Fetal Programming and Later Obesity in a Predominantly Latino WIC Population

Eric George Walsh

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FETAL PROGRAMMING AND LATER OBESITY IN A PREDOMINANTLY LATINO WIC POPULATION

By

Eric George Walsh

A Dissertation in Partial Fulfillment of the Requirements for the Degree of Doctor of Public Health in Global Health

August 2013
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ABSTRACT OF THE DISSERTATION

FETAL PROGRAMMING AND LATER OBESITY IN A PREDOMINANTLY LATINO WIC POPULATION

By

Eric George Walsh

Doctor of Public Health Candidate in Global Health

Loma Linda University, 2013

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Background: In utero stressors may work to program the metabolism of the developing fetus in such a way that predisposes him/her to obesity later on. Studies have shown that breastfeeding is protective against childhood obesity and suggest that after six months the weight gain in breastfed babies slows opposed to formula fed babies who continue with rapid weight gain. This slowing of weight gain has been shown to be protective against adiposity and later life weight gain.

Purpose: This study looks to further explore these findings in a low income Latino population adding mother’s feelings about the pregnancy and the impact of prenatal caffeine intake as a mediator to increase in utero stress hormones.

Method: A retrospective analysis of data from California’s Women, Infants, and Children (WIC) Program’s Integrated Statewide Information System (ISIS) database, and the Automated Vital Statistics System (AVSS) was conducted with 487 pregnant women
and their children participating in the Orange County WIC Program from birth through 36 months of age.

**Results:** Using Hierarchal Linear Modeling, weight to length ratios were evaluated until 24 months for breastfeeding practices. The group that breastfed exclusively more than 6 months were the most lean at 12 and 24 months. The protective effects of breastfeeding existed regardless of how women felt about their pregnancy. Maternal caffeine intake was shown to be a significant contributor to the difference in weight in the children at 12 and 24 months of age.

**Significance to Global Health:** Childhood obesity in the United States is a disease disproportionately seen in poorer individuals of certain ethnic minority groups. This health disparity falls under the purview of global health especially because in the current study the group from whom the data is gathered are predominantly immigrants or first generation descendants of immigrants from Mexico.
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CHAPTER 1
INTRODUCTION

A. Statement of the Problem

Childhood obesity is a growing problem in the United States. It is estimated that the number of overweight 6-11 year olds has tripled since the 1970’s, and doubled for 12-18 year olds (MMWR, 2009). There are now children as young as 10 years old described as type 2 diabetics (Boney, Verma, Tucker, & Vohr, 2005). Public Health efforts to stem the rising tide of overweight and obese children have largely focused on lifestyle changes. However, these efforts have been minimally effective in halting the rising number of overweight and obese children. Programs have not proven effective especially among the poorest children where the highest rates of childhood obesity exist (MMWR, 2009).

Obesity in adults is defined as a BMI greater than 35 kg/m2. Overweight is defined as a BMI of 25 kg/m2 up to 35 kg/m2. Using these definitions greater than 50% of the adults in the United States are overweight or obese (Ogden et al., 2012). In children obesity is defined by age and sex specific BMI percentiles greater than 85. The prevalence of overweight children aged 2-5 years is 13.9% and for 6-11 year olds is 18.8%. The incidence of overweight children has tripled among U.S. preschoolers and has quadrupled among children age 6-11 years old (Ogden et al., 2012).

One alarming aspect of the growing weight problem facing children in the U.S. is that the prevalence of obesity is disproportionately higher among certain racial and ethnic groups as well as among individuals from lower socioeconomic status. In particular, African-Americans, Mexican Americans, and Native Americans bare increased rates of
obesity. Mexican American children have the highest rates of being overweight (Branscum & Sharma, 2011). Among children, Latino girls and boys have the highest or second highest rates for overweight and obesity among the different ethnic categories (Wang & Beydoun, 2007). Non-Hispanic blacks are the next most affected groups and non-Hispanic Whites are the lowest (Wang & Beydoun, 2007). Independent of race or ethnicity being of a lower socioeconomic status is key predictor of higher overweight and obesity prevalence in US children (Crawford, Story, Wang, Ritchie, & Sabry, 2001).

Obesity prevalence among the poorest Californians as reported in the Conditions of Children’s in Orange County Report (CCOC, 2011) for (and based on Pediatric Nutrition Surveillance System [PedNSS] data) was 17.0% in 2009 for 2-4 year olds and after fluctuating ended at 17.4% in 2007. In Orange County California, Hispanics are reported as have the highest percentage of overweight: 13.9% in 0-4 year olds and 22.9% for 5 to 11 year olds.

Overweight among Orange County Children by Race/Ethnicity and by Age, 2007

Percent of Records with Weight Greater than the 95th Percentile on the Pediatric Growth Chart

![Bar chart showing overweight prevalence by age and ethnicity](image)

Figure 1.1
1. Socioeconomic and Global Aspects of Obesity Epidemic

There are many hypotheses as to why there is such a rise in childhood obesity in the United States, especially among lower socioeconomic groups. Some of the reasons considered have been lack of access to healthy affordable foods; lack of nutritional literacy in parents; lack of time to prepare healthy foods; and decrease in physical activity among children due in part to an increase in computer gaming and other less physical activities in children during leisure hours (Anderson & Butcher, 2006; Berkey, Rockett, Gillman, & Colditz, 2003; Block, Scribner, & DeSalvo, 2004; Kumanyika & Grier, 2006; Kumanyika S. K., 2008).

Obesity and overweight in children is no longer a disease of just the developed or western world. Wang & Lobstein (2006) report in a meta-analysis that in the past 40 years there has been a growing global obesity epidemic. They report a doubling or tripling of overweight or obesity in school aged children from the 1970’s to the end of the 1990’s in countries like Canada, Brazil, Chile, Australia, Japan, Greece and Spain.

Wang and Lobstein go on to report that in middle-income countries, members of the more affluent classes are more likely to have children at risk for overweight and obesity, as well as children residing in more urban areas more than those who live in more rural areas. One disturbing trend in the developing world is an increase in the prevalence of overweight and obese children among the poorer children in society, as cheaper western diets are made available, especially in the urban settings of these poor countries (Wang & Lobstein, 2006)

2. Weight Gain Patterns in Early Life and Utero
In the first six months of life, infant weight gain is rapid. Weight gain slows in the next six months of life. During the first 6 months of life, substantial fat is deposited. After the first six months, an increase in lean body mass decreases the ratio of fat to fat free mass. After the first year of life, weight gain is steady and continues to be predominantly lean mass. This creates a low point in body fat percentage by 5-6 years of age. After this there is again an increase in fat deposition often called the adiposity rebound. Infants with a growth trajectory characterized by rapid early postnatal growth (birth to 6 months of age) and/or who have an early age of adiposity rebound are at a significant increased risk of becoming obese.

An individual’s propensity for weight gain, particularly increased body fat percentage, has been attributed primarily to genetic make-up. However the relatively recent (and increasingly global) epidemic in obesity cannot be explained by genetic variation alone. The concept of fetal programming of health and disease risk proposes that obesity or the susceptibility to become obese can be traced back to the intrauterine period of life. According to this theory, while the developing fetus is in the womb it is affected by and responds to stressors and suboptimal conditions. Thus, while it is important to understand these post-delivery patterns of weight gain, research is now also being done to find earlier intervention points in addressing the problem of childhood obesity. Growing evidence suggests that the origins of obesity and its sequelae can be traced back to the intrauterine period of life (Boney, Verma, Tucker, & Vohr, 2005; Gillman, Rifas-Shiman, Berkey, Field, & Colditz, 2003; Whitaker, 2004). Children who were exposed to intrauterine environments of diabetes, smoking or emotional stressors have been shown to be at greater risk for large for gestational age, and childhood obesity.
In the current climate of increasing childhood obesity, prevention efforts need to target risk factors as early in development as possible.

For the first two trimesters the fetus gains predominantly lean mass. Throughout the course of the pregnancy weight gain is relatively steady and very little weight gain is fetal fat deposition until the third trimester. In the third trimester fetal fat deposition is substantial. Although there is a great deal of variability, at birth humans average about 15% fat by body mass. Although on average infant birth weight is 14% by fat mass, fat mass explains 46% of the variance.

In a stressful or suboptimal intrauterine environment during critical periods of proliferation, differentiation and maturation structural and functional changes can be produced in cells, tissues and organ systems. These changes may permanently affect the way that energy is metabolized, fat is deposited and hence increase the risk for obesity. This is especially true when the individual is facing an obeso-genic postnatal environment.

An increased risk of metabolic disorders, such as obesity, type 2 diabetes and cardiovascular disease are associated with poor birth outcomes such as low birth weight. This is true of a poor birth outcome that occurs by itself or in conjunction with rapid growth trajectories in the critical period of birth to six years of age or with early adiposity rebound. Whincup, et al. (2008) conducted a meta-analysis that showed birth weight is strongly correlated to type 2 diabetes risk in an inverse fashion. Harder, Rodekamp, Schellong, Dudenhausen, & Plagemann, (2007) also conducted a meta-analysis that also showed correlation except in a U-shaped manner.
3. **Fetal Programming in Childhood Obesity**

Studies have shown that factors that affect the developing fetus in utero may work to program the metabolism of the developing fetus in such a way that predisposes to obesity later on. Studies conducted on baboons found that female baboons that were overfed while they were pregnant, but not after birth resulted in babies that had a higher adiposity rate at five years of age (Hamosh, 1988; McGill, Mott, Lewis, McMahan, & Jackson, 1996).

Ong & Loos (2006) conducted a comprehensive review of the literature and reported that while a higher birth weight correlates to a higher BMI later in life, low birth weight is associated with a subsequent higher ratio of fat mass to lean mass and greater central adiposity and insulin resistance. Similarly, early, accelerated postnatal weight gain is associated with abdominal fatness. Individuals born at a lower birth weight in combination with early accelerated/catch up growth during the first year of life appear to be at greatest risk for later disease.

4. **Breastfeeding as Potentially Protective Against Childhood Obesity**

When there is “faster than normal” weight gain in babies, this can result in higher childhood adiposity in children aged 12 years and older. Ong, et al. (2009) found that if a baby experienced rapid weight gain during the first 9 months of life there was a higher risk of increased adiposity and early menarche in girls. Agostoni, et al. (1999) found that while breastfed and formula fed infants gained similar amounts of weight in the first six months of life, that after six months old the weight gain in breastfed babies slowed down as opposed to formula fed babies who continued with a rapid weight gain. This was supported by findings in the DARLING study (Dewey, Heinig, Nommsen,
Peerson, & Lonnerdal, 1993) and by Ziegler (2006) who found there was no difference in adiposity in babies aged 4 – 6 months old, regardless of feeding method, but that after 6 months old breastfed babies were leaner than formula fed babies.

There are two reasons why breastfeeding could act as a preventative for childhood obesity. First, the act of breastfeeding itself contains mechanisms that prevent a baby from over eating. A mother’s milk supply is directly impacted by the amount a baby will eat. This supply-demand factor means that babies are not ingesting more food than they need, or want. This contrasts with a bottle fed baby who is often encouraged to take in a specific ml amount by the mother, when in fact the amount of food the baby actually needs might be less (or more) than the amount in the bottle.

Secondly, researchers found that there were lower serum concentrations of insulin in breastfed infants that in those infants that were fed cow’s milk (Lucas, Sarson, Blackburn, Adrian, Aynsley-Green, & Bloom, 1980; Lucas, Boyes, Bloom, & Aynsley-Green, 1981). Given that insulin promotes fat storage this could be a significant finding. In a separate study, Hamosh (1988) found that babies who were fed cow’s milk fed consistently over a ten minute period. Breastfed babies, however, consumed most of the energy (80-90%) from their feed in the first four minutes. This suggests that breastfed babies consumed less energy (calories) per volume than babies fed on formula.

But the research on the link between breastfeeding and higher BMI scores in children is not definitive. Ong and Loos (2006) found that while a higher birth weight usually corresponded to a higher BMI in later life in cases where babies had an exceptionally low birth weight, the rate of fat mass to lean mass and increased adiposity can result as the babies got older. In fact, they concluded that children who were born at
a lower than normal birth weight, and who then played catch up with an increased growth rate in the first year of life appeared to be at greater risk than other babies for weight related diseases. Dewey (2003) found that while there might be a relationship between breastfeeding and childhood obesity the causal effect was very small when compared to other factors that could impact the weight in children. These factors could include the access to healthy foods, a decrease in physical activity in children; genetic factors and the impact of childhood diseases.

5. The Role of In Utero Stress Factors and Stress Hormones in Obesity

Other prenatal and postnatal factors, including excessive weight gain early in life, have been described as being able to program future obesity. Pregnant women who are undernourished, over-nourished, diabetic during pregnancy, and smoking during pregnancy have all been shown to be factors that promote later obesity (Boney, Verma, Tucker, & Vohr, 2005; Dubois & Girard, 2006; Gillman, Rifas-Shiman, Berkey, Field, & Colditz, 2003; Haggarty, et al., 2009). These factors may act during fetal development to affect the central body weight regulatory system. Cortisol, a steroid hormone secreted by the adrenal glands, seems to play a role in this process; therefore, any factor that might increase cortisol in pregnant women might play a role in later obesity. Caffeine is known to elevate cortisol levels at rest and in response to various stressors (Lovallo, Farag, Vincent, Thomas, & Wilson, 2006; Gavrieli, et al., 2011). It is a pharmacological substance widely consumed through coffee, tea, soft drinks, chocolate, kola nuts, and certain medicines. Researchers found evidence that caffeine not only increases stress, but the effects persisted through the day (Lane, Pieper, Phillips-Bute, Bryant, & Kuhn, 2002). Other studies have demonstrated a causal relationship between cortisol, also known as the
‘stress hormone,’ and obesity suggesting higher levels of stress hormone activity promotes visceral fat accumulation and insulin resistance, and not the reverse (Epel, et al., 2000; Bjorntorp & Rosmond, 2000).

B. Purpose of the Study

Hispanic children are more likely than other ethnicities to be obese. This study looked at a predominantly Mexican-American cohort in the Orange County Healthcare Agency’s Women, Infants, and Children Program (WIC). The purpose of this study was to examine two key factors possibly related to later adiposity: 1) the impact of exclusive breastfeeding on the child’s weight gain in the first 6 to 36 months of life, and 2) maternal consumption of caffeine during pregnancy as caffeine intake has been shown to elevate cortisol levels.

C. Research Questions

The following questions were addressed in this study:

1) In a low income Latino population how does breastfeeding impact weight gain of children in the first 6 to 36 months of life?

2) How does self-reported caffeine intake in pregnant women correlate with weight of children in the first 6 to 36 months of life?

D. Significance to Global Health

Childhood obesity and its prevention are important to the field of global health for several reasons. First, childhood obesity in the United States is a disease disproportionately seen in poorer individuals of certain ethnic minority groups. This analyses of potential health disparities falls under the purview of global health especially because in the current study participants were predominantly immigrants or first
generation descendants of immigrants from Mexico. Secondly, understanding possible contributing factors that are at play in poorer, more urban Latino populations in the United States might help developing nations put policies and practices into place that may help to stem the rising tide of childhood obesity in poorer nations. Thirdly, due to the costs of the treatment of consequences of childhood obesity, any strategies that might be cost effective or relatively free that work in poor populations in the United States, might be transferable to poor individuals in the developing world who may also have poor access to health care.
A. Childhood Obesity and its Consequences

Obesity has surfaced as a top concern in public health. Of particular concern is childhood obesity and its short and long term affects. Childhood Obesity has increased in all racial, ethnic, and socioeconomic groups as well as in both genders (Anderson & Butcher, Childhood obesity: trends and potential causes, 2006; Crawford, Story, Wang, Ritchie, & Sabry, 2001; Wang, Disparities in pediatric obesity in the United States, 2011). Overall, girls are more affected than boys. In a period of 20 years, between the NHANES I and NHANES III studies, prevalence of obesity and overweight in young girls increased more than 2 fold. In comparison, in young boys the increase was about 25% (Murasko, 2011; Wang, 2011). However, between 1999-2000 and 2009-2010, there has been a significant increase in BMI among adolescent males aged 12 through 19 years, but not among any other age group or among females (Ogden et al., 2012).

These figures are significant because overweight children are going to develop health problems a lot earlier than their normal BMI counterparts. Obese children are at a higher risk of being asthmatic, developing Type II Diabetes and orthopedic issues (Boney, Verma, Tucker, & Vohr, 2005; Raj & Kumar, 2010; Ogden, Yanovski, Carroll, & Flegal, 2007). They are more likely to have behavioral problems and many suffer from depression (Raj & Kumar, 2010). Children are now also showing an increased risk rate in developing high blood pressure or high cholesterol level (Crawford, Story, Wang, Ritchie, & Sabry, 2001; Raj & Kumar, 2010; Ogden, Yanovski, Carroll, & Flegal, 2007). Estimates have indicated that more than 80% of teenagers that are obese will remain
obese as adults (Ogden, Yanovski, Carroll, & Flegal, 2007; Whitaker, Wright, Pepe, Seidel, & Dietz, 1997).

Obese teenagers are three times more likely to become obese adults than children within a normal weight range. The costs involved in treating obese adults for preventable health problems was $41.2 billion in California in 2006 and is estimated to cost up to $52.7 billion in 2011 (Orange County, 2009, p.2).

Childhood obesity epidemic is sobering because it is associated with significant short and long-term health problems. It is reported that 80% of obese children will be obese adults (Ogden, Yanovski, Carroll, & Flegal, 2007). If overweight before the age of 8, adult obesity is likely to be more severe. Obesity is associated with the onset of conditions in children previously thought to be exclusive to the adult population. For example, we now find children that are obese to be more likely to be diagnosed with high blood pressure and type 2 diabetes. The metabolic and cardiovascular complications of obesity found in children are closely related to insulin resistance and hyperinsulinemia, which are the most common abnormalities of obesity.

As adults, the risks of serious health complications continue for those who were overweight and obese as children. These risks include a number of disease conditions such as strokes, heart attacks, diabetes, asthma and even certain forms of cancer which are more common in adults who were overweight or obese as children.

B. Childhood Obesity in Children under 12 years of age

There are many hypotheses as to why the obesity epidemic has impacted children. Anderson and Butcher (2006) conducted a comprehensive review of the literature as to possible causal reasons for the increase in childhood obesity. The authors could not find
one clear factor that has caused the obvious increase in childhood obesity rates. From their review of the literature they determined that there were "complementary changes" (Anderson and Butcher, 2006, p.19) in the way families operated, the foods that were available to children at home and away and reasons why children appear to expend less energy now than they used to.

Whittaker et al (1997) point out that more than 50% of children who were obese between the ages of three and six years old were still obese as adults. This is supported by Anderson and Butcher (2006) who showed that the increasing trend in childhood obesity started in the 1980's and has increased steadily since then. Other factors such as the high rates of obese children in minority groups and children from lower socioeconomic groups were also noted. The authors surmised that the fluctuations in childhood obesity figures during the 1980s might have been impacted by children who were borderline obese during one study, and overly so by the next. Anderson and Butcher (2006) concluded that a good starting point for research on childhood obesity is 1999-2002 because not only were there a consistently higher rate of obese children from that date, but the weight gains were higher per child as well.

These authors were furthermore interested in the issue of genetics and hereditary causes of obesity. They quote studies that showed that when identical twins were raised apart, the correlation coefficient of BMI (body mass index) was 0.7 which is significant and only slightly lower than the BMI scores in twins raised together (Stunkard et al, 1990). This supports the hypothesis that genetics plays some role in obesity. The World Health Organization (1997) also noted the importance of hereditary factors and a study by
Bouchard, C. et al. (1990) noted that when identical twins were over eating the correlation of weight gain is a lot higher than the 0.7 found in Stunkard et al (1990).

The increase in the availability and affordability of low nutritional quality fast foods has also been the topic of studies in overweight children but there are no replicable studies that have proven a direct correlation between being overweight and eating fast foods across all population types (Block, Scribner, & DeSalvo, 2004). However, there have been more conclusive studies conducted on preschoolers who consumed large amounts of sweetened beverages and their BMI scores (Welsh, Cogswell, Rogers, Rockett, Mei, & Grummer-Strawn, 2005). In older children (aged 9 years to 14 years) the consumption of sweetened beverages did result in small increases in BMI over longitudinal studies (Berkley, 2004; James et al, 2004; Ludwig et al, 2001; Rajeshwari et al, 2005; Skinner and Carruth, 2001; Welsh et al, 2005).

Any possible link between BMI and basal metabolic rate (BMR) is also of interest. In their literature review Anderson and Butcher (2006) couldn’t find any definitive evidence to suggest that children who were overweight had a lower BMR. Studies on the correlation between physical activity and BMI in children were also inconclusive. Watching television has been positively correlated with increases in childhood obesity but other activities such as reading, computer usage and doing homework correspond with high physical activity levels – this finding has been attributed to positive parenting but this has not been substantiated (Berkey et al, 2003; Utter et al, 2003).

Finally in the analysis of the literature review in Anderson and Butchers (2006) the authors did do some research into studies involving breastfeeding infants but their
perspective was based on what they describe as the “energy balance equation” (p. 24). They noted that cross sectional studies on older children have found them to be leaner if breastfed as a baby (Kramer, 1981) but in other studies breastfeeding only had a small impact on obesity (Arenz et al, 2004) or even that there is no consistent correlation (Dietz, 2001). Anderson and Butchers (2006) note that factors such as the amount of feed given to a baby, or the type of parental methods might have more to do with the findings than whether or not they were breastfed. These observations suggest that women who do breastfeed for longer also have more knowledge about the nutritional requirements for growing children and so are more careful about the types of foods their children eat long after the nursing is ended (Nelson, Gordon-Larsen and Adair, 2005). Anderson and Butcher (2006) noted that conclusions on the correlation between breastfeeding and childhood obesity were not conclusive and that because it was difficult to find sample families where one sibling has been breastfed and another has not, that making any conclusion about breastfeeding and weight gain in children would be difficult. They also concluded that even in cases where a mother may have decided to breastfeed one child and then not another that the reasons behind those decisions might have more of an impact on the children’s weight, rather than the issue of breastfeeding.

The Anderson and Butcher (2006) study noted other possible causes of childhood obesity. Those factors included urban travel patterns, changes in food consumption patterns including the increase of food prices, changes in schooling and childcare services and changes in parenting roles.

In the area of interventions to combat childhood obesity, Lindsay et al (2006) felt that parents were the key to addressing childhood obesity. They conducted a literature
review on school-based obesity prevention programs that include parents. They believe that the only way to reduce childhood obesity is to educate and involve parents in ensuring that children eat nutritional foods, have regular eating patterns and engage in appropriate physical exercise.

Epstein (1996) thought there were three reasons why parents should be involved in any childhood prevention programs. (1) Because obesity usually runs in families so it would be unrealistic to do an intervention on one member of the family without including others; (2) Parents are the models for their children and their participation will help reinforce positive behaviors and outcomes for the children and (3) Parents can be taught behavior changing strategies to help facilitate positive outcomes for the children. There are some successful school-based intervention programs, that include parents as part of the intervention model, that are working including Planet Health; Eat Well and Keep Moving and a Special Supplemental Nutrition Program for Women, Infants and Children (Gortmaker, Peterson et al, 1999; Gortmaker, Cheung, et al., 1999).

One area of research that is receiving attention is the idea of early life metabolic programming. Studies conducted on baboons found that female baboons who were overfed while they were pregnant but not after birth resulted in babies that had a higher adiposity rate at five years of age (Hamosh, 1988; McGill, 1996).

A number of the studies conducted on pre-natal factors influencing obesity in children have focused on issues where an intrauterine environment can negatively impact fetal development. In particular conditions such as diabetes, gestational diabetes or under- or over-nutrition, produce children who are at risk for obesity and/or gestational
diabetes later in life (Whittaker and Dietz, 1998). The role of intrauterine factors will be looked at in greater depth later in the literature review.

C. Breastfeeding vs. Formula Feeding

Armstrong et al. (2002) also suggests that breastfeeding is associated with a reduction in childhood obesity. Twells and Newhook (2010) conducted a highly focused study on whether or not exclusive breastfeeding could reduce the risk of childhood obesity for children in Canada. Their study notes that the findings on the correlation of breastfeeding and lower obesity risks in children are “inconsistent” (Twells and Newhook, 2010). One study noted that in a follow up of more than 13,000 breastfed infants that there were no significant differences in weight, BMI or adiposity when compared to non-breastfed children over the same length of time. The data was collected at aged 6.5 years (Twells & Newhook, 2010).

Twells and Newhook’s (2010) own study was based on 1,026 children that were born in 2001. The children were accessed at a Pre-Kindergarten Health Fair in 2005 which was a program set up to ensure that children get their immunizations, as well as hearing and vision tests before they start school. Attendance at these fairs is not compulsory and this study took data from ten such fairs. Research assistants took children’s height and weight details and a questionnaire was used to collect information from the parents on demographics, infant feeding, smoking status, mother’s age and level of education. Exclusive breastfeeding was defined as a diet that only includes breast milk with no additional formula, water or juice up until 3 months of age.

The Twell and Newhook (2010) is one of many studies that have found a correlation between exclusive breastfeeding and a reduction in childhood obesity and
their study also factored in a number of other variables that could impact childhood weight such as gender, maternal smoking, mothers education and whether or not the child was full term or premature. Of course the results must be carefully considered. For example a limitation is that exclusive breastfeeding was only calculated for up to three months of the infants’ life. Also variables such as socioeconomic status and ethnicity were not collected and finally the length of breastfeeding was self-reported and retrospective, asking parents to remember something that happened more than four years earlier.

Lindsay et al (2006) also noted that the findings on breastfeeding as a preventive measure for childhood obesity were inconclusive and suggested that the only studies that had been done related to Caucasian children and therefore could not be applied to other ethnicities. However, as an important point to consider, the authors raised the possibility that breastfed babies were better able to regulate their food intake as opposed to bottle fed babies that were encouraged to finish a bottle even if the infant wasn’t hungry. They posit that this would make it difficult for young and older children to regulate their food intake, or control the amount of food they ate. As a limitation however, the author’s themselves is that even though breast feeding might appear to have a protective impact on later obesity, other factors such as parental weight issues, or socio-economic factors could just as easily be applied to the same situation. In other words in studies that might indicate that breastfeeding is a preventative of childhood obesity, the effect may in fact be due to other unmeasured variables.

Another interesting point in Lindsay et al (2006) review was that they made the distinction between parents offering exposure to healthy foods, but that children should
be responsible for deciding what and how much they want to eat (Dietz & Stern, 1999). They also made a correlation between parental and child food choices, suggesting that a parent’s eating habits will impact what a child eats and tie that in with studies on the link between the consumption of sweetened beverages and weight gain in young children. Parents that breastfeed exclusively may well also be parents who will give better food options to their children later in life and support that.

To counteract some of these limitations, other studies with longer periods of exclusive breastfeeding seem to show a small but consistent protective effect against later obesity. Gillman et al (2001) found that infants who were predominantly fed breast milk, (compared with infants predominantly fed infant formula) in the first 6 months of life had a lower prevalence of overweight 9 to 14 years later. That study found an estimated relative risk reduction of approximately 22%. The study also supported the hypothesis, that there was greater protection with longer breastfeeding.

Agastoni et al (1999) showed in an Italian cohort of children that breastfed infants gained more weight in the first six months of life but in the second six months of life the growth of the breastfed infants slowed and the formula fed infants gained more weight for length. This is consistent with the findings of the DARLING study (Dewey, 1999).

Ziegler (2006) supports the idea that in the first 4-6 months of life there is no difference in adiposity between breastfed and formula fed infants. However after 6 months of life the breastfed infants are in fact leaner than formula fed infants.

Dewey (1993) showed a highly significant difference in fatness between breastfed and formula fed infants, with the greatest difference between 9 and 15 months of age. Dewey (2003) suggests that if the relationship of breastfeeding to childhood obesity is
causal the effect is probably small compared to other factors that influence childhood obesity, however in light of the obesity epidemic in the children even a small effect that moves away from childhood obesity might be very helpful in the battle against childhood obesity.

Notably Orange County, CA Hispanic women are least likely to breastfeed when compared to other race/ethnicities in the County. This finding is startlingly inconsistent with the breastfeeding data on Hispanic women in the US in general. In fact the literature supports the idea that Hispanic women are the most likely to breastfeed in America with a drop in the number breastfeeding that is related to acculturation in the United States (Gill, 2009).

Thus, if we focus in on Mexican-American women in Orange County, CA to make a strong effort to reintroduce them to the “normal” pattern of Hispanic women that they lost – for whatever reason, such a protective effect might go a long way. Again, notably, these same women also raise children who are most likely to be obese.

D. Childhood Obesity in Latino Children

Latino children are disproportionately affected by overweight and obesity. Mexican American children 6-11 years of age are reported as having the highest rates of obesity at 25% when compared with non-Hispanic Whites and non-Hispanic Blacks (Ogden et al, 2010). A study of children aged 13.6 years that were tested for high blood pressure found that left ventricular hypertrophy was evident in 70% of the Hispanics tested (Hanevold, C. et al., 2004).

Studies show a connection between inactivity and obesity. A cross sectional study of Latino children in Kindergarten through second grade in San Diego found that
overweight children were less active than their normal weight peers (Elder et al., 2010). Less acculturation in Mexican American, Puerto Rican, and Cuban adolescents found that lower acculturation was associated with a decreased prevalence of overweight in first generation Latinos (Gordon-Larsen et al, 2003).

Kumanyika and Grier’s (2006) looked at study’s targeting intervention programs for ethnic minorities and low-income populations. The statistics relevant to Hispanic children include a study in 2002 obesity was higher for Mexican American boy children at 25% against 19% of African American male children and 15% of white male children. In girls the rate of obesity is higher for African American females (24%) but Mexican American girls scored second highest at 20%. Obesity rates for Hispanic children in New York elementary schools in 2003 ranked highest at 31% (Thorpe et al, 2004). Gordon-Larsen et al (2003) completed a study on overweight (85th percentile BMI cutoff) for adolescents – once again Hispanic boys were the highest ranking with 28% and the Hispanic girls coming second with 30% (first was African American girls).

Like many of the researchers of childhood obesity Kumanyika and Grier (2006) note that various environmental factors could have a causal element in the over representation of minority and low-income children in the obesity patterns. Some of the variables include the amount of television that low income and minority children watch. This not only reduces the activity levels of these children but it also subjects them to advertising for junk foods which are a common diet staple in many low income and minority children’s homes. Part of the problem with this is that the fast food restaurants position themselves in lower income areas and healthy food vendors generally don’t (Block et al, 2004). Unsafe streets, lack of parks and facilities are also issues that keep
low income and minority children in front of the television rather than playing outside with their friends.

Minority groups tend to have lower rates of breastfeeding than other groups. For Hispanics the rate was 73% in hospital but only 33% at six months. The given rates breastfeeding (any not exclusive breastfeeding) for Hispanics, could be attributed to higher rates of teenage pregnancy, an earlier introduction of solid food and early feeding of high sugar foods to infants (Ryan et al, 2002). Kumanyika and Grier (2006) maintain that the correlation between longer term breastfeeding and lower risks of childhood obesity is “inconclusive” but suggest instead that mothers who do breastfeed for longer are also more likely to put good food practices in place when the child does start to eat solid foods. However they also note that given the other benefits of breastfeeding for both mother and infant that programs encouraging and supporting women to breastfeed for longer could be helpful among ethnic minorities.

In one study the correlation between breastfeeding and a protective effect on childhood obesity was undetermined and went on to point out that most of the studies that did support that idea were based on white populations (Grummer-Strawn & Mei, 2004). Other studies led to the speculation that short-term breastfeeding (<3 months) may be a risk factor for obesity and that only longer-term breastfeeding might be protective (Grummer-Strawn, & Mei, 2004). They also considered the idea that the high rate of teen pregnancies in Hispanic (and other ethnicity) populations could be the reason the rates for breastfeeding are lower than in other populations.

In the Kumanyika study the effect of culture on eating patterns was also considered. Again the study was conducted on African Americans but some of the
findings could have a bearing on Hispanics and other ethnic minorities. In particular mothers finding it more convenient to feed their infants at the same time as adults; the concept that it was better for infants to be heavier and that heavier babies were healthier and better cared for. Also the concept that food can be used as a reward for good behavior or as a calming method was the other perceptions in African American mothers.

Another consideration was the role that grandparents played in raising the infants. Many grandmothers in the African American community didn’t see anything wrong with adding cereal to formula bottles for babies as young as 1 – 2 weeks old and introducing semi-solid foods within the first month after birth. The influence of grandmothers on feeding patterns has also been noticed in other studies (Bentley et al, 1999).

Branscum and Sharma (2011) conducted a systematic analysis of childhood obesity prevention interventions targeting Latino children. They looked at programs that varied in length and rigor. Few of the studies showed significant improvements in weight status among children. In their analysis interventions with dedicated staff, older children, and longer intervention periods showed the most success. The authors conclude that more interventions that are culturally sensitive should be created for Latino children.

E. Fetal Programming and Obesity

An individual’s propensity for weight gain, particularly increased body fat percentage has been attributed primarily to genetic makeup. However the relatively recent (and increasingly global) epidemic in obesity cannot be explained by genetic variation alone. The concept of fetal programming of health and disease risk proposes that obesity or the susceptibility to become obese can be traced back to the intrauterine
period of life. According to this theory, while the developing fetus is in the womb it is affected by and responds to stressors and suboptimal conditions.

Since there is a higher prevalence of childhood obesity in certain ethnic minority groups in the United States and even in some developing nations, it is not impossible that stress may work to contribute to the disparities that we see in childhood obesity between ethnic groups and even between nations. It has been suggested that the health disparities that exist in poor birth outcomes between African American babies and White American babies may have to do with increased stress due to racism (real or perceived) (Shannon, King, & Kennedy, 2007). It follows that stress may work to increase the conditions in utero that are conducive to producing disparities between different populations in regards to overweight and obese children.

In a stressful or suboptimal intrauterine environment during critical periods of proliferation, differentiation and maturation structural and functional changes can be produced in cells, tissues and organ systems. These changes may permanently affect the way that energy is metabolized, fat is deposited and hence increase the risk for obesity. This is especially true when the individual is facing an obesogenic postnatal environment.

An increased risk of metabolic disorders, such as obesity, type 2 diabetes and cardiovascular disease are associated with poor birth outcomes such as low birth weight. This is true of poor birth outcomes if the poor outcome occurs by itself or in conjunction with rapid growth trajectories in the critical period of birth to six years of age or with early adiposity rebound. Whincup et al, (2008) conducted a meta-analysis that showed birth weight is strongly correlated to type 2 diabetes risk in an inverse fashion. Harder et
Ong (2006) conducted a comprehensive review of the literature and reported that while a higher birth weight correlates to a higher BMI later in life, low birth weight is associated with a subsequent higher ratio of fat mass to lean mass and greater central adiposity and insulin resistance. Similarly, early, accelerated postnatal weight gain is associated with abdominal fatness. Individuals born at a lower birth weight in combination with early accelerated/catch up growth during the first year of life appear to be at greatest risk for later disease.

If intrauterine stressors can lead to later chronic disease and increased adiposity, the literature supports the idea that stress at any stage of life can be deleterious to health. Chronic exposure to stress, poor social supports and limited social networks have been shown to increase disease risk (Institute of Medicine, 2001). Stress has also been shown to potentiate the negative affects of a high fat diet and initiate atherosclerotic plaque formation (Adams, 1994).

F. Proposed Mechanisms

The role of stress hormones and inflammatory mediators, such as cortisol, CRH, C-reactive protein, IL-6, and TNF-α in obesity is well-established. Higher levels of stress hormones and inflammatory markers have been demonstrated in obese individuals and animals (Charmandari et al., 2003; Dallman et al., 2004; Rosmond, 2005; Kyrou et al., 2006). A causal relationship for this association has recently been suggested, with increased hypothalamic-pituitary-adrenal activity promoting visceral fat accumulation and insulin resistance, and not vice versa (Purnell et al., 2009). Moreover,
glucocorticoids not only have profound inhibitory effects on the secretion of growth hormone and sex steroids but also antagonize the actions of these hormones on fat tissue catabolism (lipolysis) and muscle and bone anabolism. This effect might be enhanced by increased sensitivity of fat tissue to glucocorticoids.

A number of recent studies have shown significant associations between markers of systemic inflammation and the metabolic syndrome and its components (obesity-related conditions), particularly elevated levels of C-reactive protein, TNF-α and IL-6 (Grimble, 2002; Tjoa et al., 2003; Rush et al., 2007).

In fact there are two separate but intertwined mechanisms by which stress might do this. First a physiologic pathway (termed allostatic load) and second behavioral pathways that function as stress coping methods. Again the two mechanisms would be highly interconnected but the focus for this study will be on allostatic load as the connection between stress, poor birth outcomes and ultimately childhood obesity.

1. **Allostasis and Allostatic Load**

The concept of Allostatic load is often used to explain how external stressors translate into patho-physiologic processes. By definition Allostasis is the process by which the body maintains stability (or homeostasis) during adaptation to environmental and physiological events (Sterling & Eyers 1988). Initially, Sterling and Eyers used it to describe cardiovascular adjustments from resting to activity. However, it is now evident that broad systems function to create physiologic changes that work to maintain homeostasis.

Mediators of allostasis include cortisol and adrenaline. One example of an allostatic response is associated with adrenaline. In acute stressful situations (such as
being chased by a dog) the release of adrenaline increases concentration and heightens awareness. Adrenaline induced changes enhance the ability to escape from harm (e.g. increasing perfusion to muscles). While the body is focusing on getting out of harms way other physiological functions receive lower priority (e.g., decreased blood flow to the digestive organs).

The problem arises when this allostatic change is 1) always turned on due to constant perceived threats to survival, 2) has a prolonged response once started even when the threat has ended, 3) there is a problem with adapting to repeated threats so that the individual overreacts to stressors encountered before, or there is no response, an under-reaction, to external stressors.

Chronic stress and the increase in allostatic load that it causes can affect birth outcomes (Latendresse, 2009; Shannon, 2007). Birth outcomes are impacted by the relationship between stress hormones (such as adrenocorticotropin hormone [ACTH] and cortisol) and an altering of the cascade of events that lead to normal timely labor and delivery (Latendresse, 2009; Wadhwa, 2004). The intrauterine stressors that are implicated in preterm labor as well as the affects of early birth are also implicated in altering the physiology of the offspring including creating insulin resistance (Entringer et al, 2008).

Gestational diabetes is a significant intrauterine stressor. Infants of women with glucose intolerance (even mild) have increased body fat compared with infants of woman with normal glucose tolerance. Increased fetal adiposity secondary to gestational diabetes mellitus is likely a risk factor for obesity in early childhood (Catalano, 2003).
Despite progress in understanding the intrauterine stressors, the specific prenatal conditions most strongly associated with increased child obesity risk have not been identified. Moreover, the effect of breastfeeding as a potential moderator (or effect modifier) of the relationship between exposure to prenatal adversity and child body composition is unknown.


Pregnancy is associated with major alterations in neuroendocrine and immune function, including changes in hormone levels and control mechanisms (feedback loops) that are crucial in providing a favorable environment within the uterus and fetus for cellular growth and maturation and conveying signals when the fetus is ready for extra-uterine existence. These processes are mediated by the placenta, an organ of fetal origin. Starting at 6 weeks gestation, the placenta produces hormones, neuropeptides, growth factors and cytokines, and appears to function in a manner resembling that of compressed hypothalamic-pituitary-target systems (Yen, 1994). The fetus participates in a dynamic exchange of environmental (intrauterine) information with the maternal host over the course of gestation. All communication between the maternal and fetal compartments is mediated via the placenta. One of the major placental signals in pregnant primates (but not other mammals or non-mammalian species) is the peptide corticotrophin-releasing hormone.
(CRH). This peptide plays a key role in the maturation of the fetal HPA axis and other systems, and co-ordinates (synchronizes) events that underlie both fetal growth/maturation and the timing of onset of parturition (Sandman et al., 1999a; Sandman et al., 1999b; Sandman et al., 2006; Smith et al., 2002; Wadhwa, 2005; Wadhwa et al., 2004).

During human pregnancy, CRH is synthesized by syncytial cells in the placenta and reaches elevated levels in maternal circulation observed only in the hypothalamic portal system during physiological stress (Lowry, 1993). Placental CRH is identical to hypothalamic CRH in structure, immunoreactivity, and bioactivity. In contrast, however, to the inhibitory influence on the promoter region of the CRH gene in the hypothalamus, increased levels of glucocorticoids stimulate CRH gene expression in the placenta by interacting with proteins that bind to the cAMP response site of the CRH promoter (Cheng et al., 2000). This positive feedback loop results in an amplification of stress physiology (i.e. simultaneous elevation of cortisol and pCRH) that has implications for birth outcomes (McLean et al., 1995; Wadhwa et al., 2004; Sandman et al., 2006) and fetal development (Sandman et al., 1999b).

Placental CRH is believed to regulate fetal growth via its effects on placental perfusion and fetal cortisol production (Wadhwa et al., 2004). Human fetal adrenal cells respond to CRH stimulation with a dose-dependent rise in cortisol production and time-dependent increase in ACTH receptor expression (Rehman et al., 2007). Placental CRH elevations are associated with decreased uteroplacental flow and hypoxemia-- known risk factors for fetal growth restriction (Giles et al., 1996). Fetal cortisol plays a critical role in organ growth and maturation (Fencel et al., 1980), and placental CRH also may participate...
in this process via its positive feedback loop with fetal cortisol (Laatikainen et al., 1988; Majzoub et al., 1999; Smith, 1999).

Maternal factors, intrauterine perturbations and MPF endocrine physiology. Substantial in vitro and in vivo evidence indicates that the MPF endocrine physiology (primarily CRH and cortisol) detects and responds to a variety of maternal and intrauterine perturbations, including maternal factors that associated with increased risk of subsequent child obesity and metabolic dysfunction.

3. **Cortisol**

Maternal cortisol/glucocorticoid levels in pregnancy are dysregulated in animals on an obesogenic diet (Ford et al., 2009), maternal undernutrition (Bispham et al., 2003; Bloomfield et al., 2004; Chadio et al., 2007), and alcohol exposure (Ramadoss et al., 2008), and in humans with preeclampsia (Aufdenblatten et al., 2009; Ford et al., 1990), pregnancy toxemia (Ford et al., 1990), and smoking during pregnancy (Varvarigou et al., 2006).

4. **Inflammatory Stress in Pregnancy.**

Observational studies suggest that elevated psychosocial stress scores in pregnant women are associated with higher circulating levels of C-reactive protein (CRP) and the proinflammatory cytokines (Coussons-Read et al., 2005; Christian et al., 2009). Furthermore, higher acculturation among pregnant Hispanic women is associated with increased depressive symptoms, higher BMI, increased inflammatory marker IL-1RA (Ruiz et al., 2007), and elevated CRH (Ruiz et al., 2006). CRH has been found to be associated with higher baseline and LPS-stimulated levels of the proinflammatory
cytokines IL-1 and TNF-α, suggesting that CRH potentiates the pro-inflammatory immune response in pregnancy (Wadhwa et al., 2001a).

Cortisol and CRH have been found to be directly associated with fetal and infant developmental outcomes. There is now growing evidence that excessive levels of placental CRH during pregnancy may have developmental consequences for the fetus that extend into postnatal life. Low concentrations of placental CRH at the beginning of the second trimester are associated with precocious maturation of the human fetus (Class et al., 2008), while elevated concentrations of placental CRH concentrations during the third trimester of gestation are associated with impaired fetal learning (Sandman et al., 1999b). The developmental consequences of elevated concentrations of placental CRH during pregnancy extend into postnatal life, as higher CRH concentrations during pregnancy are associated with delayed neonatal physical and neuromuscular maturation (Ellman et al., 2008) and more fearful temperaments in infants (Davis et al., 2005). Moreover, higher CRH in pregnancy is associated with an increase in central adiposity (Gillman et al., 2006) and alterations in adiponectin levels (Fasting et al., 2009) in 3-year old children.

5. Race/Ethnicity, Stress Biology and Obesity

Growing evidence suggests that biological factors are associated, in part, with racial/ethnic differences in childhood obesity. As reviewed recently by Caprio et al. (2008) and by Goran (2008), there are racial/ethnic differences among children in patterns of fat distribution, metabolic rate, adipocyte biology, insulin secretion and response, IGF-1 levels, and lipids and lipoproteins.

6. Targets for Fetal Programming
The two primary targets of programming obesity are a) the neural networks that regulate energy balance (appetite, feeding and basal energy expenditure), and b) the developing adipocyte and secretion of adipokines such as leptin (McMillen et al., 2006). The central role of hypothalamic circuits related to appetite, food intake, and basal energy expenditure in the regulation of energy balance is well-established. The concept of energy balance refers to the maintenance of relatively stable body weight over time in the face of alterations in daily food intake and energy expenditure. Humans are well adapted to match or couple energy intake and energy expenditure. Obesity results from inappropriate matching of energy intake to expenditure (Cottrell et al., 2007). Energy balance is achieved through these hypothalamic brain circuits that influence energy intake (feeding) and energy expenditure (thermogenic) responses (Schwartz et al., 2000). These circuits integrate peripheral signals produced by perturbation of adipose tissue mass into messages to effectors of food intake and energy expenditure, so as to prevent substantial variations in the level of energy balance (Devaskar, 2001). Energy imbalance is a critically important factor underlying childhood obesity (Butte et al., 2007).

In contrast to the suggestion that the effects of intrauterine perturbations on child body composition and obesity risk are a direct consequence of alterations in fetal growth patterns (Cripps et al., 2007), a growing body of literature suggests that intrauterine perturbations produce reorganization of central neural pathways that regulate energy intake and expenditure in ways that enhance the development of obesity, and that these effects may occur much earlier than previously believed.

Several studies have convincingly demonstrated that biological stress during gestation, triggered by a variety of nutritional, inflammatory, vascular, behavioral or
psychosocial perturbations, can promote obesity in the offspring by reorganizing central neural pathways that regulate energy balance and programming of energy balance “set point” (Bouret, 2009).

The adipocyte-producing hormone, leptin, is the afferent loop informing the hypothalamus about the states of fat stores, with hypothalamic efferents regulating appetite and energy expenditure. Leptin participates in the expression of hypothalamic CRH, interacts at the adrenal with ACTH, and is regulated by cortisol. Cortisol acts directly on adipose tissue and increases leptin secretion in humans. Cortisol acts as a key modulator of body weight and food intake, increases leptin secretion in adipocytes, and limits CNS leptin-induced efferents (Leal-Cerro et al., 2001). Cortisol also redistributes stored calories to abdominal fat (Dallman et al., 2004).

7. The Programming of Adipose Tissue

The condition of obesity is impacted by increases in fat cell number, fat cell size, or a combination of the two. It is generally believed that fat cell number is dependent on the age of onset and the degree of obesity. Fetal adipose tissue development is regulated by the complex interaction of maternal, endocrine, and paracrine influences that initiate specific changes in angiogenesis, adipogenesis, and metabolism (Martin et al., 1998). Adipogenesis, the process of adipocyte development from stem cell precursors, occurs primarily during late fetal and early postnatal life in humans; this process is highly sensitive to the intrauterine biological environment at this time, in particular to concentrations of insulin-like growth factors, glucose, insulin and glucocorticoids (Ailhaud et al., 1992; Martin et al., 1998). The ability to make new adipocytes in adulthood is limited; most of the developmental work in adipose tissue is
completed early in life, and the number of adipocytes is relatively fixed after young adulthood (Ailhaud et al., 1992; Martin et al., 1998; Spalding et al., 2008), supporting the idea that fetal and early postnatal periods are crucial windows in the development of adipose depots. Animal studies have shown that fat cells exposed to an excess substrate supply during crucial windows in their development have an increased capacity for storing lipid in postnatal life (Muhlhausler et al., 2006; Muhlhausler et al., 2007). This enhanced lipogenic capacity renders these individuals more likely to store excess energy in the form of fat and increases their susceptibility to weight gain and obesity and its metabolic sequelae. In individuals exposed to low nutrition levels before birth, adipocyte development is initially sacrificed in favor of ‘essential’ organs (Padoan et al., 2004; McMillen et al., 2005). If an in utero ‘restricted’ individual is born into a postnatal environment in which nutrient supply is no longer constrained, a period of ‘catch-up’ fat deposition ensues, mainly in the visceral adipose depot (Crescenzo et al., 2003). These individuals are at increased risk of visceral obesity (Ibanez et al., 2006) and, consequently, to the development of insulin resistance and type 2 diabetes (Jaquet et al., 2000).

Biological effectors of stress exert a strong influence on adipocyte mass during development. Glucocorticoids promote differentiation of human adipose precursor cells (Ailhaud 1992), thereby programming a permanent increase in adipose tissue mass (Gregoire, 2001; Cottrell et al., 2007). It is clear, therefore, that a suboptimal intrauterine environment during adipocyte development plays a crucial part in defining an individual’s propensity for accumulating body fat later in life.
8. *The Relationship Between Caffeine and Cortisol*

As discussed cortisol (and CRH) levels in utero influence adiposity through fetal programming and impact obesity later in life. One substance of interest as a “stressor” in utero is caffeine. Caffeine is consumed by a large percentage of the population in the United States. Hughes and Oliveto (1997) found that 96% of research participants had at some time in their lives consumed caffeine. The authors also found that 83% were currently consuming 186mg of caffeine per day. Caffeine has been reported to have similar consumption rates in men and women (James, 1991). Caffeine acts on the cardiovascular system as a pressor increasing blood pressure levels for up to several hours after consumption (Pincomb et al., 1985).

Caffeine has been shown to increase cortisol levels both at rest and during stressful events (Al’Absi and Lovallo, 2004). Cortisol release is highest in the last couple of hours of sleep into the first waking hour. Cortisol levels then gradually decline during the day (Weitzman et al., 1981).

Lovallo et al. (2006) found that caffeine increases cortisol secretion at multiple time points over the day in both men and women. Caffeine increases cortisol during periods of stress above what would normally be experienced under that stressful event (Lovallo et al., 1989). One study done on a male cohort found that caffeinated coffee prevents serum cortisol levels from falling in healthy men (Gavrieli et al., 2011). Lovallo et al. (2006) found that men and women when consuming caffeine had increases in cortisol when exposed to psychological stress, however the finding was only statistically significant in women.
9. Summary

The current childhood obesity epidemic is multifactorial and difficult to address. However, we know that the consequences are many and include early onset of many medical conditions once thought to be diseases that occur only in adults. Obese children are also at a higher risk of becoming obese adults.

In order to find earlier points for interventions, research has shifted to the prenatal period and early life. Fetal programming towards increased adiposity has been shown to occur when there are increased maternal stressors. This is mediated by increases in stress hormones such as cortisol. Studies have shown that breastfeeding has a protective effect against early life weight gain. Early or rapid weight gain in the first few years of life has been shown to increase the risk of later life obesity.

Latino children suffer disproportionately from childhood obesity, as do children of lower socioeconomic status. There are not many interventions that have been shown to be very successful in reversing the disparity in childhood obesity rates in Latino children.

This study looked at how prenatal factors such as depression, how a mother feels about her pregnancy, and caffeine intake impact weight gain in the first 24 months of life. The study also looks at how exclusive breastfeeding might be protective against early life weight gain. The sample population consists of low income Latino mother-child dyads in the Orange County Heath Care Agency’s Women, Infant and Child program.
CHAPTER 3

METHODS

The study described here is based on secondary data obtained from the Orange County, CA health department

A. Sample Population

This study utilizes data collected from the Family Health Division of the Orange County Health Care Agency Women, Infants, and Children program 2004 to 2009. Subjects were 487 pregnant women participants in the Orange County Health Care Agency Women, Infants and Children program 2004 to 2009. All women were in the WIC program run by the county at the 17th St. clinic in Santa Ana. Participant selection was based upon mother's who had given birth within the past 5 years (>2000 participants), had children who stayed in the program for at least 3 years (approximately 1000 participants), and were able to be matched between both data sources (487 participants). Finally, participants that had a complete and identifiable “Pink Sheet” (369 participants) were eligible to be included in the breastfeeding analysis.

B. Data Collection

A retrospective analysis of 487 pregnant women and their children were studied from birth through 36 months of age. California's WIC program's Integrated Statewide Information System (ISIS) database was used to abstract and quantify socio-demographic (marital status, income, number of children, race/ethnicity), biophysical (pre-pregnancy BMI, weight gain in pregnancy), obstetric (gestational diabetes, pregnancy-induced hypertension), psychosocial (homelessness, physical/sexual abuse, depression) and behavioral (smoking, alcohol, illegal drug use) variables for analysis. ISIS data also
provided information on breastfeeding practices and infant growth patterns; including birth weight and length information.

Additional information on the children in the sample population was obtained from a document created by the State WIC office. The “pink sheet” is a self-reported questionnaire given to mothers to provide information related to mood, mother’s nutritional intake, and mother’s physical activity levels. In the current study the “pink sheet” was used to supplement information not captured in the ISIS database.

The second database used to create the final database analyzed for this study is the Automated Vital Statistics System (AVSS). This system was created in cooperation with local, state, and federal health agencies by the University of California to automate public health records. AVSS is used to improve the timeliness and accuracy of birth certificates by automating their production at the hospital of birth. Data related to birth outcomes were matched to the mother-baby pairs to enhance the depth of the database being analyzed.

The mothers and children were matched in the database by a unique family identifying number assigned to the mother and child. A single data set was created around the mother to include data from pregnancy to the postpartum period that was then tied to the child’s early development metrics. Many mothers in the OC WIC system had more than one child all of whom would be recognized under the unique family identifier. To account for mother’s with multiple children, only the first recorded birth during the study time period was used for analysis.

C. Data Analysis
The current study is based upon a quantitative correlation design, namely a retrospective cohort study.

The study research questions are as follows:

1. In a low income Latino population how does breastfeeding impact weight gain of children in the first 6 to 36 months of life?

2. How does self-reported caffeine intake in pregnant women correlate with weight gain in children in the first 6 to 36 months of life?

Once the data set was created, data cleaned, outliers removed, and descriptive analyses conducted, hierarchical linear modeling (HLM) was used to assess the impact of breastfeeding on early life weight gain while controlling for mother’s moods during pregnancy (research question 1). Multiple linear regression was used to assess the impact of differing environmental exposures on weight change in the first 6 to 36 months of life (research question 2).

D. Measures

In the paper looking at caffeine and its effects on early life weight gain, for the model building the dependent variable of interest was: Growth among children at 0-6, 0-12, 0-24 and 0-36 months of age. This was defined using weight to height ratios. These measures were taken each time the family came to a WIC appointment.

Important covariates assessed included: infant’s gender, birth weight, depression, feeling tired during pregnancy, breastfeeding ≤ 6 months, pre-existing conditions such as diabetes, gestational diabetes, hypertension, and/or preeclampsia, baby taking medications, caffeine intake, dairy, grains and cereal, fruit and vegetable protein intake, frequency of fruits and/or vegetables intake.
Gender and birth weight were assessed from the State of California Automated Vital Statistics System (AVSS). Depression, feeling tired during pregnancy, breastfeeding ≤ 6 months, were all assessed from the Pregnancy Nutrition Questions (PNQ) also called the “pink sheet”. The “pink sheet” is a California WIC form not created for research purposes but to aid the WIC worker in connecting with the client and in getting information that is helpful in giving the client nutritional advise. The question “What word(s) describe how you feel about being pregnant?” created the nominal variables used to assess how a woman felt about her pregnancy. These included happy, Ok, tired, depressed, sad, stressed, or angry (Yes/No). For evaluation we used depressed, sad, and stressed to see how self-reported stress and depressive symptoms impacted early life weight gain in the child. The variables on caffeine intake and feeding practices also came from the “pink sheet”.

Gestational diabetes, hypertension, and/or preeclampsia, were assessed using the AVSS system. All were checked as provider diagnosed dichotomous variables (Yes/No).

The same method was used to create variables used in the HLM analyses. Models generated in this analysis were two-level models with infants nested within mothers. Mother-level variables used included mood, depression status, and pre-pregnancy BMI. Pre pregnancy BMI was collected from the state of California’s WIC program’s Integrated Statewide Information System (ISIS) database. Infant-level variables included gender and breastfeeding status. Mothers who reported having one or more stress, sad, or depressed moods were categorized as high risk and included in model six. Likewise, mothers reporting no stress, sadness, or depression were categorized as low risk and included in model 5. Pathik’s depression score was created by weighting the variables as
having no report of being depressed, sad or stressed or having one of them as low risk, and if they had two or more they were considered high risk and a dichotomous variable was created.

1. **Impact of Breastfeeding on Weight Gain**

Univariate analysis was conducted to describe the demographic characteristic of the sample. The trajectory of weight for age, weight for length, and length for age was ascertained at 0, 6, 12, 18, and 24 months of age. Individuals with missing or inconsistent data on the pink sheet regarding breastfeeding were removed resulting in a final sample size of 369. That sample was stratified further into three breastfeeding categories: “never breastfed” (n=71), “breastfeed between 1-5 months” (n=138), and “breastfed at least 6 months” (n=160).

Hierarchical linear modeling (HLM) was used to create growth curves. HLM was chosen as the analytic approach because of the nature of the study group. When it appears that a sample is hierarchal, or nested, the sample should statistically be more similar than a truly random sample from the entire source population. In this case, the sample of Latino WIC clients within the Orange County WIC system, were nested within all mothers in Orange County, and all mothers in the Southern California region, in California, etc. Furthermore, because these mothers tend to come from a similar population, statistically they would tend to be more homogenous over time. Since these mothers tend to share more similar characteristics than other mothers in Orange County or possibly the region, the indicators for these individuals are likely not fully independent. Since independence is required for regression analyses, a model that accounts for nested (hierarchal data) like hierarchical linear modeling was used to create
the growth charts. The HLM models generated in this analysis were two-level models with infants nested within mothers. Six models were generated for both weight for length until 12 months, and weight for length until 24 months. The predictors for the 2 outcomes were modeled with two-level hierarchical regressions: mothers and infants. Mother-level variables used included mood, depression status, and pre-pregnancy BMI. Infant-level variables included gender and breastfeeding status. Mothers who reported having one or more stress, sadness, or depressed moods were categorized as high risk and included in model 6. Likewise, mothers reporting no stress, sadness, or depression were categorized as low risk and included in model 5. Model construction is presented in both tables 5 and 6.

2. Impact of Caffeine Consumption on Weight Gain

Socio-demographic characteristics of the population under study were assessed using univariate analysis. Descriptive statistics were gleaned from the database (AVSS, ISIS, and the pink sheet) to characterize the population before models were created and hypotheses tested. For the model building the dependent variable of interest was: Growth among children at 0-6, 0-12, 0-24 and 0-36 months of age. Important covariates assessed included: infant’s gender, birth weight, depression, feeling tired during pregnancy, breastfeeding ≤ 6 months, pre-existing conditions such as diabetes, gestational diabetes, hypertension, and/or preeclampsia, baby taking medications, caffeine intake, dairy, grains and cereal, fruit and vegetable protein intake, frequency of fruits and/or vegetables intake.

Stepwise multiple linear regression models for the different growth periods were developed in order to analyze the impact of prenatal factors such as behaviors, like,
mood, and physical activity on early life weight gain. Variables that showed to be statistically significant associated with the dependent variable of interest (p<.10) for each of the points in time selected were kept into the final model. Three different final models were selected explaining the greatest amount of variation in the dependent growth variable, corresponding to the period of 0-12, 0-24 and 0-36 months of age. But in some cases, covariates that did not show a statistically significant association were also included into the final model to assess their contribution to the correlation coefficient.

In all models, homoskedacity, kurtosis, and colinearity indicators were assessed to ensure validity of the analysis; no violations were found. All statistical analysis were conducted in SPSS version 19 22.

E. Strengths and Limitations

Comprehensive data collection from several sources allowing for the connection of mood of the mother related to pregnancy is strength of the study. As mood/stress is a known contributor to increased cortisol levels, which has a direct impact on fetal programming that can lead to early life weight gain, the ability to control for this in the study is strength.

Limitations include the self-reported nature of the information on mood and mothers feeling about pregnancy collected from the “pink sheet”. Caffeine intake was also self-reported. Another limitation is the inconsistent method of collection of information on breastfeeding—excluding mothers who reported their breastfeeding practices before six months.

F. Ethical Considerations
This study is IRB exempt as it involved the collection or study of data documents and records that already existed and were fully de-identified and linked by identifiers not available to the data analyses team.

Official permission was obtained from the Orange County Public Health Department and local WIC office to conduct this study. The study used only a merged fully de-identified data set completely separate from any client records.
CHAPTER 4

FIRST PUBLISHABLE PAPER

Impact of Caffeine Intake during Pregnancy and Early Life Adiposity in Offspring

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For Submission to: Obesity

Note: The formatting and referencing style is not in accordance with dissertation guidelines and is according journal specifications.
Abstract

Background: In utero stressors may work to program the metabolism of the developing fetus in such a way that predisposes him/her to obesity later on. The purpose of this study is to examine how maternal consumption of caffeine during pregnancy plays a role in this process. Caffeine intake has been shown to elevate cortisol levels.

Methods: Subjects were 487 pregnant Hispanic women and their children from birth through 36 months of age. Data was collected from California’s WIC program’s Integrated Statewide Information System (ISIS) database to analyze socio-demographic, biophysical, obstetric, psychosocial, and behavioral variables. The State WIC office supplemental form provided information related to mood, mother’s nutritional intake, and mother’s physical activity levels, and the Automated Vital Statistics System (AVSS) provided data related to birth outcomes.

Results: Maternal caffeine intake was shown to be a significant contributor to the difference in weight in the children at 12 and 24 months of age. While a number of factors contribute to the difference in weight gain early in life according to our models, maternal caffeine use is a significant correlate as well. Further study should assess the effect caffeine has on maternal and placental cortisol and other stress chemical signaling levels and the pathways to unfavorable health outcomes including adiposity in children.
Introduction

Childhood obesity is a growing problem in the United States. It is estimated that the number of overweight 6-11 year olds has tripled since the 1970’s, and doubled for 12-18 year olds (1). There are now children as young as 10 years old described as type 2 diabetics (2). Public Health efforts to stem the rising tide of overweight and obese children have largely focused on lifestyle changes. However, these efforts have been minimally effective in halting the rising number of overweight and obese children. Programs have not proven effective especially among the poorest children where the highest rates of childhood obesity exist (1).

One aspect of the growing weight problem facing children in the U.S. is that the prevalence of obesity is disproportionately higher among certain racial and ethnic groups as well as among individuals from lower socioeconomic status. In particular, African-Americans, Mexican Americans, and Native Americans on average have higher rates of obesity. Mexican American children have the highest rates of being overweight (3).

Growing evidence suggests that the origins of obesity and its sequelae can be traced back to the intrauterine period of life (2,4,5). For instance, children who were exposed to intrauterine environments involving diabetes, smoking or emotional stressors have shown to have greater risk for large for gestational age, and childhood obesity (6,7).

While an individual’s propensity for weight gain, particularly increased body fat percentage, has been attributed to genetic make-up, the relatively recent (and increasingly global) epidemic in obesity cannot be explained by genetic variation alone. The concept of fetal programming of health and disease risk proposes that obesity or the susceptibility to become obese can be traced back to the intrauterine period of life. According to this
theory, while the developing fetus is in the womb it is affected by and responds to stressors and suboptimal conditions.

Studies have shown that factors that affect the developing fetus in utero may work to program the metabolism of the developing fetus in such a way that predisposes to obesity later on. Studies conducted on baboons found that female baboons that were overfed while they were pregnant, but not after birth resulted in babies that had a higher adiposity rate at five years of age (10,11).

While a higher birth weight correlates to a higher BMI later in life, low birth weight is associated with a subsequent higher ratio of fat mass to lean mass and greater central adiposity and insulin resistance (12). Similarly, early, accelerated postnatal weight gain is associated with abdominal fatness (12). Individuals born at a lower birth weight in combination with early accelerated/catch up growth during the first year of life appear to be at greatest risk for later disease (12).

Other prenatal and postnatal factors, including excessive weight gain early in life, have been described as being able to program future obesity. Pregnant women who are undernourished, over-nourished, diabetic during pregnancy, and smoking during pregnancy have all been shown to be factors that promote later obesity (2,4,6,13). These factors may act during fetal development to affect the central body weight regulatory system.

Cortisol, a steroid hormone secreted by the adrenal glands, seems to play a role in each of the factors that promote later life obesity in the offspring; therefore, any factor that might increase cortisol in pregnant women might play a role in later obesity. Other studies have demonstrated a causal relationship between cortisol, and obesity suggesting
higher levels of stress hormone activity promotes visceral fat accumulation and insulin resistance, and not the reverse (17,18).

Caffeine is known to elevate cortisol levels at rest and in response to various stressors (14,15). Hence caffeine may be a potential stressor to the developing fetus in utero. Researchers found evidence that caffeine not only increases stress, but also the effects persisted throughout the day after early consumption (16). Caffeine is consumed by a large percentage of the population in the United States. Hughes and Oliveto (25) found that 96% of Americans had at some time in their lives consumed caffeine. The authors also found that 83% were currently consuming at least 186mg of caffeine per day.

Furthermore, Lovallo et al. (30) found that caffeine increases cortisol secretion at multiple time points over the day. Caffeine also increases cortisol during periods of stress above what would normally be experienced under that stressful event (31). One study done on a male cohort found that caffeinated coffee prevents serum cortisol levels from falling in healthy men (15). Lovallo et al. (30) also reported that men and women when consuming caffeine had increases in cortisol when exposed to psychological stress; however the finding was only statistically significant in women. Caffeine does cross the placental barrier and can increase heart rate in the developing fetus. There is very little in the literature that speaks to the effect caffeine has on early life weight gain when consumed during pregnancy.

Clearly, a rational can be made to investigate if caffeine intake among low-income pregnant women similarly adds to their stress and thus indirectly leads to fetal
programming toward overweight/obesity. The purpose of this paper is to use data collected from low income, Latino women to explore this hypothesis.

**Methods and Procedures**

The Family Health division of the Orange County Health Care Agency, as part of a process of gaining local evidence of the benefits of breastfeeding, undertook a study using local (the County’s own) Women, Infants and Children (WIC) program data.

A retrospective study in 487 pregnant women and their children (from birth through 36 months of age) was conducted using the California’s WIC program’s Integrated Statewide Information System (ISIS) database. Information on sociodemographic (marital status, income, number of children, race/ethnicity), biophysical (pre-pregnancy BMI, weight gain in pregnancy), obstetric (gestational diabetes, pregnancy-induced hypertension), psychosocial (homelessness, physical/sexual abuse, depression), and behavioral (smoking, alcohol, illegal drug use) factors were obtained for the purpose of this study. In addition, information on breastfeeding practices and infant growth patterns; including birth weight and length information were obtained. Behavior characteristics for each participating mother were collected at each program visit. The BMI for mothers who had caffeine intake versus those with no caffeine intake was also assessed by “Visit count” (Figure 1). “Visit count” represents the recorded consecutive visit. A visit count of 1, represents the initial visit, visit count 2 represents the second consecutive visit, and so on. “Visit count” is used as an indicator for time exposure based upon behaviors that occurred since the previous recorded visit.

Additional information on the children under study was supplemented by a document created by the State WIC office called “the pink sheet”. The “the pink sheet” is
a self-reported questionnaire that mothers complete to provide information related to mood, mother’s nutritional intake, and mother’s physical activity levels. This document provides information not captured in the ISIS database.

A single database was created matching mothers and their children through a unique family identifying number (ID), which was assigned to the mother’s unique ID and the child’s unique ID. This database included information from pregnancy to the postpartum period that was then tied to the child’s early development metrics. Many mothers in the OC WIC system had more than one child. These children were recognized under the unique family ID. The first pregnancy during the study period for each mother was selected for inclusion in the study.

Additionally, in order to enhance the depth of the database being analyzed, the Automated Vital Statistics System (AVSS) was used to extract information on birth outcomes. This information was then matched to our mother-baby pair database. The AVSS was created in cooperation with local, state, and federal health agencies by the University of California to automate public health records. It is used to improve the timeliness and accuracy of birth certificates by automating their production at the hospital of birth.

**Statistical Analysis**

The statistical package SPPS, version 19 was used for the analysis of this study (31). The trajectory of weight for age, weight for length, and length for age was ascertained at 0-6, 0-12, 0-24 and 0-36 months of age.

Socio-demographic characteristics of the population under study were assessed using univariate analysis. Descriptive statistics were gleaned from the database (AVSS,
ISIS, and the pink sheet) to characterize the population before models were created and hypotheses tested. For the model building the dependent variable of interest was: Growth among children at 0-6, 0-12, 0-24 and 0-36 months of age. Important covariates assessed included: infant’s gender, birth weight, depression, feeling tired during pregnancy, breastfeeding ≤ 6 months, pre-existing conditions such as diabetes, gestational diabetes, hypertension, and/or preeclampsia, baby taking medications, caffeine intake, dairy, grains and cereal, fruit and vegetable protein intake, frequency of fruits and/or vegetables intake.

Stepwise multiple linear regression models for the different growth periods were developed in order to analyze the impact of prenatal factors such as behaviors, like, mood, and physical activity on early life weight gain. Variables that showed to be statistically significant associated with the dependent variable of interest (p<.10) for each of the points in time selected were kept into the final model. Three different final models were selected explaining the greatest amount of variation in the dependent growth variable, corresponding to the period of 0-12, 0-24 and 0-36 months of age. But in some cases, covariates that did not show a statistically significant association were also included into the final model to assess their contribution to the correlation coefficient.

Results

A total sample size of 369 was used for the analysis of this study after missing or inconsistent data on breastfeeding was removed.

Demographic characteristics of the study population are presented in table 1. Mothers were in their late twenties with a low mean annual income and education level. Almost all of them reported to be married. Very few cases of gestational diabetes or
hypertension were observed. Mothers inconsistently responded to questions regarding weight gain, therefore this yielded the lowest N, 301, amongst demographic variables reported in table 1. The most common feeling about pregnancy reported by these mothers was tiredness. Similar percentage of female and male represents the infant database. These children seemed to be healthy with an average weight and length at birth.

Table 4.1: Demographics of Women, Infants, and Children (WIC) Sample (N= 487)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean (SD)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mother’s characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>487</td>
<td>27.3 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Income (monthly, in dollars)</td>
<td>487</td>
<td>1,659 (794)</td>
<td></td>
</tr>
<tr>
<td>Education Level (grade)</td>
<td>421</td>
<td>9.2 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Marital Status (Married)</td>
<td>487</td>
<td></td>
<td>457 (94)</td>
</tr>
<tr>
<td><strong>Mother's Health Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal Weight Gain (lbs.)</td>
<td>301</td>
<td>27.2 (10.9)</td>
<td></td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>487</td>
<td></td>
<td>60 (12.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>487</td>
<td></td>
<td>6 (1)</td>
</tr>
<tr>
<td><strong>Infant's Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (Female)</td>
<td>487</td>
<td>443</td>
<td>231 (47)</td>
</tr>
<tr>
<td>Birth Weight (gr)</td>
<td>431</td>
<td>3328 (496)</td>
<td></td>
</tr>
<tr>
<td>Birth Length (cm)</td>
<td>423</td>
<td>49.5 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Baby taking meds for illness</td>
<td>487</td>
<td></td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td><strong>Feelings about pregnancy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>439</td>
<td></td>
<td>35 (8)</td>
</tr>
<tr>
<td>Sadness</td>
<td>439</td>
<td></td>
<td>29 (6)</td>
</tr>
<tr>
<td>Stress</td>
<td>439</td>
<td></td>
<td>40 (9)</td>
</tr>
<tr>
<td>Tiredness</td>
<td>439</td>
<td></td>
<td>137 (31)</td>
</tr>
</tbody>
</table>

*119 were coded as missing records, total=462
The effect of the variables identified as possibly contributing to the weight trajectory of the children population is presented in table 2. These final multivariate models suggested that these factors explain 12%, 11% and 10% of the variation on infant’s growth for the period of 0-12, 0-24 and 0-36 months, respectively. From these factors assessed, infant’s gender, medications taken by the baby and caffeine consumption by the mother provided a statistically significant (p<0.05) positive effect on the variation of growth for the infants during the period 0-12 months of age while breast milk had an inverse effect. Caffeine intake also showed to have a statistically significant direct effect on the infant’s growth during 0-24 months of age. In addition, tiredness during pregnancy, pre-existing condition and intake of dairy had a direct effect on the infant’s growth pattern while grains and cereals had an inverse effect. Dairy intake as well as breastfeeding for at least 6 months, although this last one was borderline statistically significant associated, were important indicators for the baby’s growth until 36 months of age. Dairy intake particularly seemed to have the strongest positive effect on the growth of these children until the first 3 years of their life.

Caffeine was a statistically significant contributor to the model. Growth (weight and height) was more affected (increased) for those mothers who reported regular caffeine consumption. However, this model only explained 0.4% of the variation in growth amongst the infants (R² = 0.004). The model was reevaluated, and a new model adding the intake of grains and cereals was assessed. The addition of grains resulted in the model explaining 11% of the variation in infant growth at 24 months. This suggests that given two infants with the same age, growth would be affected for those mothers who ate grains and cereals most days, drank caffeine, had a pre-existing condition
including diabetes, GDM, hypertension and/or preeclampsia, and reported feeling tired during pregnancy. Again, caffeine was a statistically significant contributor to the model; therefore we can conclude given two infants with the same age, growth would be affected (i.e. more weight) for those mothers who drank caffeine (B=0.40, p=0.002).
Table 4.2: Multivariate models describing Variation in Growth among Children in WIC Program at 12, 24, and 36 months.

<table>
<thead>
<tr>
<th>Covariates</th>
<th>β (95%CI)</th>
<th>P Value</th>
<th>R</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Growth 0-12 Months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infant's Gender</td>
<td>0.18 (-0.02-0.33)</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth Weight</td>
<td>-0.0004 (0.0-0.0)</td>
<td>0.66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling Tired During Preg.</td>
<td>0.10 (-0.07-0.28)</td>
<td>0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressed&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.40 (-0.03-0.83)</td>
<td>0.07</td>
<td>0.34</td>
<td>0.12</td>
</tr>
<tr>
<td>Breast Milk&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-0.33 (-0.58--0.07)</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-existing Conditions&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.40 (-0.02-0.82)</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baby taking meds</td>
<td>2.24 (0.65-3.82)</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caffeine&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.31 (0.11-0.51)</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Growth 0-24 Months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infant's Gender</td>
<td>0.15 (-0.05-0.36)</td>
<td>0.13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth Weight</td>
<td>0.0015 (0.0-0.0)</td>
<td>0.88</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling Tired During Preg.</td>
<td>0.31 (0.09-0.52)</td>
<td>0.007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-existing Conditions&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.70 (0.16-1.24)</td>
<td>0.01</td>
<td>0.34</td>
<td>0.11</td>
</tr>
<tr>
<td>Baby taking meds</td>
<td>1.54 (-0.52-3.59)</td>
<td>0.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dairy Intake&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.15 (0.05-0.25)</td>
<td>0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grains and Cereals&lt;sup&gt;e&lt;/sup&gt;</td>
<td>-0.52 (-0.09--0.01)</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caffeine&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.31 (0.11-0.51)</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Growth 0-36 Months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infant's Gender</td>
<td>-33.36 (-188.69-121.98)</td>
<td>0.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth Weight</td>
<td>0.02 (-0.13-0.18)</td>
<td>0.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breastfeeding ≤ 6 mo.</td>
<td>-193.28 (-387.49-0.93)</td>
<td>0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caffeine&lt;sup&gt;d&lt;/sup&gt;</td>
<td>128.04 (-49.83-305.91)</td>
<td>0.16</td>
<td>0.31</td>
<td>0.10</td>
</tr>
<tr>
<td>Dairy Intake&lt;sup&gt;e&lt;/sup&gt;</td>
<td>87.79 (13.05-162.53)</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit Intake&lt;sup&gt;e&lt;/sup&gt;</td>
<td>153.99 (-318.86-626.84)</td>
<td>0.52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetable Protein Intake</td>
<td>79.54 (-14.82-173.90)</td>
<td>0.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruits and/or Vegetables&lt;sup&gt;f&lt;/sup&gt;</td>
<td>494.43 (-19.10-1007.97)</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Depression was measured using Pathik's Depression scale
<sup>b</sup> Breast milk as part of the child's diet
<sup>c</sup> Mother's who had diabetes, gestational diabetes, hypertension, and/or preeclampsia coded as yes/no.
<sup>d</sup> Caffeine was measured as 'yes' or 'no'.
<sup>e</sup> Dairy, grains and cereals, fruit, and vegetable protein intake was self-reported as 'yes' or 'no' on 'most days'.
<sup>f</sup> Fruits and vegetables was measured as reported daily consumption of
Figure 4.1 illustrates the mean infant BMI by caffeine intake status of the mother and exposure. Each exposure time point represents the succession of visits to the WIC office for participating mothers. Data collected at each visit is representative of behaviors and events since the previous visit. Mean BMI correlates to BMI data collected on the pink sheet at the corresponding visit. Table 3 summarizes the mean BMI by caffeine status of the mother by exposure. Both exposure time points 1 and 10 show significant differences in mean BMI by caffeine intake status.

Figure 4.1: Mean infant BMI by caffeine exposure and exposure time point.

![BMI by Visit Count](chart.png)

Table 3: Mean Infant BMI by Caffeine Exposure

<table>
<thead>
<tr>
<th>Visit Count</th>
<th>Time 1</th>
<th>Time 2</th>
<th>Time 3</th>
<th>Time 4</th>
<th>Time 5</th>
<th>Time 6</th>
<th>Time 7</th>
<th>Time 8</th>
<th>Time 9</th>
<th>Time 10*</th>
</tr>
</thead>
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<tr>
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<td>62.71</td>
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<td>66.36</td>
<td>64.44</td>
<td>64.54</td>
<td>58.67</td>
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<tr>
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<td>398(30.07)</td>
<td>394(29.62)</td>
<td>384(28.31)</td>
<td>377(28.51)</td>
<td>369(28.58)</td>
<td>267(28.42)</td>
<td>120(29.18)</td>
<td>55(29.26)</td>
<td>18(29.35)</td>
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<tr>
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<td>59.57</td>
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<td>55.76</td>
<td>56.78</td>
<td>62.54</td>
<td>64.36</td>
<td>60.59</td>
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<td>n(sd)</td>
<td>45(29.82)</td>
<td>48(32.37)</td>
<td>47(32.14)</td>
<td>46(34.15)</td>
<td>46(31.46)</td>
<td>45(27.88)</td>
<td>41(32.35)</td>
<td>25(31.40)</td>
<td>13(30.37)</td>
<td>6(17.87)</td>
</tr>
</tbody>
</table>

*Statistically significant difference (p-value <0.05) between caffeine consuming mothers and non-consumers
Discussion

In a stressful or suboptimal intrauterine environment during critical periods of proliferation, differentiation and maturation structural and functional changes can be produced in cells, tissues and organ systems. These changes may permanently affect the way that energy is metabolized, fat is deposited and hence increase the risk for obesity. This is especially true when the individual is facing an obesogenic postnatal environment.

Looking for the environmental factors that cause fetal programming towards increased adiposity is challenging but a better understanding of prenatal and early onset adiposity can inform effective interventions to prevent childhood and later life obesity. Our models assess many different prenatal factors. It is of great interest that caffeine is the strongest predictor of early life weight gain of all of the factors we explored.

Currently the American College of Obstetrics and Gynecology (ACOG) recommends limited amounts of caffeine for pregnant women. The findings from the study speaks to the role that caffeine intake during pregnancy might have in early life weight gain in children. The three models evaluated in this study to evaluate the contribution of the identified covariates on growth at 0-12, 0-24, and 0-36 months consistently detected caffeine consumption as a significant contributor. Additionally, measurements of BMI taken at successive time points revealed that mothers who reported consistent consumption of caffeine over a period time equating to 1 and/or 10 visits to the program, report statistically significantly higher infant BMI on average when compared to mothers who do not consume caffeine.

While caffeine use is clearly an important factor, the models also show that a complex network of factors contribute to early life weight gain in children. We realize
that this is a preliminary study that seems to point in the direction of caffeine as a significant contributor to early life weight gain that can lead to later obesity. A prospective study of women who report drinking caffeine in various amounts during pregnancy, then follows the BMI of the children would be beneficial in drawing a more firm connection between caffeine intake, early life weight gain and later life obesity.

More specifically a study that measured the impact of maternal caffeine intake on maternal and placental cortisol levels would be helpful in understanding the physiology of increased adiposity if increased BMI was found later.

Acknowledgements

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Disclosure

The authors have no conflict of interest to declare.

References

1. MMWR, 2009


CHAPTER 5
SECOND PUBLISHABLE PAPER

Impact of Breastfeeding on Childhood Obesity in a Predominately Latino WIC Population

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For Submission To: Breastfeeding Medicine

Note: The formatting and referencing style is not in accordance with dissertation guidelines and is according journal specifications.
Abstract

Background: Studies have shown that breastfeeding is protective against childhood obesity and suggest that after six months the weight gain in breastfed babies slows opposed to formula fed babies who continue with rapid weight gain. This slowing of weight gain has been shown to be protective against adiposity and later life weight gain. Maternal stressors including depression and how a mother feels about her pregnancy have also been seen as risk factors for childhood obesity.

Objective: This study looks to further explore these findings in a low-income Latino population—adding mother’s feelings about the pregnancy.

Methods: A retrospective analysis of data from California’s Women, Infants, and Children (WIC) Program’s Integrated Statewide Information System (ISIS) database, and the Automated Vital Statistics System (AVSS) was conducted with 487 pregnant women and their children participating in the Orange County WIC Program from birth through 36 months of age.

Results: Using Hierarchal Linear Modeling, weight to length ratios were evaluated until 24 months for breastfeeding practices. The group that did not exclusively breastfeed had the largest babies at 12 and 24 months. The group that breastfed exclusively more than 6 months were the most lean at 12 and 24 months. The protective effects of breastfeeding existed regardless of how women felt about their pregnancy.

Conclusions: Compared to bottle fed babies, breastfed babies experience reduced weight gain between 6 and 24 months independent of mother’s self reported feelings about the pregnancy. Since early life slower weight gain appears protective against childhood
obesity any such protection would be of importance in this low income Latino population that presents with higher rates of childhood obesity.

**Introduction**

Obesity and overweight in children is a major public health concern. In children, obesity is defined by age and sex specific BMI percentiles greater than 85. The prevalence of overweight children aged 2-5 years is 13.9% and for 6-11 year olds is 18.8%. The incidence of overweight children has tripled among U.S. preschoolers and has quadrupled among children age 6-11 years old.\(^1\)

Obesity has increased in all racial, ethnic, and socioeconomic groups as well as in both genders.\(^1\)\(^-\)\(^3\) Overall; girls are more affected than boys. In a period of 20 years, between the NHANES I and NHANES III studies, prevalence of obesity and overweight in young girls increased more than two fold. In comparison, in young boys the increase was approximately 25%. In the over six-year old child population, the increase is more equitable. Among American adolescents there has been a doubling in the prevalence of obesity in both genders.\(^2\)\(^,\)\(^4\)

Although obesity has increased in all racial, ethnic and socioeconomic groups, the prevalence of obesity is disproportionately higher among certain racial and ethnic groups as well as among individuals from lower socioeconomic populations. African-Americans, Mexican Americans, and Native Americans are three of the ethnic minority groups most affected. Mexican American children have the highest rates of being overweight followed by non-Hispanic blacks.\(^5\)\(^,\)\(^6\) Non-Hispanic Whites are the least affected.\(^6\) Independent of race or ethnicity, being of a lower socioeconomic status is a key predictor of higher overweight and obesity prevalence in US children.\(^1\) Similar to
these national data, in Orange County California, Latinos are reported as having the highest percentage of overweight: 13.9% in 0-4 year olds and 22.9% for 5 to 11 year olds.

These figures are concerning because overweight children develop health problems earlier than their normal Body Mass Index (BMI) counterparts. Obese children are at a higher risk of being asthmatic, developing Type II Diabetes and orthopedic issues. They are also more likely to have behavioral problems and many suffer from depression. Obese children are also showing increased risk of developing high blood pressure or high blood cholesterol level. Estimates have indicated that more than 80% of teenagers that are obese will remain obese as adults.

Factors that might influence childhood obesity are evident early in life. Babies who experience "faster than normal" weight gain are at risk for higher childhood adiposity at ages 12 years and older. There is evidence that breastfeeding impacts how weight is gained early in life and hence how much weight and/or adiposity the child may have later in life. Ong KK, Emmett P, Northstone K, et al. found that if a baby experienced rapid weight gain during the first nine months of life there was a higher risk of increased adiposity and early menarche in girls. Agostoni C, Grandi F, Gianni ML, et al. reported that while breastfed and formula fed infants gained similar amounts of weight in the first six months of life, after six months the weight gain in breastfed babies slowed down in comparison to formula fed babies who continued to gain weight rapidly. According to Ziegler and Darling, in the first 4-6 months of life there is no difference in adiposity between breastfed and formula fed infants. However, after 6 months the breastfed infants are leaner than formula fed infants.
However, not all studies fully support breastfeeding as protective against childhood obesity. Dewey\textsuperscript{16} concludes that while there might be some relationship between breastfeeding and childhood obesity, the causal effect was very small when compared to other factors that could impact the weight in children. Protective factors likely could include the access to healthy foods, physical activity genetic factors and the impact of childhood diseases\textsuperscript{17}.

Nevertheless, studies with longer periods of exclusive breastfeeding seem to show a small but consistent protective effect against later obesity. Gillman MW, Rifas-Shiman S, Berkey CS, et al.\textsuperscript{18} found that infants who were predominantly breast fed (compared to infants who were predominantly formula fed) in the first 6 months of life had a lower prevalence of overweight 9 to 14 years later. That study found an estimated relative risk reduction of approximately 22\% and supported the hypothesis that there was greater protection with longer breastfeeding.

Latino women in Orange County California are the least likely to breastfeed of the three major ethnic groups in the County\textsuperscript{4}. Furthermore, Mexican American children in the County are the most likely to be obese\textsuperscript{4}. Notably these low rates for breastfeeding are inconsistent with data on Latino women in the rest of the US. In fact, the literature supports the idea that Latino women are the most likely to breastfeed in the US, although breastfeeding rates drop with acculturation.\textsuperscript{18}

Previous studies have shown antenatal stressors in mothers to be associated with later childhood obesity.\textsuperscript{19} For instance; several studies have shown depressive symptoms during pregnancy to be associated with childhood obesity.\textsuperscript{20,21} Hence how a woman feels about her pregnancy may impact early weight gain in her child. There is little in the
literature on how antenatal feelings about pregnancy or depression affect early life weight gain while considering the impact of breastfeeding. Considering the higher levels of depression in lower socioeconomic individuals and certain ethnic minority groups, examining how antenatal feelings about pregnancy and prenatal depression impact childhood obesity in relation to breastfeeding should be of interest.

The purpose of this study is to examine the impact of exclusive breastfeeding on weight gain in the first 12 and 24 months of life, while taking into consideration a variety of factors including how a woman feels about her pregnancy, in Hispanic children participating in the Orange County, CA Women, Infants, and Children’s (WIC) Program.

Materials and Methods

The Family Health Division of the Orange County (OC) Health Care Agency, as part of a process of gaining local evidence of the benefits of breastfeeding to the Hispanic population, undertook a study using local (the County’s own) Women, Infants and Children (WIC) program data for the period of 2004 to 2009.

We conducted a retrospective analysis of 487 pregnant women and their children studying them from birth through 36 months of age. California’s WIC program’s Integrated Statewide Information System (ISIS) database was used to abstract and obtain socio-demographic (marital status, income, number of children, race/ethnicity), biophysical (pre-pregnancy BMI, weight gain in pregnancy), obstetric (gestational diabetes, pregnancy-induced hypertension), psychosocial (homelessness, physical/sexual abuse, depression) and behavioral (smoking, alcohol, illegal drug use) variables for analysis. ISIS data also provided information on breastfeeding practices and infant
growth patterns; including birth weight and length information and weight until 24 month of age.

Additional information not captured in the ISIS database was supplemented by a document created by the State WIC office. The "pink sheet" is a self-reported questionnaire completed by mothers to provide information related to mood, mother’s nutritional intake, and mother’s physical activity levels. Mood was assessed by a question that asked: *What words describe how you feel about being pregnant: Happy, OK, tired, depressed, sad, stressed or angry.* Mothers and children were matched in the database by assigned unique family identifiers. A single data set was created around the mother to include data from pregnancy to the postpartum period that was then tied to the child’s early development metrics. Many mothers in the OC WIC system had more than one child all of whom would be recognized under the unique family identifier. To account for this particular analysis, we only used the first pregnancy for each mother in the database and matched it to corresponding ISIS data collected from the pink sheet.

The second database used in our analyses is the *Automated Vital Statistics System (AVSS)*. This system was created in cooperation with local, state, and federal health agencies by the University of California to automate public health records. *AVSS* is used to improve the timeliness and accuracy of birth certificates by automating their production at the hospital of birth. Data related to birth outcomes were matched to the mother-baby pairs and included in the final analyses data base.

Univariate analysis were conducted to describe the demographic characteristic of the sample. The trajectory of weight for age, weight for length, and length for age was ascertained at 0, 6, 12, 18, and 24 months of age. Individuals with missing or
inconsistent data on the pink sheet regarding breastfeeding were removed resulting in a final sample size of 369. That sample was stratified further into three breastfeeding categories: “never breastfed” (n=71), “breastfeed between 1-5 months” (n=138), and “breastfed at least 6 months” (n=160).

Pathik’s depression score was created by simply weighting the variables as having no report of being depressed, sad or stressed or having one of them as low risk, and if they had two or more they were considered high risk and a dichotomous variable was created.

Hierarchal linear modeling (HLM) was used to create growth curves. HLM was chosen as the analytic approach because of the nature of the study group. When it appears that a sample is hierarchal, or nested, the sample should statistically be more similar than a truly random sample from the entire source population. In this case, the sample of Latino WIC clients within the Orange County WIC system, were nested within all mothers in Orange County, and all mothers in the Southern California region, in California, etc. Furthermore, because these mothers tend to come from a similar population, statistically they would tend to be more homogenous over time. Since these mothers tend to share more similar characteristics than other mothers in Orange County or possibly the region, the indicators for these individuals are likely not fully independent. Since independence is required for regression analyses, a model that accounts for nested (hierarchal data) like hierarchal linear modeling was used to create the growth charts. The HLM models generated in this analysis were two-level models with infants nested within mothers. Six models were generated for both weight for length until 12 months, and weight for length until 24 months. The predictors for the two
outcomes were modeled with two-level hierarchical regressions: mothers and infants. Mother-level variables used included mood, depression status, and pre-pregnancy BMI. Infant-level variables included gender and breastfeeding status. Mothers who reported having one or more stress, sad, or depressed moods were categorized as high risk and included in model six. Likewise, mothers reporting no stress, sadness, or depression were categorized as low risk and included in model 5. Model construction is presented in both tables 5 and 6.

In all models, homoskedacity, kurtosis, and colinearity indicators were assessed to ensure validity of the analysis; no violations were found. All statistical analysis were conducted in SPSS version 19.

**Results**

Demographic characteristics of the study population are summarized in table 1. The mean age of the women in the study is 27.3 years. The average monthly income of the women is $1,659 and the average level of education is grade 9.2 years of schooling. Ninety four per cent of the women reported being married. In general the women were very similar with greater than 95% of the women being of Mexican descent, 100% qualifying for the WIC program and 100% living in Orange County California.

The average length of time for any breastfeeding was 24.4 weeks. The average length of time for exclusive breastfeeding was 11 weeks. Breastfeeding mother-child pairs were grouped as never breastfed (n=71, 19%), exclusively breastfed 1-5 months (n=138, 37%) and 6 months or greater exclusive breastfeeding (n=160, 43%). Women also reported being depressed (n=35,8%), sad (n=29, 6%) or stressed (n= 40, 9%) while 61(11%) report being depressed, sad, or stressed uniquely. Eleven women (2%) reported
any two (depressed, sad or stressed), while 7 women (1%) reported being sad, depressed and stressed at once.

Breastfeeding information was collected only at one time point. The age of the infants at which this question was asked varied greatly (from 1-63 weeks). Therefore, mothers who reported breastfeeding choice before 6 months of age were not included in the breastfeeding analysis. Only those mother-child dyads that reported breastfeeding at a WIC visit after six months were used. This allowed us to assess breastfeeding practices for the first six months of life in that entire time period. Therefore, after adjustments for this were made, the original, unadjusted breastfeeding categories changed slightly: twenty percent of the infants were never breastfed, 40% were breastfed up to 5 months of the first six months of life and 40% were being breastfed exclusively for at least 6 months.

Available infant growth information varied within each age range. From 0 to 6 months we only had 2 valid time points. From 0-12 months, 3 time points; and from 0-24, 5 time points. Based on this, we calculated the growth slope between 0 to 6 months and used HLM analysis to evaluate growth patterns from 0-12 and 0-24 months. Model coefficients are summarized in tables 2 and 3. Model 1 evaluates the change in weight for length explained by infant gender and breastfeeding status, model 2 evaluates the change in weight for length explained by the mood of the mother, model 3 evaluates the change in weight for length explained by infant gender and depression status of the mother, and model 4 evaluates the change in weight for length explained by infant gender and mother’s pre-pregnancy BMI. Models 4 and 5 evaluate the change in weight for length by infant gender and breastfeeding status based upon mothers categorized as low risk and high risk for mood respectively.
Using HLM, weight for length ratios were evaluated until 24 months for factors including depression, stress, and sadness. None yielded significant results alone. Analysis was also run to evaluate weight to length ratios until 12 and 24 months for breastfeeding practices and pre-pregnancy BMI. Regardless of whether or not women reported being sad, depressed and/or stressed (all evaluated in the model) breastfeeding had a significant impact on W-L ratios. For those mothers who did not report being sad, depressed or stressed, there was a significant difference in W-L ratio based on breastfeeding practices (p=0.016, p=0.035, respectively), suggesting that stronger negative mental health status may have a third variable effect to breastfeeding.

Regarding the 0-6mo period slopes, no differences were found among pre-pregnancy BMI or breastfeeding categories. The distribution of breastfeeding categories was significantly different among women who had inter-pregnancy intervals less and above 6 months (more women in the above 6 month-inter gestation interval were breastfeeding at 6 months).
Table 5.1: Demographics of Women, Infants, and Children (WIC) Sample

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>Mean (SD)</th>
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<tbody>
<tr>
<td><strong>Mother's Characteristics</strong></td>
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<td></td>
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<tr>
<td>Age (years)</td>
<td>409</td>
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</tr>
<tr>
<td>Income (monthly)</td>
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<td>1,659 (794)</td>
</tr>
<tr>
<td>Education Level (grade)</td>
<td>421</td>
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</tr>
<tr>
<td>Pre-Pregnancy BMI</td>
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<td>27.4 (6.1)</td>
</tr>
<tr>
<td>Maternal Weight Gain (lbs.)</td>
<td>301</td>
<td>27.2 (10.9)</td>
</tr>
<tr>
<td>Marital Status (Married, %)</td>
<td>370</td>
<td>94 (16)</td>
</tr>
<tr>
<td><strong>Infant's Characteristics</strong></td>
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<td></td>
</tr>
<tr>
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<td>231 (49)</td>
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<tr>
<td>Birth Weight (gr)</td>
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<td>3328 (496)</td>
</tr>
<tr>
<td>Birth Length (cm)</td>
<td>423</td>
<td>49.5 (2.8)</td>
</tr>
<tr>
<td><strong>Breastfeeding Practices</strong></td>
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<td></td>
</tr>
<tr>
<td>Weeks of Breastfeeding</td>
<td>432</td>
<td>24.4 (22.1)</td>
</tr>
<tr>
<td>Exclusive Breastfeeding</td>
<td>370</td>
<td>11.01 (20.4)</td>
</tr>
<tr>
<td>Never Breastfed (n=, %)</td>
<td></td>
<td>71 (19)</td>
</tr>
<tr>
<td>Breastfed 1-5 months (n=, %)</td>
<td></td>
<td>138 (37)</td>
</tr>
<tr>
<td>Breastfed ≥ 6 months (n=, %)</td>
<td></td>
<td>160 (43)</td>
</tr>
<tr>
<td><strong>Feelings about Pregnancy</strong></td>
<td></td>
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<tr>
<td>Depressed (n=, %)</td>
<td></td>
<td>35 (8)</td>
</tr>
<tr>
<td>Sad (n=, %)</td>
<td></td>
<td>29 (6)</td>
</tr>
<tr>
<td>Stressed (n=, %)</td>
<td></td>
<td>40 (9)</td>
</tr>
<tr>
<td>Depressed or Sad or Stressed (n=,%)</td>
<td></td>
<td>61 (11)</td>
</tr>
<tr>
<td>Any two (Depressed, Sad, or Stressed) (n=,%)</td>
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<td>11(2)</td>
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<tr>
<td>Depressed, Sad, and Stressed (n=,%)</td>
<td></td>
<td>7(1)</td>
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</table>

*a 119 were coded as missing records, total=462*
Table 5.2: HLM Analysis Weight for Length Until 12 Months

Coeficient (Standard Error) Matrix

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5⁴</th>
<th>Model 6⁵</th>
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</thead>
<tbody>
<tr>
<td>Intercept (T0₀)</td>
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<td>0.375243**</td>
<td>0.373311**</td>
<td>0.379095**</td>
<td>0.365705**</td>
<td>0.375405**</td>
</tr>
<tr>
<td></td>
<td>(0.005524)</td>
<td>(0.002876)</td>
<td>(0.004037)</td>
<td>(0.006727)</td>
<td>(0.005278)</td>
<td>(0.020258)</td>
</tr>
<tr>
<td>Gender (Female)</td>
<td>0.002747**</td>
<td>----</td>
<td>0.002887**</td>
<td>0.001762</td>
<td>0.003064**</td>
<td>0.000789</td>
</tr>
<tr>
<td></td>
<td>(0.000880)</td>
<td>(0.000816)</td>
<td>(0.000971)</td>
<td>(0.001080)</td>
<td>(0.001830)</td>
<td></td>
</tr>
<tr>
<td>Breastfed¹</td>
<td>-0.001069*</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>-0.001227*</td>
<td>-0.000468</td>
</tr>
<tr>
<td></td>
<td>(0.000430)</td>
<td></td>
<td>(0.000509)</td>
<td>(0.000803)</td>
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<td></td>
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<tr>
<td>Mood²</td>
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<td>-0.000447</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.000824)</td>
<td></td>
</tr>
<tr>
<td>Depressed (Yes/No)</td>
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<td>----</td>
<td>-0.000750</td>
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<td>----</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.001400)</td>
<td></td>
</tr>
<tr>
<td>Pre-pregnancy BMI³</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>-0.000075</td>
<td>----</td>
<td>----</td>
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<td></td>
<td></td>
<td></td>
<td>(0.000065)</td>
<td></td>
</tr>
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</table>

²0=Not Depressed, Sad, or Stressed; 1= Either One of Them; 3=All Three of Them

⁴Low Risk Group (No: Stressed, Depressed, or Sad)

⁵High Risk Group (One or More Yes: Stressed, Depressed, or Sad)
<table>
<thead>
<tr>
<th>Model</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
<th>Model 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept ((T_{00}))</td>
<td>0.382424**</td>
<td>0.386257**</td>
<td>0.387048**</td>
<td>0.390510**</td>
<td>0.380428**</td>
</tr>
<tr>
<td>Gender (Female)</td>
<td>0.001479**</td>
<td>0.001421**</td>
<td>0.001401**</td>
<td>0.0001006</td>
<td>0.001588**</td>
</tr>
<tr>
<td>Breastfed(^1)</td>
<td>-0.000405</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>-0.000604*</td>
</tr>
<tr>
<td>Mood(^2)</td>
<td>-0.000447</td>
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<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>Depressed (Yes/No)</td>
<td>-0.000937</td>
<td>----</td>
<td>----</td>
<td>----</td>
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</tr>
<tr>
<td>Pre-pregnancy BMI(^3)</td>
<td>-0.000060</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
</tbody>
</table>

\(^{1}\)0=Never Breastfed, 1=Breastfed <6 Months, 2=Breastfed>=6 Months

\(^{2}\)0=not Depressed, Sad, or Stressed; 1= Either One of Them; 3=All Three of Them

\(^{3}\)Low Risk Group(No: Stressed, Depressed, or Sad)

\(^{4}\)High Risk Group(One or More Yes: Stressed, Depressed, or Sad)

\(^{*}\)p<0.05, \(^{**}\)p<0.01
Figure 1: Weight to Length Ratio until 12 months by Breastfeeding Time

Figure 2: Weight to Length Ratio until 24 months by Breastfeeding Time
Discussion

This study supports the existing evidence that breastfed babies slow down weight gain after 6 months\textsuperscript{13}. The group that is breastfed beyond 6 months is the leanest. In light of the research on the importance of rapid weight gain early in life and what is known about early life adiposity patterns (mainly that more weight gain in the first 18 months increases risk of later obesity) these findings are important\textsuperscript{12}. This is especially important because of the population studied.

There are two reasons why breastfeeding could be preventive for childhood obesity. First, the act of breastfeeding itself contains mechanisms that prevent a baby from over eating. A mother’s milk supply is directly impacted by the amount a baby will eat. This supply-demand factor means that babies are not ingesting more food than they need, or want. This is in contrast to bottle feeding where the baby is often encouraged to take in a specific milliliter amount by the mother, when in fact the amount of food the baby actually needs might be less (or more) than the amount in the bottle\textsuperscript{15}.

Secondly, researchers found that there were lower serum concentrations of insulin in breastfed infants than in those infants that were fed cow’s milk.\textsuperscript{23,24} Given that insulin promotes fat storage this could be a significant finding. In a separate study, Hamosh\textsuperscript{25} found that babies who were fed cow’s milk consistently over a ten minute period consumed calories evenly throughout the ten minutes. Breastfed babies, however, consumed most of the energy (80-90\%) from their feed in the first four minutes. This suggests that breastfed babies consumed less energy (calories) per volume than babies fed on formula.

It is important to note, that our analytic models take into account the self-reported states of depression and mood. Collecting data on states of depression allowed for an
analysis of the impact that a women’s own feelings had on early weight gain in her child. The “pink sheet” questionnaire we had available to us also asked about how a woman felt about being pregnant. Notably that when all variables were controlled for there was no effect of any of the reported data on mood or depression had on early life weight gain indicating that regardless of how a woman felt about her pregnancy breastfeeding for longer is statistically significantly related to leaner babies at 12 and 24 months.

The study did have some key strengths in that the data came from multiple verifiable databases, and the study confirms previous research studies around breastfeeding and early life weight gain patterns. Some limitations of the study are that pink sheet data was self-reported and the pink sheet was not designed as a research tool. Also such a study may not be applicable to other populations although there are other studies on different populations that do support our findings. Another limitation is that the breastfeeding data was not collected at regular intervals in each dyad. Data was collected as part of the clinical WIC program and not necessarily for research. Future studies that are prospective and follow children longer as well as a more comprehensive data collection tool to look at mother’s mood and attitude about pregnancy would be beneficial.

This study is unique in its focus on Latino children in Orange County California. The high childhood obesity rates in the low income Latino mothers attending WIC, combined with lower rates of exclusive breastfeeding in comparison to white mother child dyads\(^4\), makes this study compelling. Understanding any of the protective effects of breastfeeding should help guide programs and policies that support breastfeeding. Our data suggests that breastfeeding even controlling for many demographic, pre pregnancy
and mental health variables remains protective and results in leaner babies over a lengthy course of time (up to 24 months). Given the potential long term life impact of obesity and in light of escalating health care costs, this “simple” intervention to encourage exclusive breastfeeding, holds great promise as an early life strategy towards healthier babies.

**Conclusion**

In a low-income population at high risk for obesity, exclusive breastfeeding appears to be protective against early life adiposity and may have a protective effect against later life obesity. This impact is seen regardless of how the women reported feeling about their pregnancy while pregnant. Programs that promote exclusive breastfeeding for at least the first 6 months of life should be supported and policies implemented that encourage and promote women to exclusively breastfeed as they might be important in the fight against obesity. This is especially true for ethnic minority groups that suffer disproportionately from childhood obesity as exclusive breastfeeding may function as an early first step to reverse health disparities related to overweight and obesity.

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CHAPTER 6
OTHER FINDINGS

There are many aspects of this study of interest but not highlighted in the papers. Breastfeeding trends in this population were particularly of interest. The average length of time for any breastfeeding was 24.4 weeks. The average length of time for exclusive breastfeeding was 11 weeks. Although greater than 24 weeks of breastfeeding is comparatively good for US breastfeeding rates, exclusive breastfeeding is much shorter in duration although it is clearly recommended for a more lengthy time period. How acculturation or other issues such as needing to return to work might impact the shorter length of exclusive breastfeeding would be of interest for future studies.

The distribution of breastfeeding categories was significantly different among women who had inter-pregnancy intervals less and above 6 months (more women in the above 6 month-inter gestation interval were breastfeeding at 6 months). This is of interest in that it connects child spacing to longer periods of breastfeeding. This can be cyclical in nature in that breastfeeding can help space pregnancies. However, if a woman does get pregnant, whether breastfeeding or not, she may be more likely to stop breastfeeding.

A large percentage of the women also reported exclusive formula feeding at 48.2%. This is in comparison to only 6.4% that reported exclusive breastfeeding at the time of being questioned. Almost 20% (19.9) reported combo feeding. Notably the data represents a time period before the WIC program changed the food offerings to promote breastfeeding in 2009. It would be of interest to conduct similar analyses with the same population after the breast feeding promotion was instituted.
Very few cases of gestational diabetes or hypertension were observed. We did not ask about initiation of prenatal care or looked into whether or not any preconception care was given. However this relatively young group of mothers had very low rates of pregnancy related diseases.

The most common feeling about pregnancy reported by these mothers was tiredness. In addition, tiredness during pregnancy, pre-existing condition and intake of dairy had a direct effect on the infant’s growth pattern while grains and cereals had an inverse effect. This protective effect of mothers reported consumption of grains and cereals was an interesting find and one that merits further study.

Mother’s dairy intake as well as breastfeeding for at least 6 months, although this last one was borderline statistically significant associated, were important indicators for the baby’s growth until 36 months of age. Dairy intake particularly seemed to have the strongest positive effect on the growth of these children until the first 3 years of their life.

Pre-pregnancy BMI was placed in the HLM models for weight for length of the child at 12 and 24 months. At 12 months there was no difference in the size of the child. However at 24 months the women with lower pre-pregnancy BMI did have smaller children but the result was not statistically significant.
CHAPTER 7

LIMITATIONS, CONCLUSIONS, AND FUTURE DIRECTIONS

This study does have unique strengths. First of all there was comprehensive data collection from several sources allowing for the connection of mood of the mother related to pregnancy to her offspring for up to three years. The ability to tie very reliable data together to create unique mother child dyads allowed for interesting analysis. As mood/stress is a known contributor to increased cortisol levels, which has a direct impact on fetal programming that can lead to early life weight gain, the ability to control for this in the study is a strength. Also we are very comfortable with the responses of the mothers on the “pink sheet” because they were not reporting to researchers but to WIC workers with whom they form relationships and are less likely to see as outsiders trying to get information from them.

Another strength is that we nest this study into a very unique and understudied population. Latino women and children in a very small geographical area in southern California create a strong study group.

Limitations include the self-reported nature of the information on mood and mothers feeling about pregnancy collected from the “pink sheet”. Caffeine intake was also self-reported and was not scaled as to how much caffeine was being consumed.

Another limitation is the inconsistent timing of collection of information. Since the information on the pink sheet, which is where we got much of the key data, was collected when women initially made contact with WIC for services there is no set time in the pregnancy when the data was collected. Some women may have come in for services in the first trimester and others in the last month, so how she felt about her
pregnancy could have been very different at other time points in the pregnancy that we did not look at.

If a mother had only one visit in the third month post partum and never came back to WIC we could not assess whether she breast fed for at least six months or not. Excluding mothers who reported their breastfeeding practices before six months is one of the consequences of this as we only were able to look at those mothers that had been with WIC more than six months and reported on breastfeeding practices for the entire first six months.

The study was also limited in that we had no way to assess for acculturation, so where the mother was born and/or how long she had been in the United States was not addressed. Also since all of the participants are more similar (Latino, lower socioeconomic status, female etc.) This study might be limited in how much of the findings can be generalized to other populations.

With the rising prevalence of obesity in the US among the poorest children and disproportionately higher rates among certain racial and ethnic groups coupled with minimal effectiveness of current interventions the findings presented should be considered and explored further. Studying factors that might lead to early life rapid weight gain that in turn can impact obesity levels is important from a global perspective as we continue to see this epidemic increase around the world.

This study supports the existing evidence that breastfed babies slow down weight gain after 6 months (Agostoni et al, 1999). The group that is breastfed beyond 6 months is the leanest. The act of breastfeeding itself contains mechanisms that prevent a baby from over eating. Babies who were fed cow’s milk consistently over a ten minute period
consumed calories evenly throughout the ten minutes (Dewey, 2003). Breastfed babies, however, consumed most of the energy (80-90%) from their feed in the first four minutes. This suggests that breastfed babies consumed less energy (calories) per volume than babies fed on formula. Researchers reported that there were lower serum concentrations of insulin in breastfed infants than in those infants that were fed cow’s milk (Lucas et al, 1981; Lucas et al 1980).

Caffeine is known to elevate cortisol levels at rest and in response to various stressors (Haggarty et al, 2009; Lovato et al, 2006). Studies have demonstrated a causal relationship between cortisol, and obesity suggesting higher levels of stress hormone activity promotes visceral fat accumulation and insulin resistance, and not the reverse (Lane et al, 2002; Epel et al 2000). In light of the research on the importance of rapid weight gain early in life and what is known about early life adiposity patterns (mainly that more weight gain in the first 18 months increases risk of later obesity) these findings are important (Dewey et al, 1993).

The unique aspect of the study is that this is a predominantly Mexican-American cohort. This is significant because there is little such research in the literature on a cohort of predominantly Mexican-American Hispanic mothers of lower socioeconomic status in a place like Orange County California (Gill, 2009) and especially in the southwestern US population patterns suggest this as the fastest growing population sub-group and in some cases a soon to come majority population. Moreover issues of income, acculturation and obesity/health converge for this group making culturally appropriate early interventions critical in a health care system that is fast escalating.
Future research might include a prospective study on caffeine intake and effects on later life weight gain in offspring as well a study that examined levels of acculturation in this study group and how it impacts early life weight gain and behaviors that increase early life weight gain.

Another area of future research might be to conduct a clinical study collecting maternal, placental and at birth cord blood cortisol (and possibly cortisol releasing hormone CRH) levels in a similar population to see how variables (such as how the mother felt about pregnancy, pre-pregnancy depression, and self-reported stress as well as caffeine intake) correlate to cortisol (and or CRH) levels.
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APPENDIX A: "PINK SHEET" (ENGLISH VERSION)
APPENDIX B: “PINK SHEET” (SPANISH VERSION)

CUESTIONARIO DE NUTRICIÓN PARA MUJERES EMBARAZADAS

Nombre: __________________________ Edad: __________________________

Favor de circular o escribir sus respuestas a las siguientes preguntas:

1. ¿Cuándo es su siguiente cita con el doctor?
   [ ] Aumento de peso [ ] Pérdida de peso
   [ ] Lo que come [ ] Alza azúcar en la sangre [ ] Alta presión de la sangre [ ] Bajo hierro en la sangre
   [ ] Ninguno [ ] Otro

2. ¿Cuáles inquietudes tiene su doctor acerca de su embarazo?
   [ ] Vitamina prenatal [ ] Otras vitaminas/minerales [ ] Hierbas
   [ ] Pastillas con hierro [ ] Laxantes [ ] Medicamentos sin prescripción médica (Tylenol, Aspirina, etc.)
   [ ] Ninguno [ ] Otros medicamentos [ ] Remedios caseros (apunte)

3. ¿Cuáles de estos productos toma?
   [ ] Comidas [ ] Bebidas
   [ ] Leche (Descremada/Beja en grasa/Entera) [ ] Queso [ ] Yogurt [ ] Requesón [ ] Pudín/Flan
   [ ] Carnes [ ] Pollo/Pavo [ ] Pescado [ ] Hotdogs [ ] Hígados/Lentejas [ ] Crema de cacahuate [ ] Huevos [ ] Nueces
   [ ] Pan [ ] Cereales [ ] Tortillas [ ] Arroz [ ] Pasta [ ] Batidos [ ] Galletas saladas [ ] Pan Dulce
   [ ] Dulces [ ] Galletas [ ] Pasteles [ ] Donas [ ] Helados [ ] Tostadas [ ] Papas fritas
   [ ] Otros (apunte)

4. ¿Cuáles condición tiene?
   [ ] Náusea [ ] Vómito [ ] Acidez [ ] Estreñimiento [ ] Hinchazón [ ] Ninguna [ ] Otras (apunte)

5. ¿Cómo se siente acerca de su aumento de peso?
   [ ] No suficiente [ ] Está bien [ ] Demasiado

6. ¿Cuántas veces al día come?
   [ ] Comidas [ ] Bebidas
   [ ] Nunca [ ] 1-2 veces [ ] 3-4 veces [ ] 5 o más veces

7. ¿Está en alguna dieta especial?
   [ ] No [ ] Sí [ ] Si, expícle

8. ¿Qué es lo que come y toma en la mayoría de los días?
   [ ] Agua [ ] Café [ ] Té [ ] Soda regular [ ] Soda de dieta [ ] Gatorade
   [ ] Jugo [ ] Kool Aid [ ] Alcohol [ ] Cerveza [ ] Vino
   [ ] Frutas [ ] Verduras
   [ ] Leche (Descremada/Beja en grasa/Entera) [ ] Queso [ ] Yogurt [ ] Requesón [ ] Pudín/Flan
   [ ] Carnes [ ] Pollo/Pavo [ ] Pescado [ ] Hotdogs [ ] Hígados/Lentejas [ ] Crema de cacahuate [ ] Huevos [ ] Nueces
   [ ] Pan [ ] Cereales [ ] Tortillas [ ] Arroz [ ] Pasta [ ] Batidos [ ] Galletas saladas [ ] Pan Dulce
   [ ] Dulces [ ] Galletas [ ] Pasteles [ ] Donas [ ] Helados [ ] Tostadas [ ] Papas fritas
   [ ] Otros (apunte)

9. ¿Cuáles cosas, además de alimentos, se le apetecen?
   [ ] Calles [ ] Pintura descascarada [ ] Ninguna [ ] Otros (apunte)

10. ¿Cómo se siente ahora acerca de sus hábitos de comer?
    [ ] Muy bien [ ] Bien [ ] OK [ ] Mal

11. ¿Ha amamantado alguna vez?
    [ ] Sí [ ] No [ ] Si, ¿por cuánto tiempo?

12. ¿Qué tan segura estás que darás pecho a su bebé? (Círcule uno)
    [ ] (no estoy segura) [ ] (estoy seguro) 1 [ ] (estoy seguro) 2 [ ] (estoy seguro) 3 [ ] (estoy seguro) 4 [ ] (estoy seguro) 5

13. ¿Estás trabajando actualmente, o asiste a una escuela? [ ] Sí [ ] No [ ] Estoy pensando empezar

14. ¿Cuáles palabras describen su estado de ánimo de su embarazo?
    [ ] Muy contenta [ ] Está bien [ ] cansada [ ] Depresionada [ ] Inflante [ ] Tensa [ ] Enojada [ ] Otra

15. ¿Cuáles actividades físico hace en la mayoría de los días?
    [ ] Caminar [ ] Correr [ ] Andar en bicicleta [ ] Bailar [ ] Deportes [ ] Nadar [ ] Clase de ejercicio/gimnasio [ ] Cultivar un jardín [ ] Ninguna [ ] Otra (apunte)

16. ¿Alguna vez se ha quedado sin dinero o sin estampillas de comida para comprar alimentos?
    [ ] Sí [ ] No

17. ¿Qué preguntas tiene hoy sobre la nutrición y la salud?

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Date: __________________________ WIC Staff Name: __________________________

Participant WIC ID: __________________________ Height: __________________________ Weight: __________________________

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