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Ruba Cheaib Date

Effects of Breastfeeding Exclusivity and Duration on Child Cognitive Development at 5 Years of Age in Morelos, Mexico.

By

Ruba Cheaib

Master's in Public Health

Hubert Department of Global Health

Usha Ramakrishnan
Committee Chair

Effects of Breastfeeding Exclusivity and Duration on Child Cognitive Development at 5 Years of Age in Morelos, Mexico.

By

Ruba Cheaib

B.S., American University of Beirut, 2011.

Thesis Committee Chair: Usha Ramakrishnan, Ph.D.

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A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University
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2011

Effects of Breastfeeding Exclusivity and Duration on Child Cognitive Development at 5 Years of Age in Morelos, Mexico.

Author: Ruba Cheaib

Advisor: Usha Ramakrishnan, Ph.D.

Background: Several studies have attempted to assess the relationship between breastfeeding and child cognitive development. Results have been mixed and inconclusive with some studies reporting an association and others not. The many potential confounders that may interfere make it difficult to properly assess this relationship; many researchers have concluded that the possible reported benefit of breastfeeding on child development may be due to those confounding factors and not breastfeeding itself.
Objective: The objective of this analysis is to assess the effects of breastfeeding status at 3 months postpartum as well as duration of breastfeeding on child cognitive outcomes at 5 years of age using the Spanish Language version of the McCarthy Scale of Developmental Abilities in a group of women in Morelos, Mexico.
Methods: This analysis used data from a prospective mother-child cohort in Morelos, Mexico. 689 mother-child pairs were included in this analysis. Information about maternal and infant characteristics were collected and child cognition was assessed on six different scales using the Spanish Version of the McCarthy Scales of Developmental Abilities. Bivariate associations were assessed to determine potential confounders and multivariate logistic regression was used to assess the relationship between the breastfeeding status and the outcome.
Results: Mothers who predominantly breastfed or exclusively breastfed at 3 months were more likely to continue breastfeeding for a prolonged amount of time. Breastfeeding was not seen to be associated with any of the six McCarthy Scales of Children's Abilities before and after adjusting for possible confounders. Effect sizes for breastfeeding on cognitive development decreased in almost all cases after adjusting for maternal intelligence, education, infant birth weight among other variables.
Discussion: There does not appear to be an association between breastfeeding exclusivity at 3 months postpartum or breastfeeding duration and later child cognition in this study population. Possible positive benefits that have been documented in past studies may be due to other confounding factors that influence both breastfeeding and child development. More rigorous control for potential confounders and stronger study designs need to be implemented to properly assess this relationship in the future.

Effects of Breastfeeding Exclusivity and Duration on Child Cognitive Development at 5 Years of Age in Morelos, Mexico.

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Chapter 1: Literature Review.

Introduction.

Many benefits of breastfeeding have been well-established, from protecting against infant diarrheal disease to decreasing the risks of certain cancers for the mother, among many others. However, there are some issues that are still under consideration and causing much controversy about the true benefits of delaying the onset of solid foods in an infant's diet (Fewtrell, et al., 2007). One of these controversial topics is the effect breastfeeding may or may not have on later cognitive development. Until this point there have been several studies that have shown that an increased duration and exclusivity of breastfeeding does have a positive effect on child cognition (Oddy, et al., 2010) (Isaacs, et al., 2010) (Leventakou, et al., 2013) (Belfort, Rifas-Shiman, Kleinman, & Guthrie, 2012) (Y. Bernard, et al., 2012). On the other hand, there have been cases where studies have not found a significant association between breastfeeding and cognitive development (Der, Batty, & Deary, 2006). Moreover, there have been some systematic reviews that compiled current evidence on this issue and concluded that there is not substantial evidence to support the claim that breastfeeding has an effect on child cognitive development (Jain, Concato, & Leventhal, 2002) (Walfisch, Sermer, Cressman, & Koren, 2013). Most of the studies that have been conducted have been in the context of high-income countries, and few have been focused on lower-income countries. Moreover, in order to study the relationship effectively one must be able to adjust appropriately for the many factors that may influence both breastfeeding and child development as well as examine the duration of breastfeeding instead of only the exclusivity of breastfeeding at one point in time; it is these weaknesses that have been addressed by critics and reviews of studies around this topic (Drane & Logemann, 2000).

The Effects of Prenatal Omega-3 Supplementation on Child Growth and Development Study (POSGRAD) is a collaborative study between the Hubert Department of Global Health, Rollins School of Public Health at Emory University and the Instituto Nacional de Salud Publica (INSP), Cuernavaca. Mexico. The study subjects are pregnant women who were recruited between 2005-2007 from the Mexican Institute of Social Security (IMSS) in Cuernavaca, Mexico to participate in a randomized controlled trial evaluating the effects of prenatal docosahexanoic acid (DHA) supplements on infant growth and development. Data have been collected prospectively from ~900 mother-child pairs from mid pregnancy through 5 years of age and include detailed information on socio demographic characteristics, birth outcomes, infant feeding practices which include details of breastfeeding exclusivity and duration and cognitive development at age 5y.. This allows for the opportunity to study the possible association of breastfeeding on child cognitive development in a lower income, Latin American setting.

Possible Mechanisms Linking Breastfeeding and Child Cognition.

Two main pathways have been hypothesized as the main possible mechanisms by which breastfeeding could affect child development. One such pathway is through the hormones prolactin and oxytocin whose secretion has been shown to be increased by breastfeeding; there has been some evidence to show that the secretion of these hormones may enhance mothering behaviors, which in turn may positively affect the child's development (Gordon, Zagoory-Sharon, Leckman, & Feldman, 2010). The release of oxytocin has also been shown to be increased, not only by the act of breastfeeding, but by skin-to skin contact of the mother and child (Feldmen & Eidelman, 2003). This hormonal system has been shown to decrease depression and stress levels of mothers thus positively affecting maternal moods and behaviors (Feldmen & Eidelman, 2003). A study that sought to examine the effects that oxytocin levels in

mothers and fathers could have on parenting behaviors found that maternal oxytocin levels were in fact associated with certain affectionate behaviors towards her infant such as stimulating vocalizations, expressing positive moods, more skin contact and touching with the infant (Gordon, Zagoory-Sharon, Leckman, & Feldman, 2010).

Another mechanism that has been hypothesized in this relationship is related to the content of breast milk, which is high in the two long-chain polyunsaturated fatty acids, docosahexaenoic acid (DHA) and arachidonic acid (ARA). These fatty acids can buildup in the infant's brain during the first few months of life and could positively influence development of the brain (Feldmen & Eidelman, 2003). In fact, several studies have shown that fatty acid supplementation during the first few months of life may have beneficial effects on infant and child development (Ryann, et al., 2010) (Guesnet & Alessandri, 2010). A study was able to find an association between breast milk and brain development in boys which provides some empirical evidence behind the findings mentioned (Isaacs, et al., 2010). However, the extent to which DHA and ARA content in breast milk effects child development is still not well-established (Carlson, 2009).

Other possible mechanisms of this relationship that have been proposed have to do with the increased risk of malnutrition, infection and diarrhea associated with improper infant feeding practices, which could all potentially hinder proper development (Black, et al., 2008) (Grantham-McGregor, Fernald, & Sethuraman, 1999).

Potential Consequences of Malnutrition and Delayed Cognitive Development.

There are numerous factors that can potentially influence a child's development, including socio-demographic characteristics of the family, environmental influences, nutritional status of both mother and baby, genetic factors and much more. Some of these factors may be hard to influence, such as genetic predispositions, however by encouraging certain behaviors in the mother and infant that have been documented to possibly affect child development, it is possible to see an improvement in child functioning (Charlesworth, 2010).

Nutrition can play a large role in child development, especially during the first 2 years of life. During this period, the infant grows at a rate that is higher than any other point in the lifecycle, this is especially true during the period from 3 to 6 months of age; meaning that infants in this period have very high nutritional requirements that need to be met (Martorell, 1999). There has been evidence to suggest that if a child is malnourished throughout infancy and childhood the consequences spillover to adolescence and adulthood where malnourished individuals can experience a number of things from delayed motor development, decreased cognitive development and intelligence, behavioral problems and decreased educational achievement (Martorell, 1999).

Growth delays in infancy and childhood could in turn have a potential effect on later cognition and development, and it has been shown that it is easier to compensate for poor cognitive development at earlier stages than it is when the child is older, for this reason assessing such relationships are necessary to be able to intervene at the opportune moment in an infant's life (Cuhna, Hechman, & Schennach, 2010).

In 2010 globally, 27% of children under 5 were stunted and 16% were underweight, with the problem persisting in low to middle income countries including Latin America (Lutter, et al., 2011). Stunting, underweight and other nutritional deficiencies puts children at risk for a number of things including diarrheal disease, increased susceptibility to infection, delayed physical and cognitive development, among other things (Black, et al., 2008). Progress towards reaching the Millennium Development Goals related to decreasing global under-nutrition has been slow, and this has been partly attributed to low breastfeeding rates worldwide and poor infant feeding practices (Lutter, et al., 2011). If there were to be an association between breastfeeding and cognitive development this would support low cost interventions around this area to promote both infant nutrition and cognitive development.

Current Literature on the Topic.

As mentioned above, studies examining the relationship between breastfeeding and later child cognition have been mixed and varied.

A meta-analysis conducted in 1999 aggregated the findings of 20 studies that examined this relationship to conclude if breastfeeding was associated with cognitive development or if the effects were due to other confounding factors. They found that breastfed infants scored 3.16 points higher in cognitive function when compared to formula-fed infants after adjusting for potential confounders, with low birth weight infants showing larger differences than normal weight infants (Anderson, Johnstone, & T., 1999). Another systematic review carried out by Walfisch et al. in 2013 included 84 studies and sought to examine the effect of confounders on the relationships being assessed. Of the 85 studies included, 28 found positive results indicating that breastfeeding does increase child cognitive development while 21 found no effects; 18 of the

studies reported that the effects seen diminished completely after adjusting for potential confounders and 17 studies reported a decrease in the magnitude of the results after adjusting (Walfisch, Sermer, Cressman, & Koren, 2013). The review also reported that more drastic decreases in effect size were observed when the amount of confounders taken in to account increased, showing and concluding that a large portion of the seen effect of breastfeeding on cognitive development may be due to other confounding variables (Walfisch, Sermer, Cressman, & Koren, 2013).

A prospective study set in Australia concluded that infants that were breastfed for more than 4 months scored higher on motor, adaptability and communication skills than infants that were breastfed for less than 4 months after adjusting for maternal socio-demographic characteristics and stress factors (Oddy, et al., 2013). While Oddy et al. assessed the relationship using a dichotomous variable to categorize breastfeeding duration; other studies used more complex categories to capture a more detailed account of breastfeeding duration or used a continuous variable to assess for the existence of a dose-response relationship; possibly adding to the strength of their study. One such study was set in France and reported a positive linear relationship between breastfeeding duration and child cognitive development at 2 and 3 years of age (Bernard, et al., 2013). They found that with each 1 month increase in breastfeeding duration, cognitive points increased by 0.75-1 points; while this is a small increase, it was found to be statistically significant after adjusting for possible confounders (Bernard, et al., 2013). Another Study set in the United States, also reported finding a significant dose-response relationship and concluded a 0.21 point increase with each additional month of breastfeeding up to 12 months in a Peabody Picture Vocabulary Test at 3 years of age and a 0.35 and 0.29 point increase in verbal and non-verbal intelligence tests respectively per month breastfed after

adjusting for socio-demographic characteristics, maternal intelligence and home environment (Belfort, Rifas-Shiman, Kleinman, & Guthrie, 2012). A similar study conducted in Greece also found a significant dose-response relationship between increased number of month's breastfed and cognitive development at 18 months of age in all tests except fine motor skills using the Bayley Scales of Infant Deveopment (Leventakou, et al., 2013).

While most studies of this kind have been conducted in higher income setting, there have been several studies around this subject in the context of lower-income counties, and a few in Latin America specifically (Walfisch, Sermer, Cressman, & Koren, 2013). A prospective cohort study conducted in Chile in 2006 followed 784 Chilean children and measured motor and mental development on children at 5.5 years of age in relation to breastfeeding (Clark, et al., 2006). The results obtained from this study were similar to the ones discussed above; children breastfeed for longer than 2 months scored higher on cognitive testing than those breastfed for less than 2 months (Clark, et al., 2006). Interestingly however, children who were breastfed for longer than 8 months scored lower than those breastfed from 2 to 8 months. The effect sizes of these relationships decreased drastically when the model adjusted for gender, birth weight, age at examination, maternal and paternal intelligence, home environment, socio-economic status and others, but they remained statistically significant (Clark, et al., 2006). Another study conducted in Chile in 1999 found that breastfeeding for over 30 days was associated with higher text scores at 12 months of age (De Andraca, Salas, Cayazzo, & Icaza, 1999); however, these results were not adjusted for any confounders and the results reported were most likely due to socio-economic differences (Walfisch, Sermer, Cressman, & Koren, 2013). Eickmann et al. carried out a prospective cohort of this kind among a lower-socio-economic population of mother and child pairs in Brazil and found similar results where infants that were exclusively breastfed for 1

months scored 3 points higher on cognitive scoring at 12 months when compared to infants that were not exclusively breastfed for 1 month (Eickmann, de Lira, & al., 2007). However the authors did state that while these results were statistically significant it is debatable whether a 3 point increase could have a functional impact on the child or if this difference may have a relatively small impact at the individual level (Eickmann, de Lira, & al., 2007). Another study carried out in Brazil by Morris et al. measured breastfeeding in a different way than the studies previously mentioned; cognitive development was measured among around 100 normal birth weight children born in Brazil and the authors sought to see if this was associated with the number of breastfeeds an infant receives daily (Morris, Grantham-McGregor, Lira, Assunc, & Ashworth, 1999). The results found in this study mimic the ideas mentioned above, a small association of a quarter point increase was found with every extra breastfeed per day for up to 12 months; after 12 months however, this was no longer apparent (Morris, Grantham-McGregor, Lira, Assunc, & Ashworth, 1999).

In their systematic review, Walficsh et al. graded most of the studies conducted in lower-income settings a letter grade of B or C based on study design, sample size, adjustment of confounders, summary of results among other criteria related to methodology (Walfisch, Sermer, Cressman, & Koren, 2013). They also found that studies that were conducted in low and middle income countries were most likely to find no association between the exposure and outcome when compared to studies set in higher income countries; this may be because breastfeeding and non-breastfeeding mothers in lower income countries have been found to be very different within each other in many characteristics while in higher income countries breastfeeding mothers tend to be more homogenous (Walfisch, Sermer, Cressman, & Koren, 2013).

Randomized control trials are the gold standard of study designs when it comes to assessing causal relationships, however due to the string evidence supporting breastfeeding and its benefits it would be ethical in this case. The closed designs to the RCT in these types of studies are sibling pair studies and RCT's randomizing breastfeeding promotion interventions. However, even studies of these kinds have come to contradicting conclusions. An RCT conducted in Belarus randomized mother in two groups where one group received a breastfeeding intervention to promote breastfeeding modeled after the Baby Friendly Hospital Initiative, developed by the World Health Organization and UNICEF and the other group received the standard of care that was in effect at that time (Kramer, et al., 2008). Bothe groups were similar on measured characteristics that included maternal age, education, pregnancy history and socio demographic variable; they were also matched on birth weight, gestational age, type of delivery and other birth outcomes (Kramer, et al., 2008). Data was collected on breastfeeding practices and child cognition was measured at 6.5 years of age. It was found that that the intervention group had a much larger proportion exclusively breastfeeding at 3 months, and increased breastfeeding at all ages u to 12 months, compared to the control group (Kramer, et al., 2008). Moreover it was found that the intervention group scored higher on verbal, performance and overall IQ testing after adjustment, when compared to children in the control group with differences of about 7, 3 and 6 IQ points respectively further supporting the notion that breastfeeding may increase cognitive development and intelligence in childhood (Kramer, et al., 2008).

A prospective study carried out in the U.S. also sought to examine this relationship. What makes the design on this particular study strong, in the subsample of sibling pairs that was examined separately. Siblings are similar are almost all characteristics, especially those related

to maternal and paternal intelligence and education, home environment and family socio demographic and economic characteristics. Therefore comparing one sibling that was breastfed to another that was not, is the closest one can get to an RCT is this context (Der, Batty, & Deary, 2006). Among all mother-child pairs, a benefit of breastfeeding was noticed on child cognitive development, but these effects disappeared after adjusting for confounders. Among the sibling pairs, no difference in development was noticed supporting the findings that breastfeeding does not have a seen effect on child cognition (Der, Batty, & Deary, 2006). This further justifies the reasoning to adjust for as many confounders as possible to properly assess the relationship of breastfeeding on cognitive development especially in specific settings where is it has been shown that breastfeeding mothers differ in many characteristics than those that do not breastfeed

Current Breastfeeding Practices and Potential Influencers.

Before 2001, the World Health Organization (WHO) recommended that children be breastfed exclusively for up to 4 to 6 months of age (Organization, Infant Feeding Recommendation., 1995); In May of 2001, following a review analyzing the benefits of breastfeeding for a longer duration, the WHO changed their recommendations to encourage exclusive breastfeeding for up to 6 months (The Optimal Duration of Exclusive Breastfeeding: Report of an Expert Consultation, 2001)

Potential confounders in this relationship include Socio-economic and demographic characteristics, maternal education and intelligence, infant characteristics at birth among many others; and as mentioned previously many investigators claim that the association that has been

seen between breastfeeding and the outcome are due to these factors and not to feeding practices (Walfisch, Sermer, Cressman, & Koren, 2013).

Past literature has shown that many factors associated with urbanization, social and economic development have the potential of negatively influencing breastfeeding (Chaparro & Lutter, 2010). For this reason it is important to be aware of breastfeeding trends and how they may be changing in countries that may be undergoing social and economic changes. Chaparro and Lutter studied the trends of breastfeeding practices in several counties in Latin America from the years 1986 to 2005 to identify changing practices in breastfeeding among this population as well as pinpoint certain characteristics that influence different breastfeeding behaviors. Maternal education was found to be the strongest predictor of breastfeeding in their survey, with higher maternal education being associated with lower rates of breastfeeding (Chaparro & Lutter, 2010). Maternal age and parity were positively associated with breastfeeding: children born to older mothers were more likely to be breastfed and greater parity increased the probability of an infant being breastfed (Chaparro & Lutter, 2010).

Gonzalez de Cossio et al compared data from the 1999 to 2006 National Health and Nutrition Surveys of Mexico identify trends in infant feeding practices in the country. In general it was found that breastfeeding rates remained stable in the population as a whole but decreased mostly in the poorer population (Gonzalez, et al., 2012). In 2006, the median duration of breastfeeding was 10.4 months and 22.3% of infants under 6 months were exclusively breastfed, with higher rates of exclusive breastfeeding for up to 6 months in mothers living in the southern region of the country, mothers living in rural areas, those of lower socio-economic status and in unemployed mothers (Gonzalez, et al., 2012). From 1999 to 2006, the percentage of infants who were predominantly breastfed for up to 6 months decreased from about 50% to 38% among the

low socio-economic group (Gonzalez, et al., 2012). These declines are of concern especially since the benefits associated with breastfeeding have been shown to be greater in more vulnerable populations, usually those that are less educated, have lower incomes and are of lower social status (Gonzalez, et al., 2012).

Being able to properly assess the relationship between breastfeeding and later child cognition could have large implications in public health and further drive the need to support interventions to promote proper infant feeding practices, especially in low and middle income countries where breastfeeding rates may already be low and malnutrition high. The aim of this analysis to assess the relationship between breastfeeding status at 3 months of age and duration of any breastfeeding on child cognitive performance at 5 years of age using the McCarthy Scale of Children's Abilities among study participants in Morelos, Mexico. It is hypothesized that children who were breastfed at 3 months of age will show more advanced cognitive development at 5 years of age on six different scales (verbal, motor, memory, perceptual-performance, quantitative and general cognition) compared to children who are not breastfed and that longer durations of breastfeeding will be associated with higher scores on these test scales.

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Contribution of Student

For the manuscript titled, *The Effects of Breastfeeding Exclusivity and Duration on Child Cognitive Development at 5 Years of Age in Morelos, Mexico,* I performed a review of the literature, served as the principle writer, and completed the data analysis, and created tables and figures for the manuscript.

Chapter 2: Manuscript

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Author: Ruba Cheaib

Advisor: Usha Ramakrishnan, Ph.D.

Background: Several studies have attempted to assess the relationship between breastfeeding and child cognitive development. Results have been mixed and inconclusive with some studies reporting an association and others not. The many potential confounders that may interfere make it difficult to properly assess this relationship; many researchers have concluded that the possible reported benefit of breastfeeding on child development may be due to those confounding factors and not breastfeeding itself.
Objective: The objective of this analysis is to assess the effects of breastfeeding status at 3 months postpartum as well as duration of breastfeeding on child cognitive outcomes at 5 years of age using the Spanish Language version of the McCarthy Scale of Developmental Abilities in a group of women in Morelos, Mexico.
Methods: This analysis used data from a prospective mother-child cohort in Morelos, Mexico. 689 mother-child pairs were included in this analysis. Information about maternal and infant characteristics were collected and child cognition was assessed on six different scales using the Spanish Version of the McCarthy Scales of Developmental Abilities. Bivariate associations were assessed to determine potential confounders and multivariate logistic regression was used to assess the relationship between the breastfeeding status and the outcome.
Results: Mothers who predominantly breastfed or exclusively breastfed at 3 months were more likely to continue breastfeeding for a prolonged amount of time. Breastfeeding was not seen to be associated with any of the six McCarthy Scales of Children's Abilities before and after adjusting for possible confounders. Effect sizes for breastfeeding on cognitive development decreased in almost all cases after adjusting for maternal intelligence, education, infant birth weight among other variables.
Discussion: There does not appear to be an association between breastfeeding exclusivity at 3 months postpartum or breastfeeding duration and later child cognition in this study population. Possible positive benefits that have been documented in past studies may be due to other confounding factors that influence both breastfeeding and child development. More rigorous control for potential confounders and stronger study designs need to be implemented to properly assess this relationship in the future.

Introduction

The World Health Organization recommends exclusive breastfeeding for up to 6 months and continued appropriate complimentary feeding for up to 2 years of age due to the many known benefits of breastfeeding for both the mother and baby (The Optimal Duration of Exclusive Breastfeeding: Report of an Expert Consultation, 2001). Immunological and antibacterial compounds found in breast milk have been shown to decrease the risk of different forms of infection for the infant; breast milk has also been show to possibly prevent chronic disease development in the infant's life, decrease the risk of postmenopausal breast cancer and ovarian cancer in the mother, among many other benefits (Allen & Hector, 2005). Certain components and advantages of breastfeeding have also been linked to possible improvements in child cognition and intelligence (Allen & Hector, 2005). Breast milk is concentrated in long-chain polyunsaturated fatty acids, docosahexaenoic acid (DHA) and arachidonic acid (ARA) which have been linked in improved brain development and in turn more advanced cognition and intelligence (Feldmen & Eidelman, 2003). The act of breastfeeding has also be associated with increased secretion of the hormones prolactin and oxytocin in the mother; these hormones have been shown to enhance certain mothering behaviors by possibly decreasing maternal depression and stress levels, this can in turn have a positive effect on the development of the infant (Gordon, Zagoory-Sharon, Leckman, & Feldman, 2010). Moreover, breastfeeding decreases infant risk of malnutrition, infection and diarrhea, which could all potentially hinder proper development (Gordon, Zagoory-Sharon, Leckman, & Feldman, 2010) (Black, et al., 2008). However, the extent to which breastfeeding does influence later cognitive development is still unclear.

Many researchers have attempted to study this relationship but results have been mixed and inconclusive. Until this point there have been several studies that have shown that proper infant feedings practices related to appropriate introduction of complimentary foods and prolonged duration of breastfeeding has a positive effect on child cognition (Oddy, et al., 2010) (Isaacs, et al., 2010) (Leventakou, et al., 2013) (Belfort, Rifas-Shiman, Kleinman, & Guthrie, 2012) (Y. Bernard, et al., 2012). On the other hand, there have been cases where studies have not found a significant association between breastfeeding and cognitive development (Der, Batty, & Deary, 2006).

A meta-analysis conducted in 1999 aggregated the findings of 20 studies that examined this relationship to conclude if breastfeeding was associated with cognitive development or if the effects were due to other confounding factors. They found that breastfed infants scored 3.16 points higher in cognitive function when compared to formula-fed infants after adjusting for potential confounders, with low birth weight infants showing larger differences than normal weight infants (Anderson, Johnstone, & T., 1999). Another systematic review carried out by Walfisch et al. in 2013 included 84 studies and sought to examine the effect of confounders on the relationships being assessed. Of the 85 studies included, 28 found positive results indicating the breastfeeding does increase child cognitive development while 21 found no effects; 18 of the studies reported not finding any effect after adjusting for potential confounders and 17 studies reported a decrease in the magnitude of the results after adjusting (Walfisch, Sermer, Cressman, & Koren, 2013). Most of these studies have been conducted in high-income countries and settings with a lack of focus of this research in middle and low income countries.

A prospective cohort study conducted in Chile in 2006 followed 784 Chilean children and measured motor and mental development on children at 5.5 years of age in relation to

breastfeeding (Clark, et al., 2006). It was found that children that were breastfed for longer than 2 months scored higher on cognitive testing than those breastfed for less than 2 months (Clark, et al., 2006). Interestingly however, they found that children who were breastfed for longer than 8 months scored lower than those breastfed from 2 to 8 months. The effect sizes of these relationships decreased drastically when other variables were taken in to consideration and adjusted for, but they remained statistically significant (Clark, et al., 2006). Eickmann et al. carried out a prospective cohort of this kind among a lower-socio-economic population of mother and child pairs in Brazil and found similar results where infants that were exclusively breastfed for 1 month scored 3 points higher on cognitive scoring at 12 months when compared to infants that were not exclusively breastfed for 1 month (Eickmann, de Lira, & al., 2007). However the authors did state that while these results were statistically significant it is debatable whether a 3 point increase could have a functional impact on the child or if this difference may have a relatively small impact at the individual level (Eickmann, de Lira, & al., 2007).

Being able to properly assess the relationship between breastfeeding and later child cognition could have large implications in public health and further drive the need to support interventions to promote proper infant feeding practices, especially in low and middle income countries where breastfeeding rates may already be low and malnutrition high. The aim of this analysis to assess the relationship between breastfeeding status at 3 months of age and duration of any breastfeeding on child cognitive performance at 5 years of age using the Spanish Language Version of the McCarthy Scale of Children's Abilities among study participants in Morelos, Mexico. It is hypothesized that children who were breastfed at 3 months of age will show more advanced cognitive development at 5 years of age on six different scales (verbal, motor, memory, perceptual-performance, quantitative and general cognition) compared to

children who are not breastfed and that longer durations of breastfeeding will be associated with higher scores on these test scales.

Methods

Sample Population and Data

The data used for this analysis were collected from a randomized clinical trial looking at the effects of DHA supplementation on pregnancy outcomes and child development under the patronage of the Department of Health, Rollins School of Public Health at Emory University and the Instituto Nacional de Salud Publica (INSP), Cuernavaca, Mexico. During the period from February 2005 to February 2007, women were recruited at the IMSS General Hospital as well as three other associated health clinics during their regular prenatal visits and randomized in to one of two groups either receiving DHA supplementation or a placebo. Inclusion criteria included women 18 to 35 years of age, 18-22 weeks pregnant, having intents to predominantly breastfeed for up to 3 months and being a resident of Cuernavaca with the intention of delivering at the IMSS hospital and remain in the area for at least 2 years. Women were excluded from the study if they were experiencing a high risk pregnancy, had any lipid metabolism and/or absorption disorders, were taking any long-term medication for a specific illness and/or were taking fish oil supplements during their pregnancy.

Breastfeeding

Feeding practices and dietary intakes were assessed using structured 24 hour recalls that were administered by trained nurses during the mothers' visits to the hospital. Based on the infants' stated diets by their mother, they were places to in one of four possible categories:

exclusive breastfed, predominately breastfed, mixed, or not breastfed. Exclusive breastfeeding was defined in accordance in the WHO definition that states that the infant receives no solids or liquids other than breast milk. Predominant breastfeeding was defined as receiving breast milk plus additional fluids such as water or juices and less than 2 fluid ounces of any commercial infant formula per day. Mixed feeding was defined as the infant receiving more than the previously stated amount of infant formula and/or any solids in addition to breast milk; and no breastfeeding was defined as the infant receiving no breast milk as part of his/her diet. For the purposes of this analysis, two breastfeeding variables were used: 1) breastfeeding status at 3 months, using the categories above, to measure the effect of breastfeeding exclusivity on child cognitive development and 2) breastfeeding duration, a categorical variable indicating if an infant received any breast milk for less than month, 1 to 3 months, 3 to 6 months, 6 to 12 months and above 12 months to measure the possible effect of breastfeeding duration on child cognitive development.

Cognitive Assessment

Child cognitive evaluation was assessed at 5 years of age using the Spanish language version of the McCarthy Scales of Children's Abilities (MSCA). The MSCA is a comprehensive test that uses game-like tests to measure cognitive and motor function for children ages 2.5 to 8.5 years and is suitable for both genders as well as different racial, ethnic and socio economic groups. The MSCA measures development on six different scales: verbal, perceptual-performance, motor, quantitative, memory and general cognition. The MSCA Spanish language version has been used successfully in other studies and its validity has been shown to be good based on significant correlations with other achievement tests such as the Peabody Individual Achievement Test. For this analysis, scaled grades of each McCarthy test were used; raw scores

of each of the tests are converted into scale indices using the Scale Index Equivalents of Composite Raw Scores Tables and are normalized and converted to a scaled score distribution with a fixed mean and standard deviation . This is standardized for the child's age at the time of examination.

Other variables of interest

A variety of socio-demographic variables were considered as possible confounders in this analysis. Data on these variables were collected at baseline using a survey tool that has been validated for use in pregnant women from low to medium socio-economic backgrounds containing 55 questions administered by a trained nurse. These included details regarding age, marital status, education (number of years of school completed and whether or not she had completed high school), reproductive history (number of previous births), type of current delivery and occupation. Infant characteristics were also collected prospectively and included birth weight and length, sex and gestational age. Maternal intelligence was measured using Raven's Progressive Matrices, a non-verbal test of intellectual functioning which requires the participant to figure out complimentary abstract patterns.

Statistical Analysis

Two subsamples of the overall data were used for this analysis one that included mother-infant pairs that had complete data on breastfeeding status at three months as well as complete McCarthy data at 5 years of age and the other that included mother-infant pairs that had complete data on breastfeeding duration and McCarthy data at 5 years of age. Twins were excluded from the sample. Descriptive statistics were obtained for the main predictor and outcome variables as well as selected maternal baseline characteristics and infant characteristics at birth that could

serve as possible confounders. T-tests and Chi-square tests were conducted to assess whether these characteristics differed between those mother-infant pairs that were included in the analysis and those that were excluded due to missing data. Bivariate associations were assessed between the main predictor and outcome variables and the selected characteristics. ANOVA and Chi square tests of association assessed if these characteristics were associated with breastfeeding status at 3 months and/or breastfeeding duration for continuous and categorical variables respectively. Similarly, ANOVA tests and correlation statistics assessed whether the characteristics were associated with the 6 different McCarthy scales of development. Multivariable linear regression models were formulated to assess the association between breastfeeding status at 3 months and breastfeeding duration on child cognition before and after adjusting for possible confounders. Potential confounders related to both the outcome variable and the main exposure variable were included in the model at a significance level of $p<0.1$. The treatment group the mother was assigned to during the trial and the child's age at time of examination were considered as confounders from the start and were thus included in all models. Also, the effect of each confounder on the outcome was assessed by adding each variable one by one in to the model. Sensitivity analyses was conducted in which women who may have breastfed slightly over 3 months but were still classified as not breastfeeding at 3 months were excluded. All hypotheses were conducted assuming a significance level of 0.05; all data were analyzed using SAS 9.3 statistical software.

The Emory University Institutional Review Board as well as the biosafety and ethics committee of the Mexican Institute of Public Health (Instituto Nacional de Salud Publica) approved this study.

Results

Study population characteristics of mothers that had complete data on breastfeeding status at 3 months and complete McCarthy data at 5 years are shown in Table 1. The mean age of participating mothers was about 26 years old and this was the first birth for about 37% of mothers.. Just under 10% of the study sample infants were pre-tern and about the children in the mother-child pairs were male. Comparison of the study sample to those who were not included in this analysis showed no differences for several baseline maternal and infant characteristics except socioeconomic status (you should include this table at least in the appendix). Participants excluded from the study sample tended to be of a higher socioeconomic status than those included.

Figure 1 presents breastfeeding practices in terms of breastfeeding status at 3 months and duration of breastfeeding duration. At three months, 12.1% of women were exclusively breastfeeding (n=83), 12.3% of mothers were predominately breastfeeding (n=85), 57.8% of infants were receiving mixed feedings (n=398) while 17.85% were not breastfeeding at all (n=123). 3.04% of mothers breastfed for less than 1 month (n=23), 24.9% breastfed from 1 to just under 3 months (n=188) and 10.5%, 24.6% and 37.0% breastfed for 3 to just under 6 months, 6 to just under 12 months and above 12 months respectively (n=70, n=186, n=280, respectively). Of those mothers who were exclusively breastfeeding at 3 months, all breastfed for longer than 1 month and 66.3% of them breastfed for over 1 year, the highest proportion in comparison the other groups. Similarly in the group of mothers that were predominantly breastfeeding at 3 months, all breastfed for over two months and 55.3% of them breastfed for over 1 year. For those mothers that were mixed feeding at 3 months, the proportion on women that breastfed for over 1 year dropped to 38.9% while a larger proportion of women breastfed

between 1 and 12 months (61.1%). In this group, there were also no women that breastfed for less than 1 month. For those that were not breastfeeding at 3 months, 19.2% breastfed for less than one month, and a larger proportion of 58.3% breastfed for longer than 1 month but less than 3 months.

Population characteristics by breastfeeding status at 3 months are shown in Table 2. In this group, mothers for whom this was the first birth were less likely to exclusively or predominantly breastfeed compared to those who practiced mixed feeding or did not breastfeed. Mothers who completed high school were less likely to predominantly breastfeed. Population characteristics by breastfeeding duration are shown in Table 3. Mothers for whom this was their first birth were more likely to stop breastfeeding after 3 months. Those mothers that completed high school were more likely to continue breastfeeding for up to 12 months, after which the proportion of breastfeeding mothers decreased. As length of the baby at birth decreased, mothers became less likely to continue breastfeeding for a longer time. And those mothers that gave birth the premature infants (<37 weeks) were less likely to continue breastfeeding past 3 months. Table 3 shows the associations between different maternal and infant characters and the six McCarthy scale scores. First births and socio-economic status had negative relationships with overall McCarthy test scoring with children who were the first child and children of mothers with a lower socio-economic status scored lower on overall cognition. Completion of high school, mothers' age and birth weight had positive linear associations with overall cognition. Girls scored higher on overall cognition than boys.

Table 4 shows the crude effects of breastfeeding (type of breastfeeding at 3 months and breastfeeding duration) on the six McCarthy scales of cognitive development at 5 years of age.

Both breastfeeding status at 3 months and breastfeeding duration were not seen to be associated with any of the cognitive outcomes examined.

Table 5 presents the adjusted coefficients of the multivariate linear regression analysis between breastfeeding (exclusivity at 3 months and duration) and McCarthy scale scores at 5 years of age. Breastfeeding status at 3 months and breastfeeding duration both remained unassociated with all six McCarthy scales of development. Parameter estimates for the effects of breastfeeding decreased in almost all cases from the crude model to the adjusted model (results not shown). To assess the effect of each possible confounder on the association between breastfeeding and cognitive development, each variable was added separately in the models and the change in the parameter estimate was examined. The largest confounder effect on breastfeeding status at 3 months was found to be whether this was the mothers first birth, causing a decrease of 45.8% in the parameter estimate; followed by maternal education (completion of high school) causing a decrease of 26.6%. The largest confounder on assessing the relationship of breastfeeding status on the outcome was found to be infant birth weight, causing a 53.9% decrease in the parameter estimate, followed by first birth (46.9% decrease).

Discussion

The main finding of this analysis is the lack of a statistically significant association between breastfeeding status at 3 months of age and breastfeeding duration on child cognitive development at 5 years of age as assessed using the McCarthy Scale of Children's Abilities cognitive assessment test. The large sample size (n=689) allows us to be confident about the findings that have resulted from this analysis. This is one of the few studies to assess this relationship in this region and context and specifically in Mexico. These findings are consistent

with several findings of studies in this field that have not found there to be an association with breastfeeding and child cognitive outcomes (Der, Batty, & Deary, 2006) (Walfisch, Sermer, Cressman, & Koren, 2013).

It was shown that mothers that were exclusively breastfeeding at three months were more likely to continue breastfeeding for a longer amount of time, as one would expect. Implying that by encouraging exclusive breastfeeding among mothers, duration of breastfeeding could potentially be positively affected. Variables that were seen to influence breastfeeding were also what one would expect, with education being negatively associated with breastfeeding which is characteristic of low and middle income countries (Gonzalez, et al., 2012). As education, specifically completion of high school was also seen as one of the largest confounders in the relationship being assessed, targeting interventions to promote breastfeeding at mothers with higher education status may be beneficial.

Moreover, the noticed decline in parameter estimates of breastfeeding on cognitive development after adjusting for potential characteristics is consistent with many studies in this field that saw decreased or complete disappearance of the effect size of breastfeeding in adjusted models, compared to the effects sizes noted in crude models (Walfisch, Sermer, Cressman, & Koren, 2013). These results can be used to argue that significant results seen in previous studies may be due to persistent confounding for variables not taken in to account. This supports the need to collect detailed and rigorous data on the study population to properly assess this relationship.

The strengths of this study include the study design of a population based prospective nature allowing for the possibility of assessing relationship and causal links. Of the participating

mothers that gave live births, 70% were followed up with complete information up to 5 years of age. This resulted in a large sample size of 689 mother-child pairs completing the final assessment at 5 years of age. Having collected a large amount of information on maternal demographic and socio-economic characteristics as well as infant characteristics at birth allowed for the consideration of other possible confounders to be taken in to account; this has been a weakness in many studies before that were unable to adjust for potential confounders and thus unable to conclude with confidence that the documented effect was indeed due to breastfeeding (Walfisch, Sermer, Cressman, & Koren, 2013). Another issue that is dominant as a draw back in previous studies is the way in which the breastfeeding data was collected and defined. Instead of looking solely at 'ever breastfed' and 'never breastfed' infants, this data allowed for the analysis of different intensities of breastfeeding at a certain time points as well as the duration of any breastfeeding, giving two separate but related variables with which to examine the relationship (Walfisch, Sermer, Cressman, & Koren, 2013). Moreover, participants were unaware of this research question when the breastfeeding data was being collected, making misclassification unlikely. In addition to that, the McCarthy Scale for Children's Abilities has been previously examined for its strength and it was found that this test has good predictive abilities when compared to other tests used to estimate child cognition (Naglieri & P.L., 1982). Also, the Spanish language version of the McCarthy Scales has been used successfully in Mexico in the past. (Schnaas, et al., 2000).

There are limitations to this study that must be recognized. Firstly, information on the exposure variables requires some amount of recall from the participants which may result in some recall bias. In addition, data on breastfeeding status at 3 months may not have been collected at exactly 3 months of age therefore there may have been some mothers who were not

breastfeeding at 3 months but were classified as such; this can be seen as some participants having mismatched data when comparing breastfeeding status at 3 months and breastfeeding duration. However, it is unlikely that this had an effect on the results of the analysis as it was seen that after removing this group for sensitivity analysis, there was no major change in results and conclusions. There is also room for residual confounding as there is still a possibility of other confounders that were not taken in to consideration, such as paternal education and intelligence. Another possible limitation to the data is that cognitive development was only measured at one time point. It may have been useful to test child cognitive development at different time points in order to assess this relationship more intensely.

The history of inconsistencies and contradicting findings of results in studies that have tried to assess the relationship between breastfeeding and cognitive development indicate the need for further research on this topic. It would be beneficial to collect detailed information on breastfeeding status at several time points as well as conduct cognitive testing at several ages during early childhood to get a clear and detailed picture of the effects of types of breastfeeding and duration on child development throughout the first few years of life. It would also be beneficial to gather more information on other possible confounders of this relationship, for example, it has been shown that certain paternal characteristics may influence a child's development therefore having data on those characteristics will provide extra strength when studying this relationship (Leventakou, et al., 2013).

In conclusion, this analysis suggests that breastfeeding does not have an effect on child cognitive development and that associations seen in the past may be due to other factors, namely maternal education, intelligence and socioeconomic status. When grouped with other studies and

systematic reviews on this topic, it is unlikely that breastfeeding has a direct effect on child cognitive development.

Tables and Figures

Table 1: Selected Maternal Characteristics at Randomization and Infant Characteristics at Birth (n=689).

	Mean (SD) or %
Age	26.29 (4.73)
BMI	26.16 (4.36)
First birth , %	36.72
Single, %	9.14
BMI >25 kg/m, %	56.6
RAVEN score	41.0 (8.96)
Completed High School[1], %	58.58
DHA group	50.51
Socio-Economic Status, %	
low	30.48
medium	35.85
High	33.67
Birth Weight (kg)	3215.13 (459.38)
Birth Length	50.344 (2.49)
Gestational Age	39.05 (1.80)
Low birth weight, %	5.22
Sex, Male, %	52.69
Premature (37 weeks), %	9.75

[1] 1 Missing Observation

Figure 1: Breastfeeding Trends in Participating Mothers: Breastfeeding Status at 3 months by breastfeeding duration

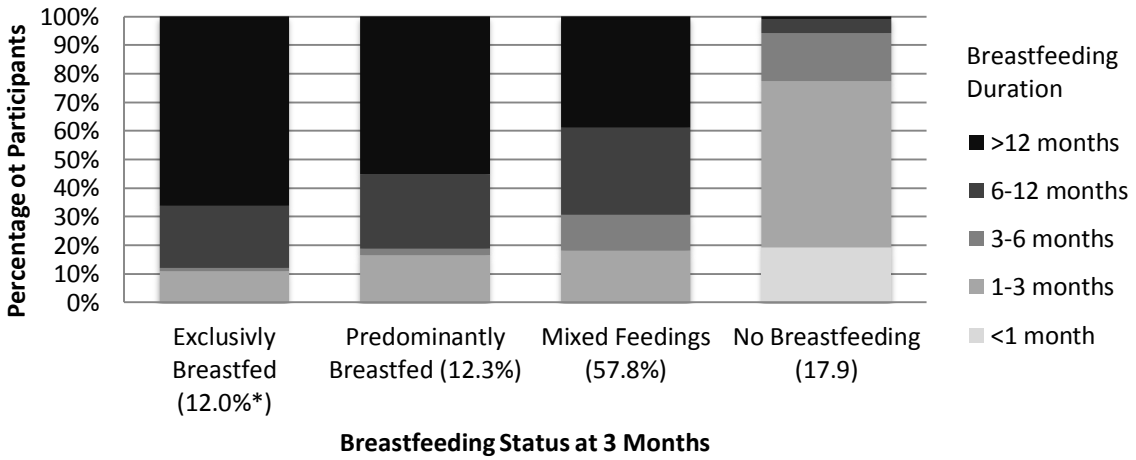

Table 2: Selected Maternal and Infant Characteristics of Study Population by Breastfeeding type at 3 months (n=689)

	Exclusively Breastfed (n=83)	Predominantly Breastfed (n=85)	Mixed Feeding (n=398)	Not Breastfed (n=123)	
	Mean (SD), or %	**Mean (SD), or %**	**Mean (SD), or %**	**Mean (SD), or %**	**P-Value†**
Maternal Age	26.29 (4.98)	25.71 (4.09)	26.55 (4.71)	25.87 (5.02)	0.33
RAVEN score	41.69 (9.22)	41.05 (9.18)	41.02 (8.89)	40.49 (8.91)	0.83
Maternal BMI	25.89 (3.71)	25.52 (3.81)	26.08 (4.13)	27.06 (5.59)	0.06
Socio-Economic Status, %					0.45
Low	31.33	38.83	29.9	26.02	
Medium	37.35	36.47	34.92	37.4	
High	31.33	24.71	35.18	36.59	
First Birth, %	**27.71**	**25.88**	**38.19**	**45.53**	**0.01***
Completed High School, %[1]	**60.24**	**42.35**	**61.96**	**57.72**	**0.01***
DHA Group, %	50.6	54.12	50	49.59	0.91
BMI >25 kg/m, %	49.4	48.24	57.79	63.41	0.08
Single, %	3.61	4.71	10.55	11.38	0.08
Gestational Age (weeks)	39.27 (1.64)	39.30 (1.79)	39.01 (1.73)	38.85 (2.12)	0.2
Birth Weight (g)	3244.63 (382.64)	3288.81 (505.10)	3207.66 (473.50)	3168.46 (423.90)	0.27
Birth Length (cm)	50.59 (2.08)	50.41 (2.89)	50.34 (2.58)	50.15 (2.16)	0.67
Low birth weight, %	0.15	0.44	3.63	1.02	0.25
Sex, Male %	6.68	6.1	31.35	8.56	0.55
Premature (37 weeks), %	8.43	7.06	10.1	11.38	0.73

[1] 1 missing observation

† P-values were obtained from Pearson's Chi-squares test for associations (for categorical variables) and ANOVA tests (for continuous variables).

*Indicates significance at 0.05 level.

Table 3: Selected Maternal and Infant Characteristics of Study Population by Breastfeeding Duration (n=686).

	Less than 1 month (n=23)	1 month - < 3 months (n=188)	3 months - < 6 months (n=79)	6 months - < 12 months (n=186)	More than 12 months (n=280)	
	Mean (SD), or %	**Mean (SD), or %**	**Mean (SD), or %**	**Mean (SD), or %**	**Mean (SD), or %**	**P-value**
Maternal Age	25.7 (4.6)	25.7 (4.7)	26.7 (4.8)	26.1 (4.7)	26.8 (4.8)	0.17
RAVEN score	37.1 (10.6)	41.4(8.8)	41.4 (7.8)	41.2 (9.0)	40.5 (9.6)	0.23
Maternal BMI	28.3 (7.4)	26.3 (4.3)	26.3 (4.7)	25.9 (4.0)	25.9 (4.0)	0.1
Socio-Economic Status, %						0.4
Low	34.8	26.1	20.6	33.5	33.7	
Medium	34.8	38.8	43.8	31.1	34.9	
High	30.8	35.2	35.6	35.5	31.4	
First Birth, %	**56.5**	**44.2**	**28.8**	**37.7**	**31.4**	**0.01***
Completed High School, %[1]	**39.1**	**56.1**	**74**	**64.7**	**53.5**	**0.003***
DHA Group, %	52.2	52.7	61.6	42.5	51.2	0.08
BMI >25 kg/m, %	65.2	60	64.4	52.1	54.3	0.2
Single, %	4.4	10.9	15.1	7.2	8.2	0.2
Gestational Age (weeks)	38.6 (2.8)	38.9 (1.8)	39.0 (1.9)	39.0 (2.0)	39.2 (1.5)	0.35
Birth Weight (g)	3129.1 (572.8)	3144.16 (430.3)	3217.78 (524.15)	3213.85 (485.19)	3263.29 (416.96)	0.08
Birth Length (cm)	**49.8 (2.7)**	**50.0 (3.0)**	**50.5 (2.4)**	**50.3 (2.5)**	**50.7 (1.9)**	**0.03***
Low birth weight, %	4.4	7.3	8.2	5.4	3.1	0.2
Sex, Male %	47.8	57	46.6	50.9	53.1	0.5
Premature (<25--g), %	**17.39**	**11.7**	**7.59**	**12.43**	**5.76**	**0.04***

[1] 1 missing observation

*Indicates significance at 0.05 level.

Table 4: Mean McCarthy Scale Scores by Breastfeeding Status at 3 months.

McCarthy Scale (Mean, SD)	**Exclusively Breastfed**	**Predominantly Breastfed**	**Mixed feeding**	**No breastfeeding**	Crude P-value	Adjusted P-value†
Memory Scale	42.79 (8.47)	41.82 (8.33)	42.46 (8.53)	42.61 (8.31)	0.89	0.99
Motor Scale	47.67 (8.39)	48.86 (9.47)	47.93 (8.69)	49.00 (8.46)	0.53	0.36
Verbal Scale	43.96 (9.24)	42.76 (8.55)	44.00 (8.03)	44.07 (8.01)	0.65	0.92
Quantitative Scale	45.11 (9.01)	44.64 (8.97)	45.61 (9.45)	44.69 (9.55)	0.7	0.76
Perceptual- Performance Scale	48.28 (7.87)	48.65 (8.30)	49.26 (8.15)	49.04 (7.95)	0.75	0.34
General Cognition	92.27 (13.47)	91.16 (13.23)	93.14 (13.22)	92.79 (12.64)	0.64	0.53

†All models were adjusted for maternal education (completion of high school), intelligence, age, whether or not this was her first birth, DHA group and infant sex, birth weight and age at examination.

Table 5: Mean McCarthy Scale Scores by Breastfeeding Duration.

McCarthy Scale Scores, Mean (SD)	**<1 month**	**1 - just under 3 months**	**3- Just under 6 months**	**6- Just under 12 months**	**>12 months**	Crude P-value	Adjusted P-value†
Memory Scale	39.74 (9.25)	42.52 (8.55)	43.10 (8.58)	42.91 (8.32)	42.23 (8.38)	0.48	0.81
Motor Scale	46.78 (7.53)	48.09 (9.21)	48.14 (8.54)	48.28 (8.98)	48.40 (8.44)	0.94	0.72
Verbal Scale	41.61 (9.05)	43.84 (8.43)	43.81 (8.55)	44.53 (7.96)	43.75 (8.53)	0.6	0.94
Quantitative Scale	41.30 (9.56)	44.76 (9.31)	45.43 (9.34)	46.28 (9.19)	45.29 (9.43)	0.16	0.47
Perceptual- Performance Scale	46.26 (7.69)	49.22 (8.37)	49.04 (8.93)	49.50 (7.93)	48.86 (7.81)	0.49	0.81
General Cognition	87.48 (14.01)	92.65 (13.51)	92.62 (12.64)	94.04 (12.64)	92.54 (12.92)	0.25	0.7

†All models were adjusted for maternal education (completion of high school), intelligence, age, whether or not this was her first birth, DHA group and infant sex, birth weight and age at examination.

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Chapter 3: Discussion, Conclusions and Public Health Implications.

Discussion and Conclusions

The main finding of this analysis is the lack of a statistically significant association between breastfeeding status at 3 months of age and breastfeeding duration on child cognitive development at 5 years of age as assessed using the McCarthy Scale of Children's Abilities cognitive assessment test. The large sample size (n=689) allows us to be confident about the findings that have resulted from this analysis. This is one of the few studies to assess this relationship in this region and context and specifically in Mexico. These findings are consistent with several findings of studies in this field that have not found there to be an association with breastfeeding and child cognitive outcomes (Der, Batty, & Deary, 2006) (Walfisch, Sermer, Cressman, & Koren, 2013).

It was shown that mothers that were exclusively breastfeeding at three months were more likely to continue breastfeeding for a longer amount of time, as one would expect. Implying that by encouraging exclusive breastfeeding among mothers, duration of breastfeeding could potentially be positively affected. Variables that were seen to influence breastfeeding were also what one would expect, with education being negatively associated with breastfeeding which is characteristic of low and middle income countries (Gonzalez, et al., 2012). As education, specifically completion of high school was also seen as one of the largest confounders in the relationship being assessed, targeting interventions to promote breastfeeding at mothers with higher education status may be beneficial.

Moreover, the noticed decline in parameter estimates of breastfeeding on cognitive development after adjusting for potential characteristics is consistent with many studies in this

field that saw decreased or complete disappearance of the effect size of breastfeeding in adjusted models, compared to the effects sizes noted in crude models (Walfisch, Sermer, Cressman, & Koren, 2013). These results can be used to argue that significant results seen in previous studies may be due to persistent confounding for variables not taken in to account. This supports the need to collect detailed and rigorous data on the study population to properly assess this relationship.

The strengths of this study include the study design of a population based prospective nature allowing for the possibility of assessing relationship and causal links. Of the participating mothers that gave live births, 70% were followed up with complete information up to 5 years of age. This resulted in a large sample size of 689 mother-child pairs completing the final assessment at 5 years of age. Having collected a large amount of information on maternal demographic and socio-economic characteristics as well as infant characteristics at birth allowed for the consideration of other possible confounders to be taken in to account; this has been a weakness in many studies before that were unable to adjust for potential confounders and thus unable to conclude with confidence that the documented effect was indeed due to breastfeeding (Walfisch, Sermer, Cressman, & Koren, 2013). Another issue that is dominant as a draw back in previous studies is the way in which the breastfeeding data was collected and defined. Instead of looking solely at 'ever breastfed' and 'never breastfed' infants, this data allowed for the analysis of different intensities of breastfeeding at a certain time points as well as the duration of any breastfeeding, giving two separate but related variables with which to examine the relationship (Walfisch, Sermer, Cressman, & Koren, 2013). Moreover, participants were unaware of this research question when the breastfeeding data was being collected, making misclassification unlikely. In addition to that, the McCarthy Scale for Children's Abilities has been previously

examined for its strength and it was found that this test has good predictive abilities when compared to other tests used to estimate child cognition (Naglieri & P.L., 1982). Also, the Spanish language version of the McCarthy Scales has been used successfully in Mexico in the past. (Schnaas, et al., 2000).

There are limitations to this study that must be recognized. Firstly, information on the exposure variables requires some amount of recall from the participants which may result in some recall bias. In addition, data on breastfeeding status at 3 months may not have been collected at exactly 3 months of age therefore there may have been some mothers who were not breastfeeding at 3 months but were classified as such; this can be seen as some participants having mismatched data when comparing breastfeeding status at 3 months and breastfeeding duration. However, it is unlikely that this had an effect on the results of the analysis as it was seen that after removing this group for sensitivity analysis, there was no major change in results and conclusions. There is also room for residual confounding as there is still a possibility of other confounders that were not taken in to consideration, such as paternal education and intelligence. Another possible limitation to the data is that cognitive development was only measured at one time point. It may have been useful to test child cognitive development at different time points in order to assess this relationship more intensely.

The history of inconsistencies and contradicting findings of results in studies that have tried to assess the relationship between breastfeeding and cognitive development indicate the need for further research on this topic. It would be beneficial to collect detailed information on breastfeeding status at several time points as well as conduct cognitive testing at several ages during early childhood to get a clear and detailed picture of the effects of types of breastfeeding and duration on child development throughout the first few years of life. It would also be

beneficial to gather more information on other possible confounders of this relationship, for example, it has been shown that certain paternal characteristics may influence a child's development therefore having data on those characteristics will provide extra strength when studying this relationship (Leventakou, et al., 2013).

The gold standard to assess causal relationships in the health related field would be to conduct a randomized control trial (RCT). However, due to the many known benefits of breastfeeding and nature of allowing a mother the choice to breastfeed or not, makes these kinds of studies unethical in the cases of assessing the relationship of breastfeeding on different outcomes. The next best thing in this case would be to look at sibling pairs. Being able to recruit mothers with siblings that has been breastfed and not breastfed would be the ideal way to properly study the effect breastfeeding may have on several outcomes, cognitive development included. However, the studies that have taken on this kind of design have also reached contradicting results (Der, Batty, & Deary, 2006) (Evenhouse & Reilly, 2005).

In conclusion, this analysis suggests that breastfeeding does not have an effect on child cognitive development and that associations seen in the past may be due to other factors, namely maternal education, intelligence and socioeconomic status. When grouped with other studies and systematic reviews on this topic, it is unlikely that breastfeeding has a direct effect on child cognitive development.

Public Health Implications

The current contradicting results on whether or not breastfeeding has a direct effect on later child cognitive development has important public health impacts. On one hand, if breastfeeding is shown to have a positive effect on neurodevelopment of infants and children,

this would warrant very cost-effective and relatively easy interventions to target child development. However, if it is shown that this relationship is non-existent, mothers who choose not to breastfeed or are unable to for certain reasons can be assured that this will not have an effect on their child's development directly.

In order for further studies to be able to result in confident conclusions, they must be able to adjust and take in to account the many characteristics and variables that have been shown to confound this relationship. Moreover, more rigorous study designs must be used, such as sibling pair analysis, in order to ensure minimal selection bias and confounding. If future studies are able to take these things in to consideration, we can get closer to reaching a conclusion to this debate.

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