triceps skinfolds, subscapular skinfold, and the sum of triceps and subscapular skinfolds were lower in infants of women who fasted every day prior to childbirth compared to women who did not fast or skipped days, but after controlling for other predictors in multivariate analyses, the differences were not significant. When adding gestational age to the models, subscapular skinfolds, daily fasting is retained as a predictor of reduced subscapular skinfolds and a reduced sum of triceps and subscapular skinfolds, although not significant ($p<0.07$ and $p<0.054$, respectively).

Summary: Daily Fasting and Infant Anthropometry

In t-tests, infants of mothers who fasted every day of Ramadan that passed prior to delivery had lower neonatal weight and birth weight, neonatal weight, length, and head circumference z-scores. However, none of these differences in neonatal anthropometry remained significant in multivariate analysis after controlling for other variables. Differences between characteristics other than daily fasting, including infant sex, gestational age, vitamin supplementation, and maternal anthropometry, account for the observed differences in infant anthropometry.

Number of Days Fasted

Increased number of days fasted was hypothesized to be negatively correlated with neonatal anthropometric measurements. However, the number of days fasted was not correlated with gestational age at birth or any infant anthropometric measurements or z-scores in pairwise correlations. If maternal fasting was associated with reduced infant anthropometry and the post-fasting period was associated with in utero catch-up growth, it remains possible that associations between fasting duration and infant anthropometry were not perceptible unless controlling for the number of days in utero after fasting is discontinued. Days fasted was therefore added to the multivariate analyses with days between fasting and labor.

Number of Days Between Fasting and Labor

The number of days between fasting and labor is expected to capture catch-up growth after any potential growth restriction resulting from fasting. Including all women who participated in any fasting, days between fasting and labor ranged from 0-43 days and averaged 9.8 days. In order to include the 11 non-fasting women in this analysis, they were added to the analysis at 45 days since fasting.

If fasting does reduce fetal growth, days between fasting and labor should be positively correlated with infant growth. Pairwise correlations supported this hypothesis. Days between fasting and labor was positively correlated with birth weight and birth weight z-scores, neonatal weight and length z-scores, head circumference and head circumference z-scores, and arm circumference (Table 6.23). All anthropometric variables were analyzed in multivariate regressions to assess if days between fasting and labor remained significantly related to each other. The number of days fasted was also included.

Table 6.23: Pairwise Correlations: Days Between Fasting and Labor and Infant Gestational Age and Anthropometry

Infant Anthropometry and Number of Days Between Fasting and Labor	N	Pearson's Correlation	p-value
Gestational Age at Birth	60		NS
Birth Weight	87		NS
Birth Weight Z-scores	56	0.43	0.001
Weight at 48-72 hours (g)	75	0.22	NS (0.060)
Neonatal Weight Z-scores	45	0.43	0.004
Length (cm)	74	0.29	0.011
Length Z-scores	45	0.47	0.001
Ponderal Index at Birth	73		NS
Ponderal Index at 48-72 hours	74		NS
Head Circumference (cm)	70	0.35	0.003
Head Circumference Z-scores	42	0.51	0.001
Arm Circumference	70	0.21	NS (0.085)
Triceps skinfold	70		NS
Subscapular skinfold	69		NS
Sum of Triceps and Subscapular Skinfold	69		NS

Fasting and Anthropometry in Multivariate Analysis

Gestational age

A multivariate regression was run that included dress, parity, gravida, anemia, and vitamin use as well as days fasted and days between fasting and labor, but neither of the latter was predictive of gestational age.

Infant Weight

Birth weight and neonatal weight were not correlated with days since fasting in univariate or multivariate analyses, with or without days fasted as a covariate. Maternal height and diabetic status and infant sex were the main determinants of infant weight. Birth weight z-scores were positively correlated with the number of days between fasting and labor in the univariate analysis. In multivariate analysis, infant sex, maternal BMI, diabetes, and taking any vitamin remained predictive. Days since fasting was retained but not significant ($p<0.054$). Neonatal weight z-scores were positively correlated with the number of days between fasting and childbirth in univariate analysis and multivariate analyses. Days fasted was only retained if days between fasting and labor was in the model as well and then was positively correlated with weight z-scores, which is counter to the hypothesis that increased fasting is associated with reduced fetal growth (Table 6.24). Hypotheses for this unexpected result follow the subsequent multivariate analyses.

Table 6.24: Multivariate Linear Regression of Days Fasted, Days Since Fasting, and Other Predictors of Neonatal Weight Z-Scores

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
Maternal BMI	0.09	0.002
Diabetes	1.29	0.048
Taking any vitamin	1.11	0.015
Days Between Fasting and Labor	0.02	0.019
Days Fasted	0.02	0.148

Neonatal Length

Infant length was positively correlated with days between fasting and labor in the univariate analysis. If not including gestational age in the multivariate model, length was not correlated with days between fasting and labor. When controlling for gestational age, days between fasting and labor was positively correlated with length (Table 6.25).

Table 6.25: Multivariate Linear Regression of Days Fasted, Days Since Fasting, Gestational Age, and Other Predictors of Neonatal Length

Independent Variables Retained in Model	Coefficient (β)	p-value
Infant Sex (Female)	-1.82	0.001
Gestational Age at Birth	0.59	0.006
Maternal BMI	0.12	0.039
Days Between Fasting and Labor	0.04	0.031

Infant length z-scores were positively correlated with an increased number of days between fasting and labor (Table 6.26). Days fasted was only retained in the output if days between fasting and labor was also included but was not significant.

Table 6.26: Multivariate Linear Regression of Days Fasted, Days Since Fasting, and Other Predictors of Length Z-Scores

Independent Variables Retained in Model	Coefficient (β)	p-value
Gestational Age at Birth	0.18	0.010
Maternal BMI	0.03	0.100
Multigravida	0.30	0.152
Taking any vitamin	0.58	0.070
Days Fasted	0.01	0.125
Days Between Fasting and Labor	0.02	0.001

Head Circumference

An increased number of days between fasting and labor positively correlated with larger head circumferences. In the multivariate analysis without including gestational age, days between fasting and labor remained a significant predictor of head circumference, along with maternal height and infant sex (Table 6.27). Days fasted was not retained. When adding gestational age to the model, days fasted and days between fasting and labor were both positively correlated with head circumference, along with infant sex and gestational age (Table 6.28). Days fasted was only retained if days since fasting was also included in the model, indicating that any association between head circumference and days fasting may be moderated by the amount of time elapsed between fasting and labor. Although days fasted was not significant, it is interesting to note that increased days fasting was associated with larger head circumference z-scores, which would be counter to the hypothesis that it would be associated with reduced infant growth.

Table 6.27: Multivariate Linear Regression of Days Fasted, Days Since Fasting, and Other Predictors of Head Circumference

Independent Variables Retained in Model	Coefficient (β)	p-value
Height	0.06	0.013
Infant Sex (Female)	-0.80	0.007
Days Since Fasting	0.02	0.016

Table 6.28: Multivariate Linear Regression of Days Fasted, Days Since Fasting, Gestational Age, and Other Predictors of Head Circumference

Independent Variables Retained in Model	Coefficient (β)	p-value
Gestational Age	0.29	0.024
Infant Sex (Female)	-1.02	0.006
BMI	0.05	0.112
Study Day	-0.04	0.100
Days Fasted	0.07	0.040
Days Since Fasting	0.05	0.005

Head Circumference Z-scores

In a stepwise multivariate analysis, head circumference z-scores were positively correlated with an increased number of days since fasting. Increased gestational age was a significant predictor of larger head circumference z-scores (Table 6.29). Fasting duration was retained but not significant, and it was only retained if days since fasting was also included in the model.

Table 6.29: Multivariate Linear Regression of Days Fasted, Days Since Fasting, Gestational Age, and Other Predictors of Head Z-scores

Independent Variables Retained in Model	Coefficient (β)	p-value
Infant Sex (Female)	-0.44	0.055
Gestational Age	0.22	0.013
Maternal Body Fat	0.02	0.183
Study Day	-0.02	0.161
Days Fasted	0.02	0.082
Days Since Fasting	0.02	0.007

Measures of Fatness: Ponderal Index, Arm Circumference and Skinfolds

In multivariate analyses with gestational age, diabetes, and maternal anthropometry, ponderal index was not related to days fasting and days since fasting. Arm circumference was positively correlated with the number of days between fasting and childbirth in the univariate analysis, but neither days fasted or days between fasting and labor were retained as significant predictors of arm circumference in the multivariate analysis, with or without gestational age as a covariate. Triceps skinfolds, subscapular skinfold, and the sum of the skinfold measurements were not correlated with days between fasting and childbirth in univariate or multivariate analyses, with or without gestational age.

Summary: Number of Days Fasted and Days between Fasting and Birth and Infant Anthropometry

The number of days mothers fasted during late pregnancy was hypothesized be inversely correlated with neonatal anthropometry measurements, while days between fasting and labor was predicted to positively correlate with infant anthropometry as an indicator of potential catch-up growth. In univariate analyses, the number of days fasted was not correlated with any infant anthropometric measurements, but the number of days between fasting and labor was significantly correlated with increased infant birth weight z-scores, neonatal weight z-scores, length and length z-scores, and head circumference and head circumference z-scores.

After controlling for other possible influences on fetal growth in the multivariate analysis, birth weight z-scores did not remain correlated with days between fasting and labor. Instead, maternal anthropometry, diabetic status, and vitamin supplementation were significant predictors, and these variables were also predictive of fasting behaviors in this sample. However, the correlations between days between fasting and labor and infant anthropometry remained significant for several variables: neonatal weight for known gestational age, length, length for known gestational age, head circumference, and head circumference z-scores. Other than head circumference, all other significant correlations accounted for gestational age, either by adding it as an independent variable or by using it to calculate z-scores.

The number of days fasted was a significant predictor of infant head circumference when gestational age was included in the analysis and was retained but not significantly correlated in the models for z-scores for neonatal weight, length, and head circumference. Days fasted was only retained when days between fasting and labor was also in the model. This indicates that in utero fetal growth may be increased after the discontinuation of fasting, which matches the hypothesis of in utero catch-up growth after fasting. However, in each of the cases in which days fasted was retained in the model, days fasted was positively correlated with infant anthropometry, counter to the hypothesis that increased fasting would result in reduced fetal growth. Since any fasting was associated with reduced weight, length, and head circumference, it is possible that there is a non-linear relationship between fetal growth and fasting duration. It is also possible that any fasting is more important to fetal growth than fasting duration.

The direct correlation between the number of days between fasting and labor and infant anthropometry along with the association between any fasting and reduced infant anthropometry may indicate in utero catch-up growth after fasting is taking place. However, the positive coefficient between days fasted and some infant anthropometric variables suggests that this relationship is more complex. There is also a possible interceding influence of maternal anthropometry. If increased fasting causes inadequate maternal weight gain during pregnancy, that may subsequently correspond to altered fetal growth. There may be a confounding influence of controlling for postnatal maternal weight or BMI without understanding the effects of Ramadan fasting on gestational weight gain in this sample. This is discussed further below.

Discussion: Fasting and Birth Outcomes

This study tested the hypothesis that participation in this fast during late pregnancy would be associated with reduced fetal growth, characterized by increased leanness, which would characteristic of acute nutritional stress (Bolten et al., 2011; Aryeh D Stein et al., 2004; Villar et al., 1986). This is in contrast to proportional weight to length reduction, which is more characteristic of chronic nutritional stress (Villar et al., 1986). Overall, this study supports the hypothesis that birth anthropometry varies by maternal fasting behaviors, as maternal fasting behaviors remained predictive of variation in infant anthropometry after accounting for several confounding factors. Any fasting was predictive of lower z-scores for known gestational ages for birth weight, length, and head circumference. In utero catch-up growth was also suggested, as days between fasting and labor was positively correlated with neonatal weight for known gestational age, length, length for known gestational age, head circumference, and head circumference z-scores. Additionally, similarly to the findings from the Dutch Hunger Winter (Aryeh D Stein et al., 2004), the results of this study do not support evidence of head sparing in this sample, as reduced head circumference was associated maternal fasting.

Relationships between fasting behaviors and infant anthropometry were not all as predicted, however. The number of days fasted was associated with increased infant anthropometry measurements, specifically head circumference. Increased fasting was not associated with increased infant leanness. Together, these discrepancies between research on situations of food restriction and famine compared to findings related to maternal fasting from this study and others suggest that maternal fasting is not likely well-modeled by situations of food restriction. Both findings will be discussed in turn, along with their possible indications for understanding and modeling the biology of maternal fasting.

Counter to the hypothesis that increased number of days fasted would predict reduced infant size, fasting duration was not negatively correlated with infant anthropometry, and in some cases, appeared to be positively correlated with infant anthropometry. Days fasted was only retained in multivariate models of infant anthropometry when accounting for days between fasting and labor, which supports the hypothesis that these variables would moderate each other. Days fasted was positively correlated with head circumference when gestational age was adjusted for and was retained in the output but not significantly correlated with z-scores for neonatal weight, length, and head circumference. However, in all models in which days fasted was retained as a predictor of neonatal anthropometry, the relationships were positive, rather than negative as hypothesized. Although it is unclear what mechanisms would account for a positive correlation between fetal growth and maternal fasting duration, particularly given that any fasting was associated with reduced neonatal anthropometry, then it is possible that the relationship between fasting duration and fetal growth is non-linear or that any fasting is more important to fetal growth patterns than fasting duration. If the relationship is non-linear, it is possible that maternal fasting results in reduced growth initially, but as adaptations are made over the several days of fasting, these adaptations may serve to allow for increased fetal growth. This would be an interesting question to address in future research to address through studies of adaptive responses to maternal fasting and dehydration. For example, it could be assessed if placental adaptations are occurring which allow for alterations in blood flow or transfer efficiency as the mother and fetus acclimatize to the environmental stimulus of extended periods without food and water daily over a period of days or weeks. Placental CRH production could additionally be assessed, as increased production of placental CRH can be a mechanism to increase blood flow to the fetus (Mclean & Smith, 1999).

Also, counter to the hypothesis that maternal fasting in late pregnancy would result in increased infant leanness at birth, measures of fatness (ponderal index, arm circumference, and skinfold measurements) were not associated with maternal fasting. These results did not suggest that fasting is associated with reduced fetal fat deposition in the third trimester. Reduced fatness at birth has been seen in studies of inadequate consumption of calories and nutrients and in cases of famine during late gestation (Aryeh D Stein et al., 2004; Villar et al., 1986). Some findings of this study remain congruent with research on the outcomes of exposure to the Dutch Hunger Winter during late pregnancy, including reduced weight, length, and head circumference for gestational age. However, exposure to that famine in late pregnancy also resulted in reduced ponderal indexes (Aryeh D Stein et al., 2004). In growth-restricted infants, proportionally reduced weight and length without a reduction in ponderal index typically characterizes chronic fetal malnutrition rather than an acute phase of growth restriction in late pregnancy and is associated with poorer long-term outcomes compared to acute phases of in utero undernutrition (Villar et al., 1986). The direction of causation cannot be concluded from this study, so it remains possible that women who fasted would have had smaller infants whether or not they fasting, and the circumstances that would lead to that also made fasting easier, such as could be the case in women who experience appetite suppression. However, that explanation does not adequately account for the indication of post-Ramadan catch-up growth.

Based on these two discrepancies between studies of food restriction and Ramadan fasting, this finding indicates that Ramadan fasting during late pregnancy is not well-modeled by situations of food restriction and famine. Rather, these findings may be more congruent with a recent study on dehydration in the third trimester, which also reported evidence of a reduction in weight, length, and head circumference associated with dehydration, although weight-to-length ratios were not included in this analysis for adequate comparison (Mulyani et al., 2018). Alternatively, the lack of an association between maternal fasting and infant leanness may be related to the duration of time spent in a fasting state, which is characterized by shifts in several metabolic hormones including cortisol, which may influence fetal growth and head circumference. Bolten et al. (2011) found increased maternal cortisol during early and late pregnancy to be predictive of reduced infant weight and during late pregnancy to be predictive of reduced length at birth. Li et al. (2012) found that maternal cortisol in late gestation was inversely correlated with several different measurements of infant head circumference but not birth weight or other anthropometric measurements. Animal studies have indicated a causal pathway of glucocorticoids in reduced brain growth by demonstrating that prenatal exposure to high concentrations of glucocorticoids results in reduced brain growth and damage to developing neurons in a dose-dependent manner (Huang et al., 1999; Li et al., 2012; Sapolsky, 1985). The hormonal responses to fasting during pregnancy and the role of hormones involved in the physiological fasting response on fetal growth need to be better understood to clarify if they play a role in fetal growth patterns.

These results demonstrate the importance of accounting for gestational age when analyzing the relationship between maternal fasting and birth outcomes. Except for head circumference, fasting behaviors were associated with infant anthropometric variables only when gestational age was included in the analysis, either by accounting for it within the infant anthropometry z-scores calculations or by adding it to the model as an independent variable. Although the gestational length was also considered in this study, larger sample sizes than available in this data set would be necessary to observe whether Ramadan fasting was associated with reduced gestational length. In larger studies of Ramadan fasting, the hypothesis that maternal fasting would be associated with shortened gestational length has not been supported (Awwad et al., 2012; Hefni, 1993; Kavehmanesh & Abolghasemi, 2004).

Infant sex, gestational age at birth, maternal anthropometry, maternal health, parity, and vitamin intake were common variables associated with infant birth size. Differences in these characteristics between women who fast, who fast but skip days, and women who do not fast accounted for some of the differences observed in infant anthropometry outcomes. The differences in birth outcomes for women who fasted daily versus those that did not disappear after controlling for maternal characteristics, infant sex, and gestational age. Univariate analyses suggested smaller measures of infant weight, length, and head circumference and possibly skinfolds in infants of women who fasted daily. However, the multivariate analyses demonstrated that variation in birth outcomes between women who fasted daily and those who did not fast daily reflected differences in variables other than fasting.

Fetal growth and fasting decisions were influenced by similar maternal factors, which poses a challenge in determining the extent to which associations between birth outcomes and maternal fasting were mediated by other variables. As discussed in Chapter 5, maternal health conditions, anthropometry, and vitamin intake were variables relevant to fasting decisions that were also important predictors of infant growth in this analysis. Gestational diabetes was a significant deciding factor in whether women fasted or could sustain fasting for the duration of the month, but infants of women with gestational diabetes were also larger on average than of non-diabetic women, and this trend accounted for some of the variation in infant birth size by fasting behaviors in this sample.

Postnatal maternal anthropometry was a significant predictor of fasting behaviors and may have been influenced by fasting, as discussed in Chapter 5. Increased fasting was associated simultaneously with reduced maternal weight and increased maternal body fat percentage, which may indicate maternal muscle loss or wasting. Maternal BMI was significantly positively correlated with several infant anthropometric measurements and maternal body fat percentage was positively correlated with some infant anthropometric measurements, particularly skinfold measurements.

Since maternal anthropometric measurements were taken post-Ramadan, it is not possible to discern causality between maternal anthropometry and fasting. Maternal anthropometry may be a determining factor in fasting behaviors, with heavier women less able to participate in fasting and giving birth to larger infants. If this is the case, controlling for maternal anthropometry in these analyses serves the purpose of controlling for differences between women that influence both fasting behaviors and fetal growth but that were not altered by participation in fasting.

Alternatively, fasting during pregnancy may result in reduced maternal weight and BMI and increased body fat, which also implies a loss of lean fat-free mass. Maternal body composition changes resulting from Ramadan fasting may also result in reduced fetal growth. If this is the case, fasting may be playing a causal role in both postpartum maternal anthropometry and in fetal growth, which might obscure associations between fasting and infant birth size in this sample.

These hypotheses are not mutually exclusive, and both may be occurring. As discussed in Chapter 5, the difference in maternal anthropometry between fasting and non-fasting women was largely accounted for by women with medical concerns such as diabetes or hypertension. After controlling for this, though, maternal weight remained predictive of fasting. A previous study in the Gambia observed weight loss amongst all pregnant women in the study during Ramadan fasting and signs of accelerated starvation amongst women fasting during late pregnancy (Prentice, Prentice, Lamb, et al., 1983). A more recent study in Lebanon during Ramadan found that fasting mothers gained weight but less than non-fasting controls (Awwad et al., 2012). Inadequate maternal weight gain during gestation can have detrimental effects to a developing fetus, so a better understanding of the effect of Ramadan fasting on maternal body composition during pregnancy is a critical next step to better understanding the effects of fasting on fetal growth.

It should be noted that there were additional maternal anthropometric measurements taken by the Tanita scale, including muscle and bone mass. Increased muscle and bone mass were significantly associated with reduced maternal fasting behaviors and positively correlated with infant anthropometry. However, the scale has not been validated for post-partum women, and the numbers obtained were outside of an expected range, so the variables were excluded from the analysis. When included in the multivariate analyses of infant anthropometry, fasting and other maternal characteristic variables were much less likely to be retained as a significant factor, with maternal muscle mass often resulting as the main predictor of infant anthropometry outcomes. Several other studies have linked maternal fat-free mass to infant birth anthropometry (Larciprete et al., 2003). In Chapter 5, fasting was associated with reduced maternal weight and increased maternal body fat, implying reduced fat-free mass as well. Whether variation in maternal anthropometry caused variation in fasting behavior or resulted from it is an important question in clarifying the influence of fasting on fetal growth.

Vitamin intake was also a significant variable in several multivariate infant anthropometry outcomes. All but one woman taking any vitamin took iron, and only about 25% of women who took vitamins took something other than or in addition to iron. Research suggests that iron deficiency increases risk for low birth weight infants (Scholl & Hediger, 1994) and that taking iron and other vitamins can have a significant impact on fetal growth (Cogswell et al., 2003; Preziosi et al., 1997; Ribot et al., 2013), so given the consistent association between vitamin supplementation and infant anthropometry in this study, vitamin supplementation may be playing a causal role in increased infant birth size in this sample. There are possible alternative explanations for this finding. For women of lower socioeconomic status such as the participants in this study, the cost of vitamins can be significant, so vitamin intake may be signifying greater access to financial resources, which could also play a role in increased infant birth size. It is also possible that increased concern over maternal and fetal health corresponded with reduced fasting and increased vitamin supplementation and possibly other lifestyle choices that would influence fetal growth. The relationship between reduced fasting and increased vitamin intake may be related to medical concerns, since women who were taking vitamins were more likely to say medical concerns were the reason that they did not fast all or some of the month.

Dress style was not associated with maternal fasting behaviors in this population (see Chapter 5), but it is reasonable to predict that it might in less homogenous populations, such as in the United States where religiosity has been associated with both style of dress and fasting behaviors (Fahmy & Mohamed, 2018; Kopp, 2002). In this study, more conservative maternal style of dress was associated with reduced arm circumference and triceps skinfold measurement. Other studies have suggested a relationship between maternal veiling, vitamin D deficiency, and fetal growth (Dror & Allen, 2010; Javaid et al., 2006; Nabulsi et al., 2008), and if maternal veiling influences neonatal birth size via vitamin D status, dress style may confound the effects of fasting in some populations.

There is also a possibility that seasonality in fetal growth patterns is also playing a role in differences in infant birth size. Z-scores for neonatal weight, length, and head circumference for gestational age were calculated based on averages previously published from the same maternity hospital for infants born at 37-42 weeks gestational age, which includes different equations by infant sex (Radouani et al., 2015). Z-scores in this sample were significantly higher than zero for birth weight ($p<0.022$), neonatal length ($p<0.000$), and head circumference ($p<0.000$). This may be due to differences between researchers and equipment or the current study sample drawing from patients that had given birth via cesarean, as the standards were based on a cohort of only 15% cesarean births. However, the doctors at this hospital frequently stated that there is a substantial increase in cesarean births during the summer months, although they said they did not know why, and it is possible that seasonal variation in fetal growth is a contributing factor. If infants born during the summer tend to be larger, this adds additional complexity to studying the effects of fasting on fetal growth.

This study was limited by the small sample size and cross-sectional study design. Ramadan fasting requires abstinence from food and water from sunrise to sunset, but dietary intake during non-fasting hours is not required to be restricted. Ramadan fasting does not necessarily correspond to reduced food availability or caloric intake, although dietary intake during non-fasting hours in this study sample was not assessed and therefore daily nutrient intake during the fast cannot be ascertained for the present study. Additionally, although several maternal variables were accounted for in this analysis, it remains possible that confounding variables that influence both fetal growth and maternal fasting behaviors were not accounted for in this analysis.

Conclusion

This study suggests that maternal fasting for about 16 hours per day from food and water during late pregnancy is associated with altered fetal growth patterns, even after accounting for many other variables that account for variation in maternal fasting behaviors and fetal growth. Specifically, infant weight, length and head circumference for gestational age were reduced with any fasting and were increased with an increased duration between discontinuation of fasting and birth, which may indicate catch up growth. However, counter to the hypothesis, no indications of reduced infant body fat or increased leanness were found other than reduced weight. These results do not lend themselves to a clear extrapolation so far as whether women *should* fast during pregnancy. What these results suggest is that the influence of fasting during late pregnancy are not comparable to results of famine, food restriction, or malnutrition. The results do suggest that infant growth may have a non-linear relationship with fasting duration, which would suggest that fasting is creating an environmental challenge that results in adaptations to maintain fetal growth, which often carry trade-offs. If this is the case, studies finding no associations between maternal fasting and fetal growth should not be considered conclusive evidence that fasting during pregnancy does not create a suboptimal fetal environment. Regardless, more data is needed to clarify the relationship between fasting and in utero growth.

The mechanisms that are involved in the association between fasting and fetal growth should be further explored but may include adaptations to food restriction, dehydration and altered metabolic hormones characteristic of the fasting state. Ramadan fasting is a multifaceted occurrence that can include water deprivation, fasting from food, an altered diet during non-fasting hours, altered activity patterns, and altered sleep patterns. Therefore, it is expected to have complex biological effects, including alterations in several hormones related to metabolism, dehydration, and possibly circadian rhythms. There are several avenues through which fasting may impact fetal growth. One potential mechanism known to be responsive to fasting and to be negatively correlated with fetal growth is cortisol. This hormone is the focus of Chapter 7, which explores the associations between fasting and postpartum milk cortisol.

Chapter 7: Results: Maternal Fasting and Breast Milk Cortisol

In this chapter, I explore the question of whether cortisol acts as a mediating hormone between maternal environmental stressors and fetal and infant life history programming. To answer this question, it would have to be demonstrated that breast milk cortisol varies predictably with maternal stressors and that this variation contributes to altered infant life history strategies. This chapter focuses on the first part of this question by assessing whether there is a relationship between maternal fasting behaviors and breast milk cortisol. A study by Dikensoy et al. (2009) demonstrated that maternal fasting resulted in elevated maternal cortisol, supporting the hypothesis that Ramadan fasting during the third trimester of pregnancy constitutes a maternal environmental stressor. Information about this stressor is predicted to be perceptible to the infant via maternal hormonal signaling through breast milk.

Cortisol in breast milk is of interest in this study as a possible hormonal messenger relaying information about the maternal environment to the offspring due to its role in metabolism, its response to fasting behavior, and its association with the stress response (Dantzer et al., 2013; Sareen & Jack, 2013). Additionally, animal studies have identified it as a potential messenger that relays information about maternal ecology to the infant and stimulates adaptations in infant biology in preparation for the maternal environment (Dantzer et al., 2013; Hinde et al., 2014). Because cortisol passively diffuses into breast milk, maternal cortisol is highly directly correlated with breast milk cortisol. Human studies have found maternal serum cortisol to account for 50-70% of the variation in maternal milk cortisol (Breakey, 2015), so it is possible that the neonate is receiving the maternal cortisol signal.

This study analyzed cortisol concentration in breast milk at 48-72 hours post-partum to determine if it is increased in women who fasted in the days leading up to delivery compared to women who did not. As discussed in Chapter 5, fasting behaviors varied with maternal biological and cultural characteristics that may also be associated with variability in breast milk cortisol, so these potentially confounding factors were considered. In Chapter 6, maternal fasting was associated with infant birth size, though the patterns of these associations were complex. Therefore, infant anthropometry measurements were also considered for their associations with breast milk cortisol in this analysis. This analysis addresses the question of whether the physiological stress of maternal fasting was associated with hormonal variation in breast milk cortisol after accounting for potentially confounding factors, such as maternal health, infant sex, and size.

Prior to the analysis of postnatal milk cortisol, it should be noted that this analysis is based on a single sample per participant taken approximately 3 days postpartum, and there are several reasons results should be interpreted with caution. First, this dataset relies largely on a cross-sectional analysis of breast milk cortisol. Ideally, several samples would have been collected from each individual to assess individual cortisol averages and diurnal patterns in order to draw conclusions about within-individual and between-individual cortisol concentrations and diurnal rhythms, along with the unique effects of labor (Hruschka, Kohrt, & Worthman, 2005; Segerstrom, Boggero, Smith, & Sephton, 2014). Although this was the original intention of this study, few participants were available to provide follow-up samples.

As described by Hruschka et al. (2005), the expected correlation among cortisol measurements from a single individual can be described statistically by the interclass correlation coefficient (ICC). The ICC indicates the reliability of using a single cortisol sample as a measure of individual cortisol variation. If ICC=0, this indicates that variation in cortisol cannot be attributed to between-individual differences, whereas if ICC=1, this indicates that individuals can be differentiated by single cortisol measurements. Using three different populations, Hruschka et al. (2005) demonstrated that, after controlling for the time of day of the sample, the ICC for cortisol ranged from 0.20-0.37. The individual level variation between cortisol is therefore high, and single sample cortisol measurements have limited, but still discernable, explanatory power.

The previous estimates did not involve studies of pregnancy, which is characterized by mild hypercortisolism beginning in the second trimester and increases throughout the rest of the pregnancy due to the placental secretion of corticotrophin-releasing hormone (CRH). The final three weeks of pregnancy are marked by a rapid rise in free plasma cortisol due to both an increase in CRH and a dramatic decrease in the percentage that is bound (Mclean & Smith, 1999). Additionally, maternal cortisol levels nearly double during labor (Jolivet, Blanchier, & Gautray, 1974). After delivery, maternal plasma CRH falls to non-pregnant levels within hours, and although the rise in cortisol that accompanies labor declines within the following six hours, maternal cortisol remains elevated for five to seven days (Jolivet et al., 1974; Mclean & Smith, 1999). How within-woman and between-woman variation in the volatility of maternal cortisol during labor influences postnatal milk cortisol is not clear.

Interpreting the results of this study may be further complicated by the fact that all participants gave birth via cesarean section, which Stjernholm et al. (2016) found to be associated with a blunted rise in free cortisol compared to normal initiation of labor and vaginal delivery, although cesarean deliveries in that study were scheduled and therefore the normal cascade of hormonal events accompanying labor may not have been triggered. In the present study, many cesareans were not scheduled, but whether they were performed before or after natural labor had begun was not assessed.

These challenges should be kept in mind during the following analyses. Still, based on the ICC of other populations, the analysis of the single samples available can be expected to capture some degree of between-individual differences and may indicate whether additional studies of fasting and breast milk cortisol are merited.

Overview of Participants with Initial and Follow-Up Breast Milk Cortisol Results

The subsample of participants with postpartum breast milk cortisol data includes 43 women from the larger sample of 92 women from this study. A total of 74 women attempted to give a breast milk sample while in the maternity ward at approximately 3 days postpartum, and 64 of these participants successfully gave samples. Of these, permission was granted to take to the United States any samples for which enough breast milk had been collected to divide between two test tubes. This analysis included only the samples that were transported to and assayed in the United States. Most of the participants whose breast milk samples were 1 mL or below were therefore not available for analysis, but some samples for which two test tubes were collected also remained in the laboratory in Morocco. Of the women who gave postpartum samples, nine were available for follow-up milk sample collection, one of whom gave two follow-up samples, though only her first milk sample is displayed here. All follow-up samples were transported to the United States and assayed. Six participants had both a postpartum sample and a follow-up sample included in this data analysis.

In this participant overview, I first summarize the breast milk samples, including cortisol concentration, which is the outcome variable of interest in this chapter. I then provide an overview of fasting behaviors, as this is the independent variable of interest. Following this, I summarize potential covariates, which includes maternal variables such as anthropometry and health, and infant variables, such as sex and anthropometry.

Breast Milk Sample Overview

Table 7.1: Summary of Postpartum and Follow-Up Breast Milk Samples

	Postpartum Breast Milk Sample Overview		Follow-Up Breast Milk Sample Overview	
Breast Milk Sample	**N**	**Mean ± St. Dev. (Range)**	**N**	**Mean ± St. Dev. (Range)**
Days Postpartum of Sample	43	3.1 ± 1.0 (2 - 9)	9	24 ± 8.5 (10 - 36)
Volume Donated for Sample	43	3.4 ± 0.9 (1 - 4.5)	9	5.9 ± 2.5 (3 - 9)
Cortisol Concentration (pg/mL)	43	6,995 ± 9,919 (430 - 52,481)	9	2,678 ± 2,810 (59 - 8,548)
Cortisol Concentration, excluding outliers (pg/mL)	39	4,260 ± 3,512 (430 - 12,157)		

For the breast milk samples that were analyzed for cortisol content, days postpartum the sample was collected, the amount of breast milk collected, and breast milk cortisol concentrations are described in Table 7.1. The initial breast milk collection was taken at an average of 3.1 days post-partum but spanned 2-9 days. Most individuals gave breast milk samples at 3 days postpartum, except four individuals that gave samples at two days postpartum, one at 5 days and one at 9 days. The amount of milk requested was 2-4 mL for the initial sample, although the amount each woman was able to give varied. The amount collected varied between 1-4.5 mL and averaged 3.4 mL.

Cortisol concentration is the outcome variable of interest in this study and varied between 430-52,481 pg/mL and averaged 6,995 pg/mL, so there was high variability in the cortisol concentrations within this sample. Four women had much higher cortisol concentrations that the rest of the participants; 39 participants had cortisol concentrations below 12,200 pg/mL. The other four concentrations were 21,263, 30,377, 30,501, and 52,481 pg/mL; all women with high milk cortisol concentrations had diabetes and/or hypertension. When removing these four outliers, the average cortisol concentration dropped to 4,260 pg/mL.

Follow-up breast milk collection took place an average of 24 days postpartum and samples averaged 6 mL of milk. One woman gave two follow-up samples, and the first sample is included in this summary. By the time of the follow-up breast milk collection, maternal plasma cortisol should have returned to pre-pregnancy levels (Mclean & Smith, 1999). Average cortisol concentration of these breast milk samples was 2,700 pg/mL, though ranged widely from 59 - 8,548 pg/mL. Six women with follow-up breast milk cortisol data also had an initial sample that was analyzed. The average cortisol of the initial samples was 3,369 pg/mL, with a range of 430-8,835 pg/mL (not shown in table). Intra-plate CVs from the cortisol assays were 8.3%, 6.1%, and 4.7%. The inter-plate CV was 10.1%

Maternal Fasting Behaviors

Table 7.2: Overview of Fasting Behaviors for Participants with Postpartum and Follow-Up Breast Milk Analysis

	Overview of Participants with Postpartum Breast Milk Analysis		**Overview of Participants with Follow-Up Breast Milk Analysis**	
Fasting Behavior	**N**	**%**	**N**	**%**
Any Fasting	39	91%	9	100%
Daily Fasting	24	56%	6	37%
	N	**Mean ± St. Dev. (Range)**	**N**	**Mean ± St. Dev. (Range)**
Days Fasted	43	18.9 ± 10.6 (0 - 29)	9	22.8 ± 7.5 (12 - 29)
Days Between Fasting and Labor	39	8.8 ± 9.4 (0 - 31)	9	4.5 ± 5.6 (0 - 18)
Reason for Opting out of Some or All Fasting	**N**	**%**	**N**	**%**
Medical Reason	7	37%	2	67%
Felt She Could Not Fast (due to exhaustion, thirst, etc.)	8	42%	1	33%
Non-health or pregnancy related exemption (ex. Travel)	2	11%	0	0%
Reason not provided	2	11%		

Fasting behavior is described in Table 7.2. For women with initial breast milk cortisol results, 9% opted out of any fasting and an additional 35% fasted some of the time but not every day. Average fasting duration was 19 days and average days between fasting and labor was 9 days. Of women who opted out of some or all fasting, 42% did so due to feeling unable to fast due to reasons such as thirst, exhaustion, or dizziness when fasting. Other than two women who opted out for other reasons fasting is exempt, such as when traveling, and two that did not provide a reason, the remaining 37% opted out for medical reasons, including maternal health concerns such as having diabetes or hypertension or a health concern related to the fetus.

Of the nine women with follow-up breast milk samples, all participated in at least some fasting. Six fasted every day of Ramadan that passed prior to going into labor. The others all fasted but not every possible day. The number of days fasted averaged 23 days and ranged from 12-29, with four of these women fasting all 29 days. Days between the last fasting day and giving birth averaged 4.6 and ranged from 0-18.

Maternal Characteristics

Maternal characteristics that are assessed as potential covariates in the relationship between breast milk cortisol and maternal fasting behavior include maternal anthropometry, maternal health, reproductive history, receiving medical advice against fasting, receiving family advice about fasting,

Maternal Anthropometry

Maternal age and postpartum anthropometry ranged widely in this sample. Their average BMI was 27.2, which is categorized as overweight, but participants ranged in BMI from being in the underweight category (below 18.5) to obese (above 30), with the highest BMI being 42.4. The subgroup who gave a follow-up sample had a higher average age by 4 years and had higher anthropometry measurements for all variables except height, which was similar. Weight averaged 5 kg higher, BMI 2 units higher, and body fat 4% higher. Maternal anthropometry is summarized in Table 7.3.

Table 7.3: Overview of Maternal Anthropometry for Participants with Postpartum and Follow-Up Breast Milk Analysis

	Overview of Participants with Postpartum Breast Milk Analysis		**Overview of Participants with Follow-Up Breast Milk Analysis**	
Maternal Age and Postpartum Anthropometry	**N**	**Mean ± St. Dev. (Range)**	**N**	**Mean ± St. Dev. (Range)**
Age	42	30.0 ± 6.6 (18-41)	9	34.1 ± 5.8 (23-45)
Weight	41	69.5 ± 14.6 (45.5-109)	9	75.7 ± 15.9 (54.1-104.6)
Height	43	159.9 ± 6.3 (148-172)	9	160.6 ± 4.6 (156-168)
BMI	41	27.2 ± 5.6 (17.9-42.4)	9	29.3 ± 6.1 (22.2-42.4)
Body Fat	40	33.5 ± 8.3 (13.1-50.1)	8	37.4 ± 7.7 (24.9-49.6)

Table 7.4: Summary of Maternal Characteristics for Participants with Postpartum and Follow-Up Breast Milk Analysis

	Overview of Participants with Postpartum Breast Milk Analysis		**Overview of Participants with Follow-Up Breast Milk Analysis**	
Maternal Health	**N**	**%**	**N**	**%**
Reported Any Health Condition	22	49%	7	78%
Diabetic	4	9%	0	0%
Hypertensive	5	12%	0	0%
Diabetic and/or Hypertensive	7	16%	0	0%
Anemic	6	14%	1	11%
Other	14	33%	7	78%
Reproductive History				
Multiparous	34	79%	9	100%
Multigravida	35	81%	9	100%
History of Miscarriage	12	27%	4	44%
Medically Advised Against Fasting	3	7%	1	11%
Family Advice				
No or Neutral Advice	30	71%	5	56%
Encouraged to fast	1	2%	0	0%
Advised Not to Fast	11	26%	4	44%
Reported Stressors				
Stressor during Pregnancy	3	7%	3	33%
Stressor during Delivery	5	12%	0	0%
Vitamin Intake				
Any Vitamin	37	86%	8	89%
Any Vitamin Other than Iron	9	21%	1	11%
Style of Dress				
More Conservative	35	85%	8	100%
Less Conservative	6	14%	0	0%
Infant Feeding Intentions				
Planned to Exclusively Breastfeed	25	59%	6	67%
Intended to Give Formula	2	5%	1	11%
Intended to Give Water or Vervain Tea but No Formula	9	21%	1	11%
Undecided	6	15%	1	11%

Reproductive History

Of women with initial breast milk cortisol results, about 80% of participants were multiparous and multigravida and 27% had a history of one or more previous miscarriages. All nine women with follow-up samples were multiparous and multigravida. Four had had one or more previous miscarriages, with one participant having had five previous miscarriages. Reproductive history is summarized in Table 7.4.

Maternal Health

Half of the women with initial breast milk cortisol data reported a health condition. Four had diabetes and five had hypertensive disorders, and two women had both conditions. Six participants had anemia and fourteen reported other health conditions. Of the nine women with follow-up samples, two reported being healthy during pregnancy. Of the other seven women, one reported having anemia, and all seven reported a condition categorized as other. Other health conditions included short inter-birth intervals, heavy bleeding during pregnancy, exhaustion, back pain, and hypoglycemia, among other conditions. Maternal health is summarized in Table 7.4.

Medical Advice

Three participants with initial breast milk cortisol data were medically advised not to fast, one due to hypertension, one due to vomiting and dizziness after fasting the first day, and one said she was told she had to drink water for the health of the baby in her last days of pregnancy. One participant with follow-up milk cortisol data was medically advised not to fast due to hypotension. Medical advice is summarized in Table 7.4.

Family Advice

Of participants with initial breast milk cortisol data, 26% were encouraged not to fast. Of the nine women with follow-up samples, four reported being advised by families not to fast, one of whom indicated family advice followed medical advice against fasting. Family advice is summarized in Table 7.4.

Reported Stressors

As summarized in Table 7.4, of the 43 participants with initial breast milk cortisol samples, three reported having stressors during pregnancy and five reported birth-related stressors. This question was not specifically asked of participants, but when asked about their health during pregnancy, some women discussed life stressors or stressors during delivery. Of the nine women with follow-up breast milk samples, three commented about stressors experienced during pregnancy.

Vitamin Intake

As shown in Table 7.4, the majority of women in both subgroups supplemented with iron during pregnancy. Of participants with initial breast milk cortisol data, 21% took vitamins other than iron, and all but one also supplemented with iron. Of participants with follow-up breast milk cortisol data, one participant took other vitamins in addition to iron.

Style of Dress

As summarized in Table 7.4, eighty-five percent of participants with initial breast milk cortisol data and all women with follow-up samples were categorized as dressing conservatively, defined as exposing at most the hands and face to sunlight.

Infant feeding intentions

As summarized in Table 7.4, about 80% of participants with initial breast milk cortisol data did not intend to give formula and about 60% intended to breastfeed exclusively, while 15% had not decided. Of the nine women with follow-up breast milk samples, six intended to breastfeed exclusively, one intended to give formula, one intended to give Vervain tea, and one was undecided.

Infant Characteristics

Table 7.5: Participant Overview, Summary of Infant Characteristics for Participants with Postpartum and Follow-Up Breast Milk Analysis

	Overview of Participants with Postpartum Breast Milk Analysis		**Overview of Participants with Follow-Up Breast Milk Analysis**	
Infant Sex	**N**	**%**	**N**	**%**
Male	21	49%	5	56%
Female	22	51%	4	44%
Reported Infant Health Concern	7	29%	2	22%
Infant Gestational Age and Anthropometry	**N**	**Mean ± St. Dev. (Range)**	**N**	**Mean ± St. Dev. (Range)**
Gestational Age (weeks)	25	39.7 ± 1.3 (37-41)	6	39.7 ± 1.5 (37-41)
Birth Weight (g)	42	3522 ± 601 (2280-5370)	9	3247 ± 364 (2700-3720)
Weight (g)	43	3410 ± 586 (2260-5400)	9	3140 ± 404 (2500-3680)
Length (cm)	43	51.0 ± 2.5 (44-57)	9	49.8 ± 2.0 (47-54)
Ponderal Index at birth	42	2.6 ± 0.3 (2.1-3.5)	9	2.6 ± 0.2 (2.3-2.8)
Ponderal Index (neonatal)	43	2.5 ± 0.3 (2.1-3.5)	9	2.5 ± 0.2 (2.2-2.6)
Head Circumference	41	35.7 ± 1.3 (33.5-38.3)	9	35.0 ± 0.8 (33.5-36)
Mid-Arm Circumference	41	11.0 ± 1.2 (8.5-14)	9	10.4 ± 1.0 (9-12)
Triceps Skinfold (mm)	41	4.3 ± 1.1 (2-7)	9	4.1 ± 1.1 (2.5-6)
Subscapular skinfold (mm)	41	4.3 ± 1.3 (2-8)	9	4.4 ± 1.5 (2.5-7)
Triceps plus Subscapular skinfold (mm)	41	8.6 ± 2.4 (5-15)	9	8.6 ± 2.6 (5-13)
Z-Scores for Weight, Length and Head Circumference				
Birth Weight Z-score (with known gestational age)	25	0.33 ± 1.10 (-1.73 - 3.59)	6	-0.04 ± 0.60 (-0.94 - 0.84)
Neonatal Weight Z-score (with known gestational age)	25	-0.02 ± 0.98 (-2.03 - 2.56)	6	-0.30 ± 0.73 (-1.39 - 0.55)
Length Z-score (with known gestational age)	25	0.97 ± 0.72 (-0.20 - 2.6)	6	0.64 ± 0.48 (0.07 - 1.45)
Head Circumference Z-score (with known gestational age)	24	1.33 ± 0.78 (-0.09 - 3.16)	6	0.86 ± 0.50 (-0.01 - 1.52)

Infant Sex

Infant sex was evenly split for both sets of data (Table 7.5). Of the 43 women with initial breast milk cortisol data, 21 had male infants and 22 had female infants. Of the nine women with follow-up breast milk samples, five had male infants and four had female infants.

Infant Health at Birth

Whether or not an infant was reported to be healthy within three days of birth is summarized in Table 7.5. Of the 43 women with initial breast milk cortisol data, 37 said their infants were healthy, and five commented on the infant's health. Three were uncertain about the infant's health and were waiting for test results. To note, on follow-up, two infants were reported as healthy and one needed follow-up x-rays on her legs. Two mothers also commented on a birth-related event; one infant had needed oxygen at birth, and one was born with the umbilical cord wrapped around its neck, but both babies had recovered from the events and were otherwise reported to be healthy.

Of the nine women with follow-up breast milk samples, seven said their infants were healthy at birth. The other two women were uncertain and waiting for test results at the time of the enrollment questionnaire. Upon follow-up, one was reported healthy. The other infant returned to the hospital at 7 days postpartum with a fever.

Infant Anthropometry and Gestational Age

Of women with initial breast milk cortisol data, gestational age at birth was known for 25 infants. Of the nine women with follow-up breast milk samples, all gave birth at full term, and gestational age was available for 6 participants. Table 7.5 summarizes gestational age and birth weight as recorded by the medical staff at the time of delivery and neonatal measurements, which I took 48-72 hours postpartum. Also included are ponderal indexes, calculated using both birth weight and weight at 48-72 hours postpartum, and z-scores, calculated for weight, length and head circumference based on data produced by researchers at the same hospital (Radouani et al., 2015). Z-scores were adjusted for gestational age if known.

Supplemental Feeding at Hospital

Of the women who gave initial samples, 55% did not supplement the infants' diet at the hospital. One third supplemented with formula. Of the ten mothers who supplemented with Vervain tea and the seven that supplemented with water, three supplemented with both. Of the nine women with follow-up breast milk samples, five of their infants were only breastfed between birth and the enrollment interview. Of the other four, two infants were given formula and Vervain tea, one infant was given formula only, and one was given Vervain tea only. None were given water. Supplemental feeding is summarized in Table 7.6.

Table 7.6: Summary of Supplemental Feeding at Hospital for Participants with Postpartum and Follow-Up Breast Milk Analysis

	Participants with Postpartum Breast Milk Analysis		Participants with Follow-Up Breast Milk Analysis	
Supplemental Feeding at Hospital	**N**	**%**	**N**	**%**
Supplemented with Anything	19	45%	4	44%
Supplemented with Formula	15	36%	3	33%
Supplemented with Water	7	17%	0	0%
Supplemented with Vervain Tea	10	24%	3	33%

Statistical Analysis of Determinants of Breast Milk Cortisol Concentration

Data collection methods were detailed previously in Chapter 4. Breast milk cortisol concentration was the outcome of interest in the present data analysis. Breast milk cortisol concentrations were right skewed rather than normally distributed, which is commonly seen in studies with cortisol analyses, and log-transformation of cortisol concentration has successfully been used to create a normal distribution (Hruschka et al., 2005). Therefore, in this dataset, cortisol concentrations were log-transformed, which created a normal distribution. The back-transformed cortisol concentrations were reported for all statistical analyses. Breast milk cortisol concentration was assessed in univariate analysis with fasting behaviors, maternal characteristics, and infant characteristics.

Fasting behaviors were quantified in four ways: the number of days fasted, the number of days between fasting and labor, non-fasting versus any fasting, and some or no fasting versus daily fasting. Several maternal characteristics were considered for their potential mediating influence on breast milk cortisol concentration, including maternal health, reproductive history, anthropometry, family advice about fasting, medical advice about fasting, vitamin intake, style of dress, supplemental feeding, and infant feeding intentions. Infant characteristics considered included sex, health, and anthropometry. Univariate analyses were first used with each independent variable using pairwise correlations for continuous variables and student t-tests for binomial variables. Two-tailed p-values were used throughout this analysis unless otherwise noted.

To determine if fasting variables were associated with breast milk cortisol after accounting for other differences between women and infants, variables found to be significant in univariate analysis were added to stepwise multivariate linear regressions. Maternal characteristics were first added with fasting variables, then infant characteristics were assessed with fasting variables, and then these two models were combined. Significance level was set at $p<0.05$; however, for the purpose of identifying potentially confounding variables, any variable that was significant at the 0.10 level in the univariate analysis was included into the stepwise multivariate analyses. The stepwise model significance level was set to 0.2, with variables that have over a 0.2 p-value removed from the analysis.

As noted in previous chapters, women with diabetes and hypertension were included in the study. The prevalence of both Type 2 and gestational diabetes in Morocco is believed to be around 12% (Utz et al., 2017) and there has been concern over the increase in the occurrence of hypertension related to pregnancy due to the increasing average BMI in the country (Mochhoury et al., 2013). Pregnant women with these conditions must, therefore, navigate a cultural environment in which maternal fasting during pregnancy is the norm. Research on the effects of fasting with these conditions is therefore warranted. A risk of including diabetic and hypertensive women in this data analysis is that these conditions have been associated with higher maternal circulating cortisol or higher CRH, which may lead to higher cortisol (Ahmed & Shalayel, 1999; Laatikainen, Virtanen, Kaaja, & Salminen-Lappalainen, 1991; Perkins et al., 1995), and this may skew the present analysis since there is a strong relationship between maternal and breast milk cortisol (Breakey, 2015). The impact of including women with diabetes is evident given that the four previously discussed breast milk cortisol concentrations that were outliers were all from women with diabetes and/or hypertension. To address this challenge, the analyses were run on a subsample that excluded these outliers. Variables that became significant were discussed and included in the multivariate models.

Predictors of Breast Milk Cortisol

Variables tested for their relationship to the cortisol concentration in breast milk were categorized into three sections: fasting behaviors, maternal characteristics, and infant characteristics. Maternal characteristics that were significant in univariate analyses were added to a multivariate regression with relevant fasting behavior variables. This was repeated with infant characteristics. Variables retained in each of these models were added to another multivariate model combining maternal and infant characteristics with fasting variables.

Fasting

Days Fasted and Days Since Fasting Based on pairwise correlations, neither the number of days fasted nor the number of days between fasting and labor was associated with breast milk cortisol concentration. Study duration, which was positively correlated with days fasted ($p<0.000$) and inversely correlated with days between fasting and labor ($p<0.000$) was also not associated with breast milk cortisol.

Fasting Categories Breast milk cortisol concentration did not differ by fasting versus non-fasting, but women who fasted every day of Ramadan prior to going into labor had significantly lower cortisol than women who skipped days or did not fast at all (Table 7.7). As discussed in Chapter 5, women who did not fast daily were more likely to have diabetes or hypertension, and, as discussed in the following analysis of maternal characteristics, women with these health conditions also had significantly higher cortisol. To test if this relationship was driven by the inclusion of these participants, a two-tailed t-test was repeated with only participants who did not have diabetes or hypertension; the relationship between fasting daily and a lower cortisol concentration was no longer significant ($p<0.092$).

Table 7.7: T-tests of Log of Breast Milk Cortisol Concentrations by Any Fasting and Daily Fasting

Fasting Behavior	**N**	**Cortisol, Mean ± St Dev**	**p-value**
No Fasting	4	11,168 ± 13,247	NS
Any Fasting	39	6,567 ± 9,637	
No or Some Fasting	19	10,691 ± 13,260	0.019
Fasted Daily	24	4,069 ± 4,673	

Reasons for Not Fasting Women who did not fast or skipped days were asked why they did not fast and their responses were categorized as medical reasons, feeling physically unable to fast, or reasons unrelated to pregnancy. Women who did not fast all or some of the month because they did not feel they could, which was typically attributed to feeling exhausted, weak, thirsty, or dizzy, had significantly higher breast milk cortisol than women who fasted (Table 7.8). Although this group included women who were diabetic and hypertensive and included two of the high breast milk cortisol outliers, breast milk cortisol remained higher among this group when excluding the four outliers from the analysis ($p<0.017$).

Table 7.8: Linear Regression of Log of Breast Milk Cortisol Concentrations by Categorized Reasons for Not Fasting All or Some of Ramadan

Reasons for Not Fasting or Skipping Days	N	Cortisol, Mean ± St Dev	Coefficient (β)	p-value
Fasted Daily	24	4,069 ± 4,673	Reference Group	
Medical Reasons	7	8,465 ± 10,325	1.9	NS
Didn't feel she was able	8	16,370 ± 16,855	4.3	0.001
Other reason for exemption (ex.travel)	2	5,469 ± 264	2.2	NS

Maternal Variables and Breast Milk Cortisol

Table 7.9: T-Tests of Log of Breast Milk Cortisol Concentrations with Maternal Characteristics

Maternal Health Concern	N	Cortisol, Mean ± St Dev	p-value
Not Diabetic	39	5,904 ± 8,827	0.022**
Diabetic	4	17,628 ± 14,976	
Not Hypertensive	38	5,065 ± 5,492	0.012**
Hypertensive	5	21,660 ± 21,208	
Not Diabetic or Hypertensive	36	4,289 ± 3,574	0.001**
Diabetic and/or Hypertensive	7	20,908 ± 18,559	
Reproductive History			
Primiparous*	9	6,320 ± 4,237	0.042**
Multiparous*	30	3,642 ± 3,082	
Style of Dress			
Hijab or More Conservative*	32	4,014 ± 3,504	NS (0.097)
Less Conservative than Hijab*	5	6,480 ± 3,540	
Stressors During Pregnancy			
No Birth Related Stress Reported	38	7,744 ± 10,325	0.001
Birth Related Stress	5	1,301 ± 1,000	

* T-tests excluded four outliers

** P-value of a one-tailed t-test

Health In t-tests, breast milk cortisol did not vary by women who reported any health condition versus none, by women who reported anemia compared to non-anemic women, or by women who reported a condition categorized as other. Previous studies have demonstrated that diabetes and hypertension are associated with increased maternal cortisol (Ahmed & Shalayel, 1999; Laatikainen et al., 1991; Perkins et al., 1995), so a one-tailed t-test was used for these conditions. Breast milk cortisol was significantly higher in women with diabetes or hypertension (Table 7.9). When excluding the four outliers, three women in with diabetes and/or hypertension remained in the subsample and the difference between groups disappears. This was considered in other statistical analyses in this chapter, and significant differences in results when removing the four outliers from the analysis are reported.

Reproductive History Primiparous mothers tend to have higher cortisol levels than multiparous mothers (Breakey, 2015), so a one-tailed t-test was used. However, in this sample, t-tests did not reveal significant differences in breast milk cortisol between primiparous and multiparous or primigravida and multigravida mothers with t-tests. However, when removing the four outliers from the analysis, average breast milk cortisol of primiparous mothers was significantly higher than multiparous mothers ($p<0.042$, see Table 7.9). Previous miscarriages were not significant to breast milk cortisol concentration.

Age and Anthropometry Maternal age and anthropometry were analyzed for their relationship to breast milk cortisol in pairwise correlations and together in a multivariate linear regression. When including all mothers, no maternal anthropometry measurements were correlated with breast milk cortisol concentrations. If excluding the four outliers, maternal height was positively correlated with breast milk cortisol ($r=0.447$, $p<0.004$). In a stepwise multivariate linear regression of maternal age and all anthropometry variables except weight, only height was significantly predictive of increased breast milk cortisol (Table 7.10).

Table 7.10: Stepwise Multivariate Linear Regression of Log of Breast Milk Cortisol Concentrations with Maternal Anthropometry

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
Age (Years)	1.0	0.096
Body Fat Percentage	1.0	0.181
Height (cm)	1.1	0.028
BMI	1.1	0.096

Style of Dress In a two-tailed t-test, average breast milk cortisol of women who dressed less conservatively was not significantly different than women who dressed more conservatively. However, breast milk cortisol was higher in women who dressed less conservatively at a significant level of $p<0.1$ removing the four outliers ($p<0.097$, Table 7.9), so this variable was included in the multivariate model.

Pregnancy and Birth-Related Stress Breast milk cortisol did not vary by whether women reported stressors during pregnancy. These variables were assessed for their relationship to cortisol due to the responsiveness of cortisol to stressors. Given the fact that birth related stressors may have led to a cesarean delivery prior to the initiation of labor and a corresponding rise in cortisol, a two-tailed t-test was used. Participants who reported complication or stressor during the birthing process, such as a cord wrapped around the infant's neck, had significantly lower breast milk cortisol than women who did not (Table 7.9).

Family Advice, Medical Advice, Infant Feeding Intentions, and Vitamin Intake Family advice and medical advice about fasting, infant feeding intentions, and vitamin intake were associated with fasting behavior, as discussed in Chapter 5, and were therefore included in the present analysis. Breast milk cortisol did not vary by advice received from families about fasting, medical advice, infant feeding intentions, or vitamin intake.

Multivariate Analysis

Stepwise multivariate analysis was used to determine which maternal characteristics predict breast milk cortisol. Maternal variables that were found to be significant at $p<0.10$ included maternal age, height, and BMI, style of dress, reporting birth related stressors, multiparity, and having diabetes and/or hypertension. Daily fasting versus no fasting or skipping days was found to be associated with lower cortisol, so daily fasting was added. The number of days fasted was the primary variable of interest to this study, so it was included. Any potential effect of days fasting on breast milk cortisol was predicted to be moderated by the number of days between fasting and labor, so this variable was included. Study duration and the number of days postpartum of the breast milk sample were also controlled for in the model, although neither were significant in univariate analyses.

The result of the stepwise model is displayed in Table 7.11. Having diabetes or hypertension, increased height and increased BMI were retained and positively associated with breast milk cortisol. Daily fasting remained associated with lower breast milk cortisol. This trend remained when controlling for diabetes and hypertension, when taking women with these conditions out of the model, and when removing just the outliers. To note, if running the same model without the four breast milk cortisol outliers, having diabetes and/or hypertension was no longer significant and no other variables changed in significance or the direction of the correlation. Higher average cortisol among women who did not fast daily cannot, therefore, be attributed to the effect of these health conditions, which were associated with reduced fasting, as discussed in Chapter 5.

After controlling for these other variables that were associated with breast milk cortisol, increased number of days fasting was retained in the model as predictive of increased milk cortisol ($\beta=1.1$, $p<0.004$). Days between fasting and labor and study duration were not retained in the model.

Table 7.11: Stepwise Multivariate Regression of Log of Breast Milk Cortisol Concentrations with Significant Maternal Variables, Fasting Daily, Days Fasted, and Days Between Fasting and Labor

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
Less Conservative Dress	2.1	0.081
Height (cm)	1.1	0.036
BMI	1.1	0.044
Diabetes and/or Hypertension	3.9	0.001
Number of Days Fasted	*1.1*	*0.004*
Fasted Daily	*0.5*	*0.019*

Infant Variables and Breast Milk Cortisol

Infant Sex and Health At the end of pregnancy, mothers of female infants have been observed to have higher levels of circulating cortisol than mothers of male infants (Dipietro et al., 2011). Mothers of females were therefore hypothesized to have higher postpartum milk cortisol, but there was no significant difference by infant sex, whether outliers were included or not. Breast milk cortisol also did not vary by whether the infant was reported as healthy or not.

Infant Anthropometry

Table 7.12: Pairwise Correlations Between the Log of Breast Milk Cortisol Concentrations and Infant Gestational Age and Anthropometry, Non-Significant Correlations Excluded from Table

Infant Gestational Age and Anthropometry	**R**	**p-value**
Birth Weight (g)	0.33	0.032
Weight (g)	0.35	0.023
Length (cm)	0.35	0.023
Arm Circumference	0.37	0.018

Gestational age and infant anthropometry were assessed for their relationship with milk cortisol. Anthropometry included weight at the time of birth, weight at the time of neonatal measurements (48-72 hours postpartum), length, head circumference, arm circumference, and triceps and subscapular skinfold. Ponderal indexes based on birth weight and neonatal weight were also analyzed. Additionally, z-scores for birth weight, neonatal weight, length, and head circumference were analyzed for infants of known gestational age. Pairwise correlations identified positive correlations between breast milk cortisol and birth weight, neonatal weight, length, and arm circumference. Significant correlations are shown in Table 7.12.

Supplemental Feeding in Hospital A previous study found bottle-feeding to be associated with higher maternal salivary cortisol compared to breastfeeding for multiparous but not primiparous mothers (Tu, Lupien, & Walker, 2006), which may be due to the suppressive effects of breastfeeding on cortisol (Amico, Johnston, & Vagnucci, 1994; Tu et al., 2006). Although a greater percentage of this sample was multiparous and it may, therefore, be predicted that women who exclusively breastfed at the hospital may have lower breast milk cortisol, many women who were supplementing were not exclusively bottle feeding either. Therefore, the t-test remained two-tailed. Based on t-tests, supplemental feeding with formula was associated with higher breast milk cortisol (Table 7.13). When removing the outliers, this was no longer significant.

Table 7.13: T-Tests of Log of Breast Milk Cortisol Concentrations by Supplemental Feeding Behaviors in the Hospital

Infant Feeding in Hospital	**N**	**Cortisol, Mean ± St Dev**	**p-value**
No Supplements	23	4,286 ± 3,334	NS (0.057)
Supplements	19	10,594 ± 13,815	
No formula	27	4,671 ± 4,579	0.043
Formula	15	11,584 ± 14,852	

<u>Multivariate Analysis</u>

Infant anthropometric variables that were associated with cortisol were considered for the multivariate analysis. Arm circumference was included in the multivariate model. Birth weight, birth weight z-scores, neonatal weight, and neonatal weight z-scores were significantly positively correlated with breast milk cortisol. As one birth weight was missing and two infants z-scores were not calculated, neonatal weight was used to maintain the sample size. Length and length z-scores were also identified; length was included because the two z-scores were not calculated. To note, z-scores were not calculated for the two infants because their charts did not have an indication of whether they were or were not full-term at birth. Anthropometry measurements of one of the infants was well within the range of the other full-term infants so this infant was most likely full term, while the other was the smallest infant in this sample and slightly under what is considered healthy length and weight for a full-term infant. Additionally, supplementing with formula was included in the model.

Fasting variables were also added. Fasting daily was included since daily fasting was associated with lower cortisol in the univariate analysis. As the association with fasting was of interest for the present analysis, the number of days fasted was added to the analysis, and study duration was also included. If the number of days fasted is associated with breast milk cortisol, the relationship would be predicted to attenuate with increased duration after the discontinuation of fasting prior to labor, so this variable was also included. Additionally, since the days postpartum of the breast milk sample collection varied, days postpartum was added to the model.

In the multivariate model, significant predictors of increased breast milk cortisol included increased infant length, having opted out of some or all fasting, and having supplemented the infant's diet with formula (Table 7.14). To note, if running the same model without the four breast milk cortisol outliers, number of days between fasting and labor was also inversely correlated with breast milk cortisol ($p<0.016$).

Table 7.14: Stepwise Multivariate Linear Regression of Log of Breast Milk Cortisol Concentrations with Significant Infant Characteristics, Daily Fasting, Days Fasted, and Days Between Fasting and Labor

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
Infant Length (cm)	1.22	0.004
Supplementing with Formula	2.40	0.014
Fasted Daily	*0.44*	*0.011*
Independent Variables Retained if Infant Sex is Included	**Coefficient (β)**	**p-value**
Infant Sex (Female)	2.14	0.012
Infant Length (cm)	1.33	0.000
Supplementing with Formula	2.34	0.010
Fasted Daily	*0.30*	*0.000*
Study Duration (Days)	*1.02*	*0.077*
Days between Fasting and Labor	*0.98*	*0.075*

Infant sex was also considered for inclusion in the multivariate analysis. Although not significant in the univariate model and therefore did not meet the qualifications for inclusion in the multivariate analysis, infant anthropometry varied by sex, so it was considered that controlling for infant anthropometry may reveal differences in breast milk cortisol by infant sex. Adding infant sex into the previous model, being female was a predictor of significantly higher breast milk cortisol content (Table 7.14).

Full Multivariate Model

The variables that were retained in the previous multivariate models were added together with the same fasting variables. The multivariate model that included maternal, infant and fasting variables included: maternal diabetes and/or hypertension, height, BMI, and style of dress; infant length and supplementing with formula; and fasting daily, days fasted, days between fasting and labor, and study day.

Significant predictors of increased cortisol included maternal diabetes and/or hypertension, increased infant length, less conservative maternal style of dress, opting out of some or all fasting, and increased number of days fasted (Table 7.15). Maternal BMI and days between fasting and labor were retained but not significant. Without the four outliers, having diabetes and/or hypertension were not significant predictors of breast milk cortisol, but no other variables changed in significance or direction of the correlation.

Table 7.15: Stepwise Multivariate Linear Regression of Log of Breast Milk Cortisol Concentrations with Significant Maternal and Infant Characteristics, Daily Fasting, Days Fasted, and Days Between Fasting and Labor

Independent Variables Retained in Model	**Coefficient (β)**	**p-value**
Diabetes and/or Hypertension	3.61	0.002
Maternal BMI	1.06	0.076
Maternal Height	1.04	0.086
Less Conservative Dress	1.99	0.084
Infant Length (cm)	1.12	0.063
Number of Days Fasted	*1.06*	*0.002*
Fasted Daily	*0.45*	*0.011*
Independent Variables Retained if Infant Sex is Included	**Coefficient (β)**	**p-value**
Diabetes and/or Hypertension	2.98	0.006
Less Conservative Dress	1.67	0.185
Supplemental Feeding with Formula	1.79	0.060
Infant Sex (Female)	1.81	0.033
Infant Length (cm)	1.26	0.000
Number of Days Between Fasting and Labor	*0.97*	*0.011*
Study Duration (Days)	*1.03*	*0.012*
Fasted Daily	*0.40*	*0.002*

As infant sex was considered in the previous model and found significant, this was repeated in this model. Being female was again a significant predictor of increased breast milk cortisol, along with increased infant length. The number of days fasted was no longer significant and instead, study day was positively correlated with breast milk cortisol ($p<0.012$), and the number of days between fasting and labor was inversely associated with breast milk cortisol ($p<0.011$). Without fasting variables, infant sex was no longer retained in the model.

Summary of Predictors of Postpartum Breast Milk Cortisol

Increased breast milk cortisol was associated with having diabetes and/or hypertension and not participating in fasting daily. Fasting duration was positively correlated with milk cortisol only after accounting for these variables and other covariates in the model of maternal variables and in the full model. Variables that predicted increased breast milk cortisol in the multivariate model of maternal characteristics included maternal height and BMI, but these were not retained in the full model. In the model with infant characteristics, increased infant length and formula feeding predicted higher breast milk cortisol, but these were also not significant in the full model, with the exception of length when including infant sex. Although infant sex was not related to breast milk cortisol based on t-tests, its addition to the multivariate models demonstrated that it was a significant predictor of breast milk cortisol. However, the addition of infant sex to the model influenced the significance of fasting duration, and infant sex was only retained if fasting variables were included in the model. This may indicate that the relationship between fasting and breast milk cortisol varies by infant sex.

Predictors of Follow-Up Breast Milk Cortisol

For the nine women with follow-up milk cortisol data, the previous analyses were repeated, excluding the multivariate models due to the small sample size.

Fasting

Follow-up breast milk cortisol was not associated with any fasting behaviors or reasons for opting out of fasting.

Maternal Variables

Follow-up breast milk cortisol was not associated with any maternal characteristics that varied in this group. For the six individuals that have initial and follow-up breast milk cortisol data, cortisol concentration in the first sample predicted cortisol in the follow-up sample in a linear regression ($p<0.013$). When using the logs of both measurements, the initial and follow-up cortisol were not correlated.

Infant Variables

Follow-up breast milk cortisol did not vary by infant sex or health in t-tests. Using the log of the cortisol concentration, subscapular skinfold measurements were positively correlated with breast milk cortisol concentration in pairwise correlations (Table 7.16).

Table 7.16: Pairwise correlations between the log of follow-up breast milk cortisol concentrations and infant birth anthropometry (non-significant variables omitted from the table)

	Cortisol Concentration (Log)	
Infant Gestational Age and Anthropometry	**R**	**p-value**
Arm Circumference (cm)	0.61	NS (0.077)
Subscapular skinfold (mm)	0.74	0.022
Triceps plus Subscapular skinfold (mm)	0.64	NS (0.061)

Summary of Determinants of Follow-Up Breast Milk Cortisol

Given the small sample size, multivariate modeling was not completed for follow-up breast milk cortisol. In univariate analysis, breast milk cortisol was positively correlated with initial breast milk cortisol content and infant subscapular skinfolds.

Discussion

The primary research question of this chapter was whether maternal fasting behavior contributed to variation in breast milk cortisol. The results of these analyses demonstrate that maternal fasting behavior was associated with postpartum milk cortisol in four ways: fasting daily versus some or no fasting, reasons for not fasting daily, and days fasted. Additional variables associated with breast milk cortisol included maternal diabetes and/or hypertension, maternal style of dress, maternal anthropometry, infant anthropometry, and infant sex.

These results should be interpreted cautiously given that this is based on a single cortisol sample per individual, the small sample size, and the cross-sectional nature of this study. Women also gave birth via cesarean, so the hormonal cascade of events that typify labor and delivery may have been altered in this sample. Also, many women were advised not to eat for a period of time after giving birth, though drinking water was permitted, so some participants may have still been in a fasting state. It was primarily women who were unable to give milk samples that commented on this and I did not recognize this until later in the study, so this factor cannot be controlled for in the analyses. Variation in postpartum food intake is likely randomly distributed throughout the sample in comparison to the number of days fasted during Ramadan or that most women were not eating prior to giving the milk sample and therefore possible that this had minimal influence on the analyses. Additionally, cortisol during pregnancy and labor is elevated compared to non-pregnant individuals, so the variability between and within individuals in this sample may not be comparable to other studies that have assessed cortisol in biological samples. Breast milk samples were taken at approximately 3 days postpartum, which is a transitional period for maternal cortisol, though days postpartum was not correlated with breast milk cortisol in any analysis. The surge of cortisol that occurs during labor would have passed, but the high levels of maternal cortisol that characterize pregnancy would not yet have returned to pre-pregnancy levels (Jolivet et al., 1974; Mclean & Smith, 1999). However, some variables associated with breast milk cortisol were consistent with other studies, which is encouraging as to the validity of the present analysis. Additionally, although the follow-up breast milk sample data set is too small to analyze within or between individual variability in cortisol, the correlation between maternal milk cortisol concentrations taken at the two time points does bode well for the within-individual variability in postpartum milk cortisol and therefore for the reliability of the analyses of the initial breast milk cortisol samples.

Fasting Variables and Breast Milk Cortisol

Fasting every day of Ramadan that passed prior to going into labor was consistently associated with lower breast milk cortisol in all models compared to fasting some of the time or not fasting at all. In the multivariate analyses, controlling for or excluding participants with diabetes and hypertension from the analysis did not reduce the association between daily fasting and lower breast milk cortisol, so the difference in cortisol between these groups cannot be fully attributed to the inclusion of women with diabetes and hypertension.

Participants who did not fast or skipped days were asked about the reason for their fasting decision, so the group that did not fast daily was further categorized by their reasons for opting out of fasting. Reasons were categorized as exemptions not related to pregnancy or health (such as travel), medical reasons, or feeling unable to fast for non-medical reasons such as thirst or exhaustion. The group that cited feeling unable to fast was the group that had significantly higher cortisol than the group of women who fasted daily. Even after removing outliers or all women with gestational diabetes and hypertension from the analysis, this group still had significantly higher breast milk cortisol than the participants who fasted daily. Comparatively, when asked about fasting decisions, women who fasted every day of Ramadan essentially said they did so because they felt able to. The percentage of women who did not, therefore, find fasting during pregnancy to be excessively difficult was 56% in the present sample, which is similar to what was found by Joosoph et al. (2004).

Although most women did not express feeling social pressure to fast, the relationship between opting out of some or all fasting and higher breast milk cortisol may indicate that there is stress involved in the decision to be non-compliant with the social norm of fasting or with a religious obligation. If this is the case, the decision to opt out of fasting influences maternal cortisol. In Chapter 5, reduced fasting was also associated with increased weight, and BMI was also positively associated with breast milk cortisol. However, other than medical concerns, including diabetes, there were no identifiable differences in the group that listed feeling unable to fast as their reason for opting out. An alternative explanation for these findings is that increased breast milk cortisol in the group that felt unable to fast daily may indicate differences in underlying metabolic physiology of women who find fasting during pregnancy to be too difficult versus women who find it to be manageable. Evidence that supports this hypothesis includes studies demonstrating the effect of glucocorticoids on eating behaviors. For example, Epel, Lapidus, Mcewen, and Brownell (2001) found that cortisol reactivity accounted for individual differences in food intake, with higher cortisol reactivity associated with higher caloric intake and consumption of more sweet foods when exposed to stressors. Although cortisol as a continuous variable was not as strongly associated with food intake as cortisol reactivity, cortisol may reflect or mediate other factors involved in the stress response that more directly influence eating behavior, such as leptin, neuropeptide Y or cytokines. This research mirrors findings from animals studies on the manipulating of glucocorticoids that produce effects on dietary choice and weight via mechanisms such as overriding the appetite-regulating effects of leptin (Bell et al., 2000; Solano & Jacobson, 1999).

Because of this association between daily fasting and reduced cortisol, fasting duration appeared to be inversely but not significantly correlated with breast milk cortisol in univariate regression. After controlling variables that were associated with reduced fasting and increased cortisol, including daily fasting, having diabetes or hypertension, and maternal anthropometry, increased fasting duration was positively associated with cortisol, as predicted. Fasting duration was significantly correlated with milk cortisol only when controlling for daily fasting. In both the multivariate model with maternal variables and in the multivariate model that included both maternal and infant variables, the number of days fasted was positively correlated with breast milk cortisol. Causal relationships cannot be determined by the present analysis, but these results support the hypothesis that maternal fasting contributes to variation in postpartum breast milk hormones.

It was predicted that increased duration of fasting would be positively correlated with breast milk cortisol. It was also predicted that this correlation would be moderated by the amount of time that had elapsed since fasting had ended and the initiation of labor. The duration between fasting and labor, however, was not correlated with reduced breast milk cortisol as predicted. One hypothesis to explain this finding is that maternal fasting during late pregnancy may have prolonged effects on placental function, as was reported in a study by Alwasel et al. (2010). This study found that placental size at birth was decreased but placental efficiency was increased in women who had fasted in the second and third trimesters of pregnancy, which may have helped to increase blood flow and nutrient availability to the fetus as an adaptive response to fasting. Since cortisol during pregnancy is so strongly controlled by the placenta, it is possible that fasting leads to adaptations in the placenta in order to increase blood flow and nutrients and that these adaptations remain after normal eating behaviors resume.

The possible confounding effect of study duration also may be important, because when adding infant sex to the full models, days fasted was no longer retained but study day and reduced duration between fasting and labor were predictive of increased cortisol. However, it may be difficult to parse out the differences between study duration and fasting duration in the relationship to breast milk cortisol. Study implementation began as Ramadan began, so pre-Ramadan data is unfortunately not available for comparison, and few participants in the study opted out of fasting completely. Study duration was also positively correlated with the number of days fasted and inversely correlated with the number of days between fasting and labor ($p<0.000$ for both). It is, therefore, possible that this variable is still indicating an association between breast milk cortisol and fasting duration, especially if fasting during pregnancy has prolonged effects. Alternatively, the seasonal increase in temperatures that occur from late May to late July may correspond with an increase in maternal cortisol levels throughout the study (Braig et al., 2015; Kanikowska et al., 2019). Study day may also be important regardless of fasting decisions because fasting during the month of Ramadan is a community experience, and even if not fasting, pregnant women may experience a disrupted food environment during the month (Yamauchi et al., 2009).

Non-Fasting Variables and Breast Milk Cortisol

Several non-fasting variables were also related to breast milk cortisol. Additional predictors of increased milk cortisol included having diabetes and/or hypertension, increased maternal height and BMI, supplemental feeding, infant length, and female infant sex.

Diabetes and Hypertension

Increased breast milk cortisol was observed in participants with diabetes and/or hypertension. In this sample, the four breast milk samples that were atypically high in cortisol compared to the rest were from women with either or both conditions. Some previous studies have found that women with diabetes and hypertension during pregnancy had high maternal cortisol or CRH (Ahmed & Shalayel, 1999; Laatikainen et al., 1991; Perkins et al., 1995), although this has not been consistently demonstrated (Braig et al., 2015; Grigorakis et al., 2000; Ho et al., 2007).

Although maternal and placental cortisol during pregnancy cannot be established based on this study, it seems reasonable to predict that circulating maternal cortisol during pregnancy may also have been atypically high in these individuals. Cortisol is necessary for normal fetal growth and development, but abnormally high levels are associated with poor birth outcomes, including lower birth weight and length, premature birth, and miscarriage (Bolten et al., 2011; Christian, 2012; Field & Diego, 2008; Thayer & Kuzawa, 2014). If fasting is found to further exacerbate already high cortisol in women with these conditions, as this study suggests may be the case, fasting may also increase the risk of poor birth outcomes. Although these conditions have been grouped together for this analysis, they have different etiologies and birth outcome risks. The outcomes of maternal fasting for women with these conditions deserves further research.

Maternal Anthropometry and Infant Anthropometry

When considering only maternal variables and fasting behaviors, maternal height and BMI were positively correlated with breast milk cortisol. In the model that included infant anthropometry variables, maternal BMI was retained but not significant, although when removing style of dress, BMI was significant. Since those variables were related, dress may have confounded the influence of maternal anthropometry in this analysis. Additionally, maternal size is a strong predictor of fetal size, so that may also have influenced the result that breast milk cortisol was predicted by infant anthropometry but not maternal anthropometry in the full model.

In utero exposure to high levels of glucocorticoids is typically associated with reduced fetal size at birth (Bolten et al., 2011; Field et al., 2006). It is unclear to what degree postpartum milk cortisol would be indicative of circulating maternal cortisol during pregnancy, but if it were, an inverse association would be predicted between infant birth anthropometry and breast milk cortisol. This does not appear to be the case, as length was positively correlated with breast milk cortisol in the multivariate model with infant characteristics, and several other infant measurements were positively correlated with breast milk cortisol in univariate analyses.

Supplementing with Formula at the Hospital

Supplemental feeding implies reduced breastfeeding. Due to the suppressive effects of breastfeeding on cortisol (Amico et al., 1994; Tu et al., 2006) and research demonstrating that bottle-feeding is associated with higher maternal salivary cortisol (Tu et al., 2006), supplemental feeding at the hospital was predicted to be associated with increased breast milk cortisol. This prediction was supported, as supplemental feeding with formula was associated with increased breast milk cortisol in a t-test and in a multivariate analysis with infant anthropometry variables. However, in the full multivariate model, supplemental feeding was not significant. Maternal variables, particularly diabetes and hypertension, were more relevant.

Infant Sex

Mothers of females decreased cortisol in early pregnancy and increased cortisol in late pregnancy compared to mothers of males (Dipietro et al., 2011). Therefore, if postpartum breast milk cortisol is related to maternal cortisol in late pregnancy, mothers of females would be predicted to have higher postpartum milk cortisol based on variation in maternal cortisol during pregnancy by fetal sex. In this analysis, breast milk cortisol did not vary by infant sex in univariate analysis, but when added to multivariate analyses, breast milk of mothers with female infants had significantly higher cortisol content.

The addition of infant sex to the full model altered the significance of fasting behaviors on breast milk cortisol, and infant sex was only significant when fasting variables were included. This may indicate that the correlation between fasting and breast milk cortisol varies by fetal sex. This hypothesis is supported by other research that indicates response to maternal nutrition during pregnancy varies by fetal sex, which tends to find males to be more vulnerable. Males appear to be less buffered against environmental stress during fetal growth and development, respond more strongly to nutritional supplementation, and are more strongly affected by intrauterine exposure to nutritional deficits (Stinson, 1985). For example, males were more affected by the Dutch Hunger Winter in the prevalence of conditions related to undernutrition such as spina bifida (Brown & Susser, 1997). Males appear to be more responsive to a mother's current nutritional status, reflected in maternal BMI, and more affected by malnutrition during pregnancy, while females appear to be more responsive to lifetime nutrition, reflected in height (Alwasel et al., 2011). Testing this hypothesis requires further research, but the implication that fasting may have differential effects by fetal sex presents an interesting question for future research.

Conclusion

This analysis of determinants of postpartum breast milk cortisol suggests that fasting behavior may be related to breast milk cortisol. After controlling for other covariates, the duration of fasting was positively correlated with breast milk cortisol. This finding supports the hypothesis that maternal fasting during late pregnancy contributes to variation in the hormonal milieu experienced by the neonate and indicates that cortisol may signal the neonate about the stressor created by maternal fasting. Given that this data is based on a single sample per participant and relies on a small sample size, more research is needed to confirm these findings, but they merit further research into the relationship between maternal fasting and the hormones offspring are exposed to in utero and in breast milk.

However, the relationship between fasting duration and postpartum breast milk cortisol is complex. The correlation was only significant when controlling for whether participants fasted daily or opted out of some or all fasting because breast milk cortisol was significantly higher overall in women who opted out of some or all fasting for various reasons. As discussed in Chapter 5, women who fast are different from women who opt out of some or all fasting. Reasons women opted out of fasting included having diabetes or hypertension or feeling physically unable to fast for non-medical reasons, such as thirst and exhaustion experienced when fasting. Women who reported these health conditions and experiences also had higher breast milk cortisol. Because of this, if daily fasting was removed from the multivariate analyses, fasting duration was no longer significantly related to breast milk cortisol. It is possible that between-woman variation in baseline metabolic hormones influences how difficult the experience of fasting is during pregnancy.

Although these results should be interpreted with caution, they demonstrate that this topic should be explored further and contribute to the current research to better understand causes and consequences of variation in milk composition between and within women (Neville et al., 2012). These results also prompt several additional research questions. Follow-up questions include whether fasting has differential effects by fetal sex, the role of baseline metabolic hormones in how difficult fasting is during pregnancy and whether fasting duration causes prolonged changes in cortisol or other hormones, perhaps via adaptive efforts to increase placental blood flow and nutrient transfer. Even if cortisol exposure in utero or via breast milk is responsive to environmental stressors, as suggested by this study, to demonstrate that variation is contributing to lactational programming requires additional research on the role of within-individual variation in breast milk hormones in altering infant growth and development, which is outside of the scope of the present study. In the following chapter, I aim to synthesize the results of this chapter on the determinants of postnatal breast milk cortisol with the results of the previous two chapters, which considered determinants of maternal fasting behaviors and the relationship between maternal fasting behaviors and birth outcomes.

Chapter 8: Relationships Between Maternal Fasting, Fetal Growth, and Breast Milk Cortisol

This dissertation research addressed questions about the role of maternal ecology on fetal growth and the hormonal milieu the newborn is exposed to in postpartum breast milk. These questions are embedded in a theoretical framework from life history theory and developmental programming. Drawing on Ramadan fasting as a natural experiment, I used a biocultural approach to consider how differences between women shape maternal fasting behaviors during late pregnancy and assessed the associations between maternal fasting, infant birth size, and postpartum breast milk cortisol concentration. Ramadan fasting is not simply a biological experience of food and water abstinence but is intertwined with the cultural and religious backdrop in which it takes place.

Biological outcomes of fasting during pregnancy and lactation are embedded in this complex religious, cultural experience and therefore cannot be fully understood apart of the sociocultural environment in which it takes place. Although more extensive ethnographic work could better address the cultural backdrop than was possible within the constraints of this research, the present data can speak to some aspects of the religious fasting during pregnancy as both a cultural and biological experience. Considering various levels of causal pathways that connect the social environment to the biological outcomes, I considered how the cultural experience of fasting may influence biology, from the behavioral and social aspects of fasting to the impact on hormonal and cellular processes, and how biological variation between individuals shape the experience of religious fasting (Dufour, 2006). Given the variability in the duration of daily fasting, climate, and populations which practice Ramadan fasting, cross-cultural comparisons of outcomes of Ramadan fasting have the potential to yield an increased understanding of the intrauterine environmental and breast milk composition responses to maternal food and water abstinence. This research can help address questions about how infant life history strategies are shaped by maternal ecology, including what trade-offs are made to the specific stressor posed by maternal fasting. Moreover, by combining methods and theory of cultural and biological anthropology in addressing these questions, the biological aspects of fasting can be contextualized within the cultural and religious experience.

In this dissertation, I tested three main hypotheses. I hypothesized that women who fasted during late pregnancy differed from women who opted out of fasting and that these differences could confound the relationships between maternal fasting and outcome variables. I also hypothesized that increased maternal fasting would be associated with reduced fetal growth. Lastly, I hypothesized that the physiological stress associated with maternal fasting would be perceptible to a newborn via variation in maternal cortisol present in postpartum breast milk. These hypotheses were supported by the findings of the study, albeit not always as predicted. Predictors of reduced fasting during late pregnancy included having diabetes, hypertension, anemia, higher maternal body weight and lower body fat, being advised not to fast by medical personnel or family members, and taking vitamins. Several of these variables were associated with infant birth size and postpartum breast milk cortisol. Any fasting was associated with lower z-scores for known gestational ages for birth weight, length, and head circumference. Days between fasting and labor was positively correlated with neonatal weight z-scores for known gestational age, length, length z-scores for known gestational age, head circumference, and head circumference z-scores for known gestational age, which suggests in utero catch-up growth. Duration of fasting was not associated with any infant anthropometry variables. Postpartum breast milk cortisol was higher amongst women who opted out of some or all fasting and particularly among women who opted out of fasting because they felt unable to fast rather than for medical reasons or non-health related reasons. After accounting for this, increased fasting duration predicted increased breast milk cortisol.

In this discussion of the findings of this dissertation, each of these three main hypotheses, how they relate to each other, and how the findings from this research contribute to the current literature are addressed in turn. I then consider how these findings relate to the hypothesis that abstinence from food and water for 16 hours per day for several days during late pregnancy is a physiological stressor that may trigger in utero adaptations. If so, maternal fasting may play a role in shaping life history strategies via fetal and lactational programming, which may include prolonged changes in the intrauterine environment after maternal fasting. I then discuss several questions for future research evoked by this research. I also offer guidance in the translation of the results of research on maternal fasting during Ramadan to the public sphere, including recommendations for harm-reduction approaches. Because recommendations on maternal and infant health too often focus on individual responsibility and mother blaming without considering the overarching role of broader social structures (Richardson et al., 2014), I follow with a critical assessment of the broader social and religious determinants of maternal fasting before discussing study limitations and concluding thoughts.

Determinants of Maternal Fasting

As predicted, many maternal characteristics that were related to variation in fasting behaviors also had implications for fetal growth and milk cortisol. Variables such as maternal anthropometry, health conditions, vitamin intake, and infant sex were associated with fasting behaviors and were predictive of neonatal anthropometry and postpartum breast milk cortisol.

Having a diagnosis of diabetes had an important negative influence on fasting and was found in this study and in other research to be associated with increased infant size (Brydon et al., 2000; Catalano et al., 2003; Persson et al., 2009) and maternal cortisol, which would suggest breast milk cortisol may also be increased (Ahmed & Shalayel, 1999). Maternal size was overall positively correlated with infant birth size, as other studies have also demonstrated (Kramer, 2003; Voigt et al., 2010). Infants are often found to be smaller when born to anemic women (Scholl & Hediger, 1994) or hypertensive women (Kramer, 1990; Oluwafemi, Njokanma, Disu, & Ogunlesi), although these maternal health conditions were not significantly related to infant anthropometry in this study. Hypertension is additionally associated with elevated maternal cortisol (Laatikainen et al., 1991; Perkins et al., 1995), which was also true of this sample. Maternal vitamin intake was associated with reduced maternal fasting, and to the best of my knowledge, vitamin supplementation has not before been considered as a predictor of fasting. Yet, this is an important variable to control for when considering birth anthropometry outcomes, as vitamin intake was associated with increased fetal growth in this study and in other studies (Cogswell et al., 2003; Preziosi et al., 1997; Ribot et al., 2013). Clearly, biological and cultural factors are important determinants of maternal fasting and are important to control for in analyses of fasting outcomes, as fasting decisions and fetal growth were often shaped by similar maternal variables.

Increased maternal fasting was also associated with reduced maternal weight and increased maternal body fat. Women who weigh less and have higher body fat may have greater difficulty sustaining fasting. Alternatively, Ramadan fasting during late gestation may result in reduced gestational weight gain and reduced fat free mass, as was found in a study by Awwad et al. (2012), or even weight loss and signs of accelerated starvation as reported by Prentice, Prentice, Lamb, et al. (1983). These hypotheses are not mutually exclusive, but more data is needed to understand this finding. Dikensoy et al. (2009) did not observe differences in gestational weight gain between fasting and non-fasting women, so fasting duration and other factors may influence gestational weight gain during fasting.

The relationship between fasting and maternal body composition is important to understand, as fetal growth is largely a product of the intrauterine environment, to which maternal anthropometry and diet are important contributions (Cameron & Bogin, 2012) and inadequate gestational weight gain can increase the risk of reduced fetal weight, length and ponderal index, and neonatal death (Cnattingius et al., 1998; Stein et al., 1995). As expected, maternal weight and BMI were related to several infant anthropometric measurements, including length, weight, and skinfold measurements. If Ramadan fasting influenced maternal body composition, deconstructing the relationship between fasting, maternal weight, and infant anthropometry is more complicated.

Family advice and medical advice against fasting were both also predictive of reduced fasting. Women in this study expressed general support from family members in their decisions, but this study and others have reported high incidence of maternal fasting in Muslim populations (Ertem et al., 2001; Joosoph et al., 2004; Mubeen et al., 2012; Ozsoy et al., 2014; Robinson & Raisler, 2005; Saleem et al., 2010). Additionally, women in this study who did not fast never gave pregnancy in itself as a reason for not fasting but always justified the decision with additional reasons. Fasting during pregnancy is the norm in this population. Women have reported feeling criticized for being "soft" if they don't fast (Sacirbey, 2010). It is reasonable to expect that a certain amount of social pressure exists regarding fasting. Social support for non-fasting, indicated in this study through the advice of family members about fasting decisions, probably makes the decision to opt out of fasting easier. Although more extended interviews had been planned to try to better assess social pressures around fasting, it was not possible within the constraints of the study.

Medical advice was also taken seriously in this population. As fasting during pregnancy is the norm, women probably observe year after year their friends, family members, and neighbors fast without any obvious adverse consequences. Given that, advising all women against fasting is unlikely to be taken seriously, a point which was argued by Robinson and Raisler (2005). However, when doctors consider advising against fasting on a case by case basis if there is an additional medical concern, as is the case in this Moroccan population, the advice was always followed immediately. This means health care professionals play an important role in identifying high-risk pregnancies in which maternal fasting may add extra concern. The role of health care providers will be discussed further below when considering recommendations about maternal fasting.

Maternal Fasting and Infant Anthropometry

To the question of the relationship between maternal fasting and birth outcomes, this research contributes evidence that fasting is associated with reduced infant weight, length, and head circumference for gestational age. This research also contributes evidence that infant birth size increased with a longer duration between fasting and birth, possibly indicating in-utero catch-up growth after the discontinuation of fasting. Although birth size was associated with any fasting and an increased duration between the discontinuation of fasting and labor, fasting duration was only associated with head circumference. However, in this case, and where days fasted was retained but not a significant predictor of infant size, the correlation between infant birth anthropometry and fasting duration was positive, rather than negative as was hypothesized. Since any fasting was associated with reduced infant size, I hypothesize that the number of days fasting may have a non-linear relationship with fetal growth.

Infant size at birth after exposure to maternal fasting may be predicted to be similar to findings from other studies of acute nutritional restriction in the third trimester, characterized by an increased risk of infant leanness, which would have been indicated by reduced weight, ponderal index and body fat (Villar et al., 1986). For example, exposure to the Dutch Hunger Winter in the third trimester was associated with reduced weight to length ratios at birth, along with reduced weight, length, and head circumference. In utero-catch up growth was also seen, as neonatal size rebounded within weeks of discontinued exposure to the famine (Aryeh D Stein et al., 2004). Alternatively, in undernourished Indian populations, babies have been categorized as having a "thin but fat" phenotype, retaining adequate fat disposition but reduced lean muscle mass, resulting in a reduced ponderal index but no change in other assessments of fat on the trunk or appendages (Yajnik et al., 2003). In this study, these trends associated with food restriction or undernutrition were not observed. While reduced weight, length, and head circumference were congruent with these findings, I found no associations between fasting and measures of infant leanness based on ponderal index, arm circumference, and skinfold measurements.

Results of other studies on infant anthropometry after in utero exposure to maternal fasting have not aligned with outcomes that would be expected based on other studies of acute food restriction. Only one study, conducted by Yamauchi et al. (2009), found a reduction in birth weight in infants born shortly after Ramadan, as would be expected based on studies from cases such as the Dutch Hunger Winter (Heijmans et al., 2008; Lumey & Van Poppel, 1994). However, other studies have found a significant reduction in birth weight associated with exposure to maternal fasting only earlier in pregnancy (Almond & Mazumder, 2011; Awwad et al., 2012; Savitri et al., 2014; Ziaee et al., 2010) or not at all (Arab & Nasrollahi, 2001; Cross et al., 1990; Kavehmanesh & Abolghasemi, 2004). Taken together, these findings suggest that Ramadan fasting during pregnancy may not be well captured by studies of famine and food restriction. Therefore, studies of dehydration and hormonal mechanisms involved in fasting will be considered.

The results of this study may reflect a recent finding of the impact of maternal dehydration during the third trimester, in which dehydration was associated with reduced weight, length, and head circumference after controlling for pre-pregnancy weight, maternal gestational weight gain, and intake of calories and other nutrients (Mulyani et al., 2018). Ponderal index was not assessed in this study. Although during Ramadan women can drink as much water as desired in non-fasting hours, spending long periods of time dehydrated during the day may be having more of an impact than many hours without food on fetal growth. The risk of spending several hours each day dehydrated while fasting is increased when Ramadan occurs over the summer solstice in areas north of the equator, when daily fasting duration is longest and when temperatures are high. Since hydration status was not assessed in this study, the relationship between dehydration and birth outcomes cannot be directly assessed from this study.

The association between maternal fasting and reduced infant anthropometry may be related to the duration of time spent in a fasting state, which is characterized by shifts in several metabolic hormones including increased glucocorticoids (Sareen & Jack, 2013). Glucocorticoids may play a role in infant growth during pregnancy. Bolten et al. (2011) found increased maternal cortisol during early and late pregnancy to be predictive of reduced infant weight and during late pregnancy to be predictive of reduced length at birth. Li et al. (2012) found that maternal cortisol in late gestation was inversely correlated with infant head circumference but not birth weight or other anthropometric measurements. Animal studies have indicated that this may be due to a causal pathway of glucocorticoids by demonstrating that prenatal exposure to high concentrations of glucocorticoids results in reduced brain growth and damage to developing neurons in a dose-dependent manner (Huang et al., 1999; Li et al., 2012; Sapolsky, 1985).

This hypothesis regarding birth size and fasting-induced elevation in glucocorticoids may be supported by the finding from Chapter 7, in which increased fasting was associated with increased postpartum breast milk cortisol. However, that relationship was complex, and it is not clear how well postpartum milk cortisol would reflect prenatal maternal circulating cortisol. Additionally, even if postpartum milk cortisol was indicative of prenatal maternal cortisol, it may not reflect intrauterine exposure to cortisol, as fetal exposure is moderated by the placenta via 11β-hydroxysteroid dehydrogenase, which converts cortisol to an inactive form (Benediktsson, Calder, Edwards, & Seckl, 1997). Food restriction in animal studies has been found to result in a decrease in placental 11β-hydroxysteroid dehydrogenase, thereby increasing fetal exposure to glucocorticoids (Dupouy, Lesage, Blondeau, BréAnt, & Grino, 2001), so this may also be the case with fasting, but, again, maternal fasting during Ramadan does not appear to be readily comparable to situations of food restriction.

Ramadan fasting involves food and water abstinence and therefore disentangling influences of one or the other is difficult. Still, comparison of research on Ramadan fasting with studies of famine, food restriction, and malnutrition suggests that different physiological mechanisms may be at play in mediating the interplay between these maternal environments and birth outcomes. Ramadan fasting may be better modeled by studies on the impact of dehydration and elevated glucocorticoids induced by fasting rather than situations of food restriction per se. Because of this, studies of Ramadan fasting contribute to the understanding of physiological effects experienced in conditions of water insecurity, a topic of current interest within the field of biological anthropology (Wutich & Brewis, 2014).

Participation in Ramadan fasting is a religious experience rather than due to ecological constraints. Food and water are not necessarily restricted during non-fasting hours, and the fast can be broken when necessary. Abstaining from food and water as part of Ramadan fasting, therefore, differs from situations of food or water scarcity, famine, and drought, which are very psychologically stressful (Wutich & Ragsdale, 2008). Unless practicing Ramadan in a food or water insecure setting, Ramadan fasting is not expected to be accompanied by the same sense of psychological stress. Whether the participants in this study were food or water insecure was not specifically addressed during data collection. One participant noted being intensely stressed about her financial situation, support, and access to resources, but no other participant commented on it directly or indirectly. Given the socioeconomic status of individuals served by this hospital and the rural areas they live in, it is possible that some were food or water insecure, with possible lack of access to treated water, which is the case in some rural communities. Psychological stress might also accompany the experience of opting out of fasting in a community in which fasting, even during pregnancy, is the norm. Participants in this study did not express feeling social pressure to fast and largely expressed feeling supported by their families for their decisions about fasting. While it is possible that the discussion about family input about fasting may have been shaped by my position as a foreign researcher, since other sources describing women's feelings about fasting during pregnancy do include expressions of social pressure to fast (Sacirbey, 2010; Wadud, 2010), the participants in this study did not express that sentiment.

Psychological stress is known to have implications for birth outcomes. For example, maternal depression, anxiety, or exposure to a traumatic event such as natural disasters and terrorist attacks have been associated with low birth weight and other indicators of reduced fetal growth (Bolten et al., 2011; Henrichs et al., 2010; Lederman Sally et al., 2004; Maric, Dunjic, Stojiljkovic, Britvic, & Jasovic-Gasic, 2010; Xiong et al., 2008). Mechanisms behind these relationships are still unclear, but perceived stress has not been demonstrated to be well-captured by maternal cortisol or cortisol reactivity in humans (Bolten et al., 2011). Therefore, studying physiological responses to Ramadan fasting during pregnancy may help elucidate biological adaptations to water deprivation and disentangle the physiological and psychological influences of water insecurity on birth outcomes.

Previous studies on maternal fasting and infant birth size have focused largely on birth weight as an indicator of fetal growth during fasting (Almond & Mazumder, 2011; Alwasel et al., 2010; Arab & Nasrollahi, 2001; Cross et al., 1990; Yamauchi et al., 2009). This analysis, therefore, expands the array of neonatal anthropometric measurements that have been examined in association with maternal fasting and demonstrates that indicators of fetal growth and development beyond birth weight are relevant to this topic. To my knowledge, there is only one study that had previously analyzed infant head circumference in relationship to maternal fasting (Ziaee et al., 2010) and none that control for the duration between fasting and labor in the analysis of birth outcomes, and this research reveals that these are meaningful variables to consider. Previous studies have also been unclear about whether gestational age was controlled for in the analysis, which is an important variable to consider, as illustrated by this research.

Postpartum Breast Milk Cortisol

This study provides evidence that maternal fasting during late pregnancy contributes to variation in the hormonal milieu experienced by the neonate in postpartum breast milk. As factors that impact within and between woman variability of breast milk is of current interest to those studying lactational physiology (Neville et al., 2012), this demonstrates that maternal abstinence from food and water for about 16 hours per day may be one of those factors. This supports the hypothesis that cortisol may signal to the neonate information about the stressor created by maternal fasting and may contribute to variation in infant life history strategies (Dantzer et al., 2013; Hinde, 2013; Hinde et al., 2014; Khulan & Drake, 2012; Peaker & Neville, 1991). Although more research is needed to verify this finding and a causal direction cannot be determined by these data, this finding is consistent with another study on fasting during pregnancy that reported elevated maternal cortisol during Ramadan in comparison to non-fasting controls (Dikensoy et al., 2009).

Interestingly, the positive relationship between fasting duration and milk cortisol was not attenuated by the duration between fasting and labor, as expected. A similar finding was reported by Khoshdel, Kheiri, Nasiri, Tehran, and Heidarian (2014), who found evidence of long-lasting adjustments in metabolic hormones in pregnant women after fasting, with increased neuropeptide Y and leptin during Ramadan fasting that did not decline after the discontinuation of fasting. This differed from the hormonal pattern observed in non-pregnant fasting controls for whom these biomarkers decreased after fasting, but as non-fasting pregnant controls were not included, the authors noted that it was not clear if this observation was a normal trend through pregnancy. In the present study, this result may be related to the small sample size, but it is also possible that these study results are suggestive of prolonged metabolic effects resulting from fasting during pregnancy.

The positive relationship between fasting duration and postpartum breast milk cortisol was additionally complex because it was only found after controlling for whether women fasted daily or not. Women who fasted daily had much lower postpartum breast milk cortisol compared to women who skipped days, particularly those whose reason for skipping days was that fasting was too difficult. Although Chapter 5 illustrated many of the ways in which women who fasted more differed from women who fasted less, the higher breast milk cortisol among the group that opted out of some or all fasting suggests an additional difference between women that may be related to fasting decisions.

Categorized by the reason women provided when asked why they opted out of fasting, women who said they felt they could not fast had significantly higher breast milk cortisol compared to women who fasted daily, women who opted out of fasting for medical reasons, or women who had an exemption unrelated to health or pregnancy. This association remained after removing outliers and removing women with diabetes or hypertension. Compared to women who fasted daily, women who felt unable to fast for non-medical reasons were taller and were more likely to be primiparous. Although they did not attribute their difficulty fasting to medical reasons, they were also more likely to have anemia or diabetes. Other than anemia, these variables also were associated with higher postpartum breast milk cortisol. However, these variables were controlled for in the multivariate analysis, yet the differences between groups remained significant. As breast milk cortisol and maternal cortisol are highly positively correlated (Breakey, 2015), this may be indicative of underlying differences in maternal cortisol between women who find fasting during pregnancy to be too difficult to sustain compared to those who find it to be manageable.

Women who find fasting during pregnancy to be too difficult may differ in metabolic hormones from women who fasted daily, who commonly said they did so because they felt they could. If this hypothesis is accurate, metabolic hormones may play a role in shaping women's experiences of fasting and their ability to participate in the religious fast. Having to opt out of fasting may cause distress for women who want to participate in fasting, which may compound already elevated stress hormones. On the other hand, given the relationship between high maternal cortisol during pregnancy and adverse birth outcomes (Bolten et al., 2011; Christian, 2012; Field & Diego, 2008; Thayer & Kuzawa, 2014), and the research linking glucocorticoids to appetite regulation and food intake (Bell et al., 2000; Epel et al., 2001; Solano & Jacobson, 1999), it is also possible there is a protective mechanism at play for women who have high cortisol levels during pregnancy. In this case, feeling that fasting is unsustainable may be a biological prompt to drive behavioral to increase food intake to mitigate the physiological response associated with the fasting state.

This finding may also be of interest to researchers studying appetite regulation, dietary adherence, and obesity, as this may be indicative of biological mechanisms that make adherence to dietary recommendations more difficult for some individuals. Although pregnant individuals are not often prescribed diets to induce weight loss, healthy pregnant women are typically given food rules to follow while pregnant, both based on western medical advice and cultural beliefs about pregnancy and food, and women with conditions like gestational diabetes are usually recommended to follow dietary plans as part of the medical management of that condition (Serlin & Lash, 2009).

Ramadan, Prolonged Post-Fasting Adaptations, and Developmental Programming

The overarching question in the bioanthropological aspect of this research is whether maternal abstinence from food and water for 16 hours per day during the month of Ramadan creates a stressor that influences the intrauterine environment, fetal growth, and postpartum breast milk cortisol. Is the intrauterine environment altered, such that a fetus is required to make trade-offs in growth and development? Does maternal fasting contribute to variation in the hormonal milieu that the fetus is exposed to in utero or that the infant is exposed to via breastmilk?

The results of this research support the hypothesis that maternal fasting is associated with variation in infant birth size. Altered fetal growth patterns suggest adaptations to a suboptimal intrauterine environment. Adapting to adverse environments often come with costs, as adaptation implies a trade-off or compromise (Fisher, 1985; Wiley, 1992). Adaptation to suboptimal intrauterine environments can overlap with critical periods of development, and the associated cost may be to fetal growth or development. This can result in developmental programming, wherein long-term, irreversible effects result from biological responses to stressors (Waterland & Michels, 2007). Although long-term impacts are not assessed in this study, other studies have found associations between exposure to maternal fasting in utero and consequences to cognitive development, including worse academic performance (Almond et al., 2015; Oosterbeek & Van Der Klaauw, 2013) and increased incidence of cognitive disabilities and hearing and sight impairment (Almond & Mazumder, 2011).

The number of days fasted was positively associated with increased milk cortisol, but this was not attenuated with an increased number of days between the discontinuation of fasting and delivery. This finding suggests that adaptations to fasting during pregnancy may persist after fasting is discontinued. Previous studies have demonstrated potentially prolonged effects following maternal fasting. Khoshdel et al. (2014) demonstrated prolonged alteration in metabolic hormones, specifically neuropeptide Y and leptin, in pregnant women that did not rebound after the discontinuation of Ramadan fasting. Additionally, Alwasel et al. (2010) found reduced placental weight and reduced placental to birth weight ratio in infants of mothers who had fasted in the second and third trimesters but not the first trimester. This is consistent with findings from human and animal studies of reduced placental size during when food restriction occurs later in pregnancy (Stephenson & Symonds, 2002). Reduced placental to birth weight ratio is characteristic of intrauterine growth restriction and suggests adaptations occur to improve the efficiency of placental transfer (Stephenson & Symonds, 2002), which Alwasel et al. (2010) hypothesized may be occurring in infants exposed in utero to maternal fasting during later gestation. Given that placental size and ratio to body weight was reduced when exposure occurred in the second trimester as well as the third, catch-up growth of the placenta did not appear to occur, and the adaptations to enhance placental transfer with a reduced placenta size may have been maintained after fasting was discontinued.

That a reduction in placental size may result from a decline in placental transfer during maternal fasting is supported by a study from Iran when fasting was 12 hours per day, which observed reduced fetal renal artery flow during maternal fasting (Bayoglu Tekin et al., 2016). However, maternal fasting has not been shown to lead to reduced uterine artery flow when daily fasting duration was about nine hours in the United Arab Emirates (Mirghani et al., 2007), or in Iran when fasting hours were about 15 hours per day (Moradi, 2011), so more research on placental transfer and both maternal and fetal artery flow may elucidate these results.

Results from this study also hint at a possibility that adaptations to maternal fasting persist throughout the remainder of the pregnancy, which could be explored further in future research. In Chapter 7, fasting duration was consistently a predictor of increased breast milk cortisol, but surprisingly, this was not attenuated by the number of days between fasting and labor. However, some women noted that they were advised against eating after the cesarean section. Therefore, there is a chance that some women were in a fasting state when giving the milk sample, creating an unaccounted-for confounding variable in this analysis. If there is variation in postpartum diet prior to providing the sample, it is likely randomly distributed among the sample. If the variation in postpartum diet is minimal, it should not alter the relationship between postpartum breast milk cortisol and fasting variables. Given the cross-sectional nature of the study, causality cannot be determined, but this finding in combination with the findings of Alwasel et al. (2010) and Khoshdel et al. (2014) engender a hypothesis that the duration of maternal fasting may induce alterations in placental size and efficiency of transfer that persist beyond the fasting period to impact post-fasting fetal growth. Whether regulation of placental CRH is interrelated with this would also be of interest, as increased placental release of CRH is a hypothesized response to fetal stress due to its role in accelerated fetal organ maturation, increased blood flow to the fetus, and possibly the initiation of labor if there is a threat to survival in utero (Mclean & Smith, 1999). This mechanism to increase blood flow to the fetus may help explain the associations in this study between increased postpartum breast milk cortisol and increased infant length, weight, and arm circumference.

Additionally, in Chapter 6, it was predicted that fasting duration would be associated with reduced infant size, moderated by the length of time between fasting and labor. This hypothesis was supported in that any fasting was associated with reduced infant size and the duration between fasting and labor that was positively associated with neonatal anthropometry. However, as previously discussed, fasting duration was positively associated with head circumference. This suggests that accelerated growth may have occurred after the discontinuation of fasting. If prolonged alterations in placental function or hormonal regulation occur due to maternal fasting, they may be related to mechanisms that promote accelerated catch-up growth. In that case, increased duration of fetal exposure to the adaptation that occurred in response to fasting may be more important than the duration of the stressor that caused it. It is also possible that the relationship between fasting duration and fetal growth is not linear. If changes to the placenta size and efficiency of transfer occur during maternal fasting, as suggested by the study by Alwasel et al. (2010), growth trajectories may change before the discontinuation of fasting in response to placental changes.

This study also suggests that maternal fasting contributes to variation in postpartum breast milk cortisol, which supports the hypothesis milk hormones may act as mediators between maternal ecology and infant life history strategies and play a role in lactational programming. However, since maternal cortisol in this early postpartum period is expected to reflect placental control of CRH and cortisol, I might hypothesize that the postpartum duration for which fasting during pregnancy continued to predict variation in milk cortisol would only remain so long as the effects of placenta CRH remain. Placental CRH is responsible for elevated maternal cortisol levels for about one week postpartum. Still, if breast milk cortisol is responsive to maternal stressors such as fasting, this allows for the possibility that lactational programming may be taking place. However, demonstrating that programming is occurring requires additional evidence that variation in breast milk cortisol alters infant growth or development. Although evidence for this is outside of the scope of the present study, other studies offer insight into this possibility.

Although milk cortisol concentration has been linked to increased offspring growth in animal studies (Dantzer et al., 2013; Hinde et al., 2014), this has not been observed in humans (Breakey, 2015). However, several studies suggest that variation in milk cortisol may contribute to variation in infant behavioral development (De Weerth et al., 2003; Glynn et al., 2007; Grey et al., 2013), which has also been suggested in a study of primates (Hinde et al., 2014). More research on this topic is needed, and since maternal fasting may be perceptible in breast milk via variation in glucocorticoid concentration, Ramadan provides an ideal context within which to frame questions about breast milk glucocorticoids and infant growth and behavioral development.

Additional Future Research Directions

The results of this research raised several questions about the relationships between maternal fasting, fetal growth, and maternal and milk cortisol. In addition to the questions discussed above, which include adaptive mechanisms related to maternal fasting, prolonged alterations in the placenta, and whether variation in postpartum milk hormones has prolonged effects on infant development, several other relevant topics arose from this research. Further considerations for this research topic include more in-depth analysis of social pressures to fast, gestational weight gain during fasting, the role of infant sex in maternal fasting decisions and fasting outcomes, whether baseline differences in metabolic hormones contribute to the experience of fasting and the role of dehydration and metabolic hormones in birth outcomes.

Although more extensive interviews had been the original intention of this study, they were not possible due to various constraints during the study implementation. This leaves several questions unaddressed about the social experience of being pregnant or breastfeeding during Ramadan in Morocco. Ethnography, interviews, and participant observation could help better understand women's experiences of fasting in several ways. Interviews could help clarify how women think about and strategize about diet, activities, hydration, and other challenges faced when fasting during pregnancy. A more in-depth cultural analysis could also help elucidate whether women worry about fasting during pregnancy if they feel additional anxiety about fasting for any reason when pregnant, the role of social support both for her decisions in fasting and in other aspects of her life, and how social support interrelates to fasting decisions. Additionally, this could help assess what risks and concerns women have while fasting and clarify whether there is perceived stress associated with fasting. This could help understand how women experience Ramadan when they choose not to fast, including whether there is emotional distressful involved in this decision, and, if it is emotionally stressful, whether that stress is due to feeling judged for going against social norms, failing to meet an important religious obligation, or other reasons.

A better understanding of the circumstances in which women are able to maintain adequate weight gain while fasting would be beneficial to the study of maternal fasting. Understanding the interplay between maternal weight gain and fetal growth during fasting may help to elucidate reasons for the incongruent findings of studies of fetal growth during maternal fasting. This may also help to clarify the roles of other factors that influence maternal responses to fasting and birth outcomes, such as fasting duration, climate, and hydration.

This research suggests that infant sex may be an important mediating factor in maternal fasting behaviors and in the relationship between fasting and milk cortisol. Women with medical concerns were less likely to fast if the infant was male, although medical concerns did not vary by infant sex. As many of these women received medical advice or had medical care due to their health conditions, it is likely that this subset of women had access to prenatal care and thus had an opportunity to learn the sex of the fetus before birth. Therefore, this finding may be due to cultural factors such as son preference, which has been noted in Morocco (Obermeyer & Cárdenas, 1997). However, doctors report that many women giving birth at this hospital do not have an opportunity to find out the infant sex before birth. If infant sex was not known, it is possible that biological mechanisms are at play.

In the analysis of breast milk cortisol and maternal fasting, infant sex contributed to variation in postpartum breast milk cortisol, but only if accounting for maternal fasting variables. This suggests that the relationship between postpartum breast milk cortisol and maternal fasting may vary by infant sex, although this may be a product of the small sample size and limited cortisol data. Research with a larger sample size may be able to more clearly illustrate if this is occurring and if so, illustrate the nature of the association. Future research on maternal fasting might consider the potential impact of infant sex, both as a contributing factor in maternal fasting decisions and as a mediator in the outcomes of maternal fasting.

The finding of high cortisol in women who opted out of fasting because fasting felt difficult may indicate underlying metabolic differences between women who find fasting more difficult compared to those who find it to be manageable. Further research is needed to clarify what metabolic factors may be playing causal roles in this relationship, which could include the assessment of the pre-fasting metabolic state, maternal cortisol levels and cortisol reactivity, and other hormones regulating food intake such as leptin and Neuropeptide Y in comparison with individual variability in the ability to withstand Ramadan fasting. Elucidating the role of biological variation in metabolism and dietary intake may help better support the general population and pregnant individuals in particular in managing a healthy diet.

The findings of this study are not fully congruent with outcomes of acute food restriction in late pregnancy. While there were some similarities in terms of reduced size for gestational age, this study did not find evidence of increased leanness, as would be expected. Further research into birth outcomes after exposure to dehydration and altered metabolic hormones may help better understand the patterns of fetal growth outcomes observed in relationship to Ramadan fasting. Research comparing outcomes of Ramadan fasting versus extended periods of time without food (such as an extended overnight fast) versus hydration status during different points in gestation may help clarify how and why this fast differs from outcomes of food restriction. Outcome variables to consider for comparison in these circumstances could include placental transfer to assess fetal blood supply, placental production of CRH, placental anthropometry after birth, and infant anthropometry measurements that account for gestational age and include measures of leanness. To better isolate the effects of dehydration specifically, the study by Mulyani et al. (2018) on the impact of dehydration in late pregnancy on infant birth weight, length, and head circumference could be extended to include measures of fatness and placental measurements to better understand how birth outcomes are associated with dehydration independently of food restriction. Because the Ramadan fast can be broken when needed and is part of a religious practice, it is not accompanied by the psychological stress associated with food and water insecurity. Therefore, with a better understanding of how birth outcomes are associated with Ramadan fasting, along with the discrete consequences associated with dehydration and with the metabolic changes associated with periods of abstinence from food consumption, comparing Ramadan fasting with outcomes of food and water insecurity may help elucidate any additional impacts of psychological stress accompanying these situations.

Translating Results to the Public Sphere

When translating research to the public sphere in the form of public health recommendations, guidance for health care providers, and advice for individual-level use for a decision as personal as the observance of a religious obligation, the aim should be to increase women's sense of autonomy over their behaviors and decisions. Offering specific instructions about fasting decisions based on research or using blame or judgment when discussing fasting decisions will not be as effective as offering advice aimed at harm reduction and presenting information respect for women in making their own decisions about fasting. Fasting may have biological implications, but it is experienced as a central facet of the religious and cultural environment. As it is the norm to fast during pregnancy in many populations, the probable social pressure should also be acknowledged. With this in mind, I first discuss the context in which Muslim women find themselves in a position in which fasting during pregnancy is the norm. By situating maternal fasting during Ramadan in the context of the broader social structure, I critically consider the patriarchal religious and social structure in which this particular pattern of maternal fasting takes place. I then turn to recommendations for maternal fasting based on this research and the results of previous studies.

Who Decided Pregnant Women Should Fast in the First Place?

Studies of birth outcomes in relation to maternal behavior, stress, diet, and developmental origins of health and disease too often result in mother-blaming and in prescribing actions women can take on an individual level to reduce risks that ignore the larger social structure and other variables that shape women's decisions (Richardson et al., 2014). In the case of Ramadan fasting, pregnant and breastfeeding women are not making decisions about fasting in a vacuum. Although women express autonomy over fasting decisions and a desire to fulfill the religious obligation, fasting decisions are fundamentally shaped by the larger social and religious structure, including religious leaders who make rulings on fasting and exemptions for fasting and social norms to which women are exposed.

As such, women's fasting decisions are dominated by the influence of males within the religion, society, and home. In her article *Defining Women's Health: A Dozen Messages from More than 150 Ethnographies*, Marcia Inhorn (2006) described the health-demoting consequences of patriarchy as a major theme in women's health concerns globally, which plays out in macrostructural to microstructural realms of women's lives and should be considered as part of the societal structure that endorses maternal fasting. Until very recently, men have entirely dominated the arena of religious leadership in the Islamic religions, although a trend of female leadership has begun to emerge in some places in recent decades (Bano & Kalmbach, 2011). As the primary policymakers and religious leaders, men make decisions that influence women's bodies on a large scale, including whether pregnant and lactating women should fast. Examples are seen in the ruling by the religious leader of Muslims in Singapore that it is obligatory for pregnant women to fast if the pregnancy is healthy (Joosoph et al., 2004) and in both the writings and interpretation of Islamic law that define the circumstances in which pregnant and breastfeeding women can opt out of fasting (Hallaq (2007) as cited in Kridli (2011)). The additional influence of husbands' opinions on women's fasting decisions (Joosoph et al., 2004; Robinson & Raisler, 2005; Van Bilsen et al., 2016) demonstrates that micro-structural level how men can alter maternal fasting behavior within the home.

A religious ruling allows any woman to opt out of fasting if she fears for her own or the infant's wellbeing (Hallaq (2007) as cited in Kridli (2011)). Several studies have demonstrated adverse outcomes of maternal fasting, including reduced male to female birth ratios (Almond & Mazumder, 2011; Friger et al., 2009; Hoffmann, 2014; Johnson et al., 1975), reduced birth weight (Almond & Mazumder, 2011; Awwad et al., 2012; Yamauchi et al., 2009), reduced placenta size (Alwasel et al., 2010), reduced fetal heart rate (Hisham M. Mirghani et al., 2004), and reduced fetal breathing movements (H. M. Mirghani et al., 2004). Studies have also found an increased incidence of gestational diabetes, induction of labor, cesarean section, and admission of the infant to the special care unit (Mirghani & Hamud, 2006). Long term consequences in cognitive function and disability risk have also been reported (Almond & Mazumder, 2011; Almond et al., 2015; Oosterbeek & Van Der Klaauw, 2013). Although some studies have not found fasting to adversely affect their chosen outcome variables, these have largely focused on a single outcome such as birth weight or preterm labor (Arab & Nasrollahi, 2001; Cross et al., 1990; Kavehmanesh & Abolghasemi, 2004), which does not constitute adequate evidence to support the claim that maternal fasting has no adverse consequences, although that is sometimes the conclusion drawn.

Overall, there is a growing body of research describing the consequences of maternal fasting such that a pregnant woman might experience legitimate concern over the health and wellbeing of her offspring. However, how well these research findings are made publicly accessible is not clear, particularly in places where there are high rates of illiteracy. Still, women who feel able to fast often desire to do so and opting out is not always an easy decision.

This decision to opt out of fasting is made harder by an important aspect of the exemption: all days in which women opt out of fasting must be made up later. This presents a barrier to women's ability to choose not to fast, as women often report that they would rather fast with everyone else rather than make up the days later by themselves (Kridli, 2011; Robinson & Raisler, 2005). Considering that women who are pregnant will likely be breastfeeding for the following two years if observing the guidelines from the Quran, the expectation to make up those days within the year represents a naïve interpretation of the reproductive effort involved in maternal care. In a blog post titled "Women's Double Duty", Amina Wadud (2010), Professor Emeritus of Islamic Studies at Virginia Commonwealth University, questioned the rationale of the "exclusively male jurists" who determined that women must make up days of fasting missed due to normal reproductive biology. She drew on both her voice as a scholar and her own experience of missing days of fasting during reproductive years to question the validity of relating reproductive biology to exemptions for illness and to question how reasonable the expectation is that days are to be made up. She additionally argued that if she was able to make a ruling on the issue, women would not be required to make up days of fasting missed due to menstruation, pregnancy, and breastfeeding, as she would not have equated these circumstances to illness.

This begs the question, how might the rules of fasting during pregnancy and lactation be different if women had at any time been allowed positions of decision-making power or had been the ones writing and interpreting Islamic law? Women who participated in this research and other studies have largely expressed autonomy over the decision on whether to fast or not (Joosoph et al., 2004; Robinson & Raisler, 2005). Yet, true autonomy in this decision requires females to be in leadership positions with the power to interpret and rule on the types of religious questions that impact women's bodies. Providing females with a voice in Islamic scholarship and religious rulings would allow for increased conscious awareness of the hardship imposed by the expectation to fast when pregnant and lactating and by the requirement to make up days missed.

Recommendations about Fasting During Pregnancy

In their article "Each One is a Doctor for Herself", Robinson and Raisler (2005) provided excellent guidance for health care providers of pregnant Muslim women that focuses on harm-reduction, with advice on assessing intentions to fast and creating a plan to fast safely during pregnancy, risk factors and warning signs to discuss with patients, and what additional medical supervision might be necessary. However, several studies have come out since the time of this article that suggests that the fetal environment might be altered by maternal fasting such that fasting may carry a higher risk than was thought at the time of the publication of this article. Still, given the agency women express in making decisions about fasting, the advice provided on medical guidance for women considering fasting is as valid now as it was then. As reported by Robinson and

Raisler (2005), women want to be given the facts and information about research and medical advice but not blanket prohibitions on fasting during pregnancy or commands about what decision to make. Maternal fasting is the social norm in many Muslim populations. Many Muslim women live in areas in which they see other women fast during pregnancy and nursing without obvious consequences and in which fasting is part of a community experience, so they may feel less connected to their religious community if they do not participate in fasting. Therefore, advice against fasting many not align with women's lived experience or desired community religious experience. Harm-reduction approaches, therefore, remain the most practical avenue to take when translating research to the public sphere, and these approaches should continue to be explored and encouraged regarding maternal Ramadan fasting.

Still, the current state of research regarding outcomes of maternal fasting could be better made available to women who are making decisions about fasting. It would be ideal if more information was available through doctors and possibly also through media formats accessible to illiterate women and provided without the intention of persuading women's decisions. Rather, information aimed at harm-reduction methods should be emphasized. Appropriate harm-reduction approaches were well-described by Robinson and Raisler (2005). Their recommendations included: assessing patients intentions and plans for fasting, including how to maintain adequate nutrition and hydration during fasting; discussing individual risk factors that the patient should be aware of if choosing to fast, particularly for women who have medical conditions that contraindicate fasting; discussing how to fast safely and raising awareness about warning signs that indicate fasting should be discontinued; and increasing patient prenatal supervision during fasting. Sharing information about the potential consequences of fasting on birth outcomes should be accompanied by practical steps to take if opting to fast. Additionally, health care providers can have an impact on maternal fasting, as was demonstrated in this study, as they play an important role in identifying high-risk pregnancies that may be complicated by maternal fasting and assessing risks for conditions that are associated with dehydration or dietary restriction.

It also may be recommended that health care providers ask patients and members of the community they serve about fasting norms during pregnancy and lactation to be better aware of fasting practices in their patients. During the feasibility study and prior to study implementation, several doctors stated that it may be difficult to find women who were fasting to participate. Doctors working at public hospitals in Morocco serve communities of lower socioeconomic status and they may be less familiar with the norms of these communities. Given that most of the participants in this study did fast, it may be beneficial to patients if medical professionals are aware of fasting behaviors in their patients and potential associated risks. Husbands and family members, whose support is important in decisions to opt out of fasting, should be included in discussions with health care professionals about research on maternal fasting, birth outcomes, and assessment of risk factors.

Based on the results of this study, it would be advisable to monitor gestational weight gain and hydration status of women who opt to fast during pregnancy, as these variables may help estimate how physiologically stressing fasting is for the mother and assess risks to fetal growth. The most practical ways for an individual to assess hydration status is to recognize signs of dehydration, including thirst, headache, fatigue, increased heart rate, and overheating (Cheuvront & Kenefick, 2014) and to assess urine color (Mckenzie & Armstrong, 2017), but it can also be assessed with laboratory analysis of blood or urine or with bioelectrical impedance methods (Cheuvront & Kenefick, 2014; Lukaski, Hall, & Siders, 2007). If women are not gaining weight as advised or if dehydration is constant during fasting, it may be advisable to stop fasting, or, if continued fasting is desired, to supplement the diet with nutrient dense foods and developing strategies to stay better hydrated, such as reducing physical activity, staying in temperature controlled environments when possible, and increasing water intake in the non-fasting hours. In locations where there is variation in sunlight hours between years, fasting during the month of Ramadan may be more difficult in some years than others, and making up days fasted when daylight hours are shorter may present reduced risks to pregnant and lactating women and their infants.

It would also be ideal to address the social pressure to fast in order to make the decision to opt out of fasting more socially accessible for women who find fasting difficult. Women have reported feeling criticized as being "soft" if they opt not to fast (Sacirbey, 2010). However, the results of the milk cortisol analysis in the present study suggest that there may be physiological differences in the metabolism of women who find fasting more difficult than others. This finding and further exploration of this potential biological difference will hopefully provide support to those that are finding fasting to be difficult, as their experience may be reflecting a real biological difference. Ideally, this information would help shape the narrative around non-fasting, lead to increased support for fasting decisions, encourage women to listen to their bodies, and help to reduce feelings being weak if unable to participate in fasting during pregnancy.

Study Limitations

Limitations include the small sample size and the primarily cross-sectional nature of the data. As such, this analysis does not lend itself to interpretations of cause and effect. Pre-pregnancy maternal anthropometry and maternal gestational weight gain were also not available. As maternal BMI and body fat percentage were associated with various infant anthropometry variables, being unable to determine whether fasting had an intermediary effect on maternal body composition was a limitation of this study. An additional limitation was basing the statistical analysis of breast milk cortisol on a single sample per individual, which does not yield robust results (Hruschka et al., 2005), as discussed in detail in Chapter 7.

These results may not be generalizable to other populations. The hospital serves lower socioeconomic status communities, and poverty is associated with increased average cortisol and cortisol reactivity in mothers and infants (Clearfield, Carter-Rodriguez, Merali, & Shober, 2014; Thayer & Kuzawa, 2014) and with increased risk of altered fetal and infant growth (Ball, Jacoby, & Zubrick, 2013; Karlberg, 2006; Layte, Bennett, Mccrory, & Kearney, 2014). Additionally, a large proportion of participants delivered by cesarean section.

Collecting postpartum breast milk cortisol was a challenge for several reasons. Delayed initiation of breastfeeding and supplemental feeding within 72 hours postpartum were common among study participants. Most participants delivered by c-section, which is associated with difficulties initiating breastfeeding (Gale et al., 2012). Another contributing factor to delayed initiation of breastfeeding was women not eating after cesarean section deliveries, sometimes for days. Due to gas pain that some women experience after surgery, most women said that they were advised not to eat anything until it passed, and because they would not have milk until they were able to eat, they would give formula until then. This was a reason that women did not give a breast milk sample; among women who did give a sample, this issue was not discussed because I did not become aware of it until well into the study implementation phase and participants did not mention it during interviews. Therefore, it unclear if this was a common situation for study participants who did give samples. If so, some of them may have been in a fasting state due to this medical mandate, which may have a confounding effect on the data analysis. This also may have contributed to increased supplemental feeding at this hospital. However, another factor may be perceptions of milk production and lack of awareness about the benefits of postpartum breast milk. Women at the hospital often did not believe they were producing enough milk for their infants within the first 48 hours. Even when milk was expressed from the breast, many women would say that it was like water, not milk.

Due to constraints of the research setting, my ability to interview women about diet during Ramadan, social support, and stress was more limited than intended. Circumstances also did not allow for further assessment of milk composition, such as nutritional quality. However, as other research has not found a significant effect of Ramadan fasting on the nutritional quality of breast milk, any confounding effects of nutritional quality of the milk are expected to be minimal (Rakicioglu et al., 2006).

Concluding Thoughts

A biocultural approach to the study of Ramadan fasting can help contextualize the biological responses to food and water abstinence within the cultural environment in which the religious fast is practiced. This research provides insight into cultural and biological factors that shape maternal fasting behaviors and the experience of fasting during pregnancy. It also provides evidence that maternal fasting is associated with reduced fetal growth and in utero catch-up growth and may contribute to variation in postpartum breast milk cortisol concentration. These results support the hypothesis that in utero adaptations occur in response to maternal fasting and lay a foundation for understanding whether lactational programming is occurring in association with maternal fasting. The results of this study reveal several directions for future research and demonstrate that Ramadan fasting provides a valuable model to better understand the effects of water deprivation and the role of glucocorticoids in utero and in breast milk. Ramadan fasting can provide a unique opportunity to better understand the interplay between maternal ecology and fetal and infant growth and development. This research can also contribute to the body of information used to form recommendations and harm-reduction approaches for pregnant women who are considering participating in this religious fast.

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Appendix A: Enrollment Questionnaire

Date:______________ Participant ID______________

Infant's Date and Time of Birth: Month________Day_______2017, Time: ____Sex of Infant: Boy/ Girl

Infant Birth Weight (Normal: 2,500-4,000 grams):_______________

Was the infant born at full term? Yes / No How many weeks gestation?_____ Due Date:_________

Health issues for the infant? If so, list:____

Dominant Hand: Right / Left Identify Sample Breast (opposite Dominant Hand): Right / Left

Birth: Natural / C-Section Epidural: Yes / No

Any health issues for the mother during or after pregnancy?______________________________

Number of previous children: _______________ Number of previous births: _______________

Fasting behaviors:

Did the participant fast during Ramadan? Yes / No Number of Days:___

If no, why did you choose not to fast?

If yes, how many days of Ramadan did you fast?

If there were days when you did not fast, why did you not fast?

Does the participant's husband or family (or anyone) tell her she should fast or should not fast? Yes (should) / Yes (should not) / No

(If yes, who?)

Vitamin D:

How do you dress most days? Jilbab? Hijab? Western clothing?____________________

Specifically, how much of your skin is typically exposed to sunlight? __________________

Do you take any vitamins? Yes / No If so, what? ___________________

Specifically, do you take vitamin D supplements? Yes / No

Breastfeeding:

Does the participant intend to exclusively breastfeed for 6 months (no water or food or juice or tea): Yes / No

If no, why?

How long does she intend to exclusively breastfeed? ________

Interest in participating in the longitudinal research: Yes / No / Maybe

Appendix B : Follow-Up Questionnaire

Participant number:____________ Date of call:_____________

Has she been breastfeeding? Yes / No

How has breastfeeding been going? Has it been easy or difficult? If it has been difficult, why?

Has she given the baby formula, louisa, water, or anything else?

Does she feel like she has been producing enough milk?

Has the mother been healthy?

Has the baby been healthy?

Has the baby been to get vaccines? If so, are there any new weight or length measurements?

Date of measurements:

Weight:

Length:

Would she allow us to take another milk sample? Yes / No

If so, where does she live?

Would she come in to the hospital for follow up infant measurements?

Meagan Marie Guilfoyle
Curriculum Vitae

EDUCATION

Indiana University Bloomington, IN
Ph.D. in Anthropology, concentration in Bioanthropology *July 2019*
Dissertation: The Impact of Ramadan Fasting on Birth Outcomes and Breast Milk Cortisol
M.A. in Anthropology *2016*

Purdue University West Lafayette, IN
B.A. in Health Promotion and Anthropology *2008*
Dean's List, National Society of Collegiate Scholars, Phi Kappa Phi Honors Society

AREAS OF INTEREST

Biocultural Medical Anthropology, Lactational Physiology, Human Biology, Nutrition, Maternal and Infant Health, Human Growth and Development, DOHaD, Life History Theory, Reproductive Ecology, Endocrinology, Morocco, Middle East and North Africa Region

TEACHING EXPERIENCE

Indiana University Bloomington, IN
Associate Instructor, *Ethical Dilemmas: Human Gestation and Prenatal Care* *Spring 2019*
Human Biology Department (HUBI B-300)
Associate Instructor, *Introduction to Biological Anthropology* *Fall 2017, Spring 2018, Fall 2018*
Anthropology Department (ANTH B-200)

GRANTS AND FELLOWSHIPS

Wenner-Gren Dissertation Fieldwork Grant *2016*
Skomp Summer Research Feasibility Award, Indiana University *2015*
National Science Foundation Graduate Research Fellowship Program *2013-2018*
Foreign Language and Area Studies Fellowships (FLAS), Center for the Study of Global Change to study Arabic at the Indiana University SWSEEL Summer Language Workshop *2013*
Foreign Language and Area Studies Fellowships (FLAS), Center for the Study of the Middle East to study Arabic at Indiana University *2013*

PRESENTATIONS

Guilfoyle, M, EM Chester and AS Wiley. *2019*
Determinants of Ramadan fasting during late pregnancy and postpartum milk cortisol concentration in Rabat, Morocco. Poster session to be presented at the annual meeting of the Human Biology Association (upcoming, poster accepted).
Guilfoyle, M and AS Wiley. *2018*
Determinants of Ramadan fasting during the third trimester of pregnancy and influences on infant anthropometry and feeding practices in Rabat, Morocco. Poster session presented at the annual meeting of the Human Biology Association.
Guilfoyle, M. *2016*
Breastfeeding and Ramadan Fasting. Poster session presented at the annual symposium of the Anthropology Graduate Student Association.

OTHER TRAINING, CERTIFICATIONS & SKILLS

Certified Breastfeeding Specialist, *Lactation Education Resources* *2016*
Pedagogy course in Anthropology: Teaching Anthropology, *2013*
Ethnographic methods course *2014*
Bioanthropology research methods *2015*
Basic biometric measures (including venipuncture and blood pressure) *2014*
Anthropometric measurements training for adults and infants *2015*
Bayesian Statistics *2015*
Statistical software: familiar with Stata and R
Yoga Teach Training Program (200-hour), *LifePower* *2012*

EDUCATIONAL TRAVEL

Institute for Research and Learning in Archaeology and Bioarchaeology Lucca, Italy
Field School in Medieval Archaeology & Bioarchaeology at Badia Pozzeveri *2011*

University of New South Wales Sydney, Australia
Study Abroad *Spring 2006*

PROFESSIONAL ORGANIZATIONS

Human Biology Association
Student Member *2013 – present*

SERVICE

Indiana University Bloomington, IN
Student Member *2012-2013*
Darwin Club (Bioanthropology Reading Group), Indiana University, Bloomington
Steering Committee *2013 – 2014*
Darwin Club (Bioanthropology Reading Group), Indiana University, Bloomington

PROFESSIONAL EXPERIENCE

Community Foundation of Bloomington and Monroe Country Bloomington, IN
Administrative Assistant, (intermittent, temporary) *September 2016-June 2018*

- Conducted quantitative, statistical evaluations of effectiveness of grants administered by the organization and presented the analysis to members of the organization involved in grant application selection
- Provided administrative and clerical support and occasionally served as an assistant to the CEO

Health Solutions Services Chicago area
Health Screening Technician (contract) *October 2011-July 2012; November 2008-February 2009*

- Provided health coaching for individuals based on screening results; determined individual blood pressure, body fat and body mass indexes; administered blood cholesterol and glucose tests

Peace Corps Morocco
Community Health Educator, Volunteer *March 2009-April 2011*

- Integrated into the culture of a tribal village living agricultural and herding lifestyles and learned their unwritten dialect
- Conducted needs assessments to determine health priorities within the community
- Authored grant proposals to obtain funding for maternal and infant health programs
- Recruited participants for and administered a traditional birth attendant training for 31 women and structured outreach opportunities for the newly trained attendants to educate other women from their rural communities
- Conceived of and set up a pilot capacity building seminar for local associations and cooperatives which will be implemented on a larger scale by successive Peace Corps volunteers
- Developed curriculum and designed educational materials to conduct prenatal workshops
- Launched weekly lessons on maternal and child health at the local clinic
- Created a Life Skills Day for teenage girls unable to continue schooling to learn about women's health, self-esteem and peer pressure and to network with a nearby organization that helps women in rural areas develop income generating projects
- Created a one-day Life Skills Day Camp for teenage and young adult men to learn about sexual health, men's role in family health and family planning, women's rights under Moroccan law, setting goals, identifying individual and community strengths, weaknesses, opportunities and threats, and creating an action plan for change
- Conducted a sports club for kids three days a week during the summer break, which consisted of sports, games, dance, self-defense, and other physical activities, followed by health lessons, English lessons, self-esteem activities, or life skills activities.
- Taught weekly English classes in the local elementary school to various age groups

International Society for the Prevention of Child Abuse and Neglect West Chicago, IL
International Events Intern *August 2008*

- Created promotion materials, composed professional correspondences, and compiled data

Edward Hospital Health Promotion Department Naperville, IL
Health Promotion Intern *April 2008-August 2008*

- Developed, implemented, and evaluated a dance-inspired fitness program for three distinct demographics within the community
- Conducted activities and lesson plans according to participant needs and program objectives
- Assisted with an employee wellness program by explaining confidentiality paperwork, utilizing Excel to input and track participant data, and preparing weekly progress reports
- Evaluated an Edward program and provided feedback that resulted in updating the curriculum
- Gained skills in health education methods, adult and child learning strategies, and behavior change motivation
- Created educational materials, quizzes and handouts focusing on safety, nutrition, physical activity, emotional wellbeing, and other health related topics as needed
- Conducted a statistical evaluation of Edward Speaker's Bureau
- Prepared for and assisted with health fairs and program set-up
- Represented Edward at various community meetings and committees

LANGUAGES

Moroccan Arabic, intermediate conversation skills
Tamazight, unwritten language, advanced conversational skills