Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

______________________________ ______________

Kimberly Marie Vellano Date

Association between Infant Breastfeeding and Childhood Body Mass Index

By

Kimberly M. Vellano
Master of Public Health

Epidemiology

____

Carolyn Drews-Botsch, PhD
Faculty Thesis Advisor

Association between Infant Breastfeeding and Childhood Body Mass Index

By

Kimberly M. Vellano

Bachelor of Arts
Wake Forest University
2006

Faculty Thesis Advisor: Carolyn Drews-Botsch, PhD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2011

Abstract

Association between Infant Breastfeeding and Childhood Body Mass Index
By Kimberly M. Vellano

Objective: In light of the growing prevalence of obesity in the United States, it is critical to identify effective interventions for obesity prevention. Evidence from observational studies suggests that breastfeeding may protect against obesity in later life. The aim of this study was to examine whether breastfeeding is associated with a decreased risk of overweight and obesity in a racially and economically diverse population of preschool aged children.

Methods: Data on infant feeding and child body mass index status were obtained from the Fetal Growth and Development Study. Participants included a cohort of infants born in two hospitals in Atlanta, Georgia from 1993-1994. After delivery, mothers were interviewed for demographic information, as well as behavioral, reproductive, and medical factors of interest. A sub-sample of the cohort was selected for the Follow-Up Development and Growth Experiences Study at preschool age. These subjects received a follow-up questionnaire and anthropometric measurements were obtained for calculation of BMI. Logistic regression analysis was conducted to compare the risks of childhood overweight (BMI between the 85^{th} and 94^{th} percentile) and childhood obesity (BMI in the 95^{th} percentile or higher) among breastfed and non-breastfed children.

Results: During infancy, 50% of subjects were never breastfed, 28% were breastfed for less than 6 months, and 22% were breastfed for at least 6 months. At preschool age, 10% of the children were overweight and 7.6% were obese. After adjusting for potential confounders, breastfeeding for at least 6 months was associated with a significant reduction in the risk of childhood obesity (AOR, 0.32; 95% CI 0.09-0.99), compared with those never breastfed or breastfed for less than 6 months. There was no association between breastfeeding duration and childhood overweight.

Conclusion: The results highlight the importance and possible protective effect of early nutrition in the development of childhood obesity. Increasing the initiation and duration of breastfeeding may provide an effective strategy to reduce childhood obesity in the United States and elsewhere.

Association between Infant Breastfeeding and Childhood Body Mass Index

By

Kimberly M. Vellano

Bachelor of Arts
Wake Forest University
2006

Faculty Thesis Advisor: Carolyn Drews-Botsch, PhD

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2011

TABLES OF CONTENTS

Introduction **1**

The Obesity Epidemic in the United States 1

Breastfeeding Practices in the United States 2

The Association between Breastfeeding and Childhood Obesity 4

Methods **11**

Study Design 11

Data Collection 11

Statistical Analysis 13

Results **15**

Characteristics of the Sample 15

Feeding Mode and Early Growth 16

Discussion **18**

Strengths and Weaknesses 18

Potential Biological Mechanisms 20

Future Directions 21

Recommendations for Intervention 22

References **24**

Tables and Figures **29**

Table 1: Characteristics of Preschool Age Children by Delivery Hospital, Atlanta, Georgia, 1993-1994 29

Table 2: Characteristics of Preschool Age Children by Infant Feeding Mode, Atlanta, Georgia, 1993-1994 30

Table 3: Weight Status of Preschool Age Children by Mother's Weight Status 31

Table 4a: Duration of Breastfeeding and Prevalence of Overweight and Obesity Among Preschool Age Children 32

Table 4b: Duration of Breastfeeding and Prevalence of Overweight and Obesity Among Preschool Age Children, Stratified by Sex 32

Figure 1: Prevalence of Overweight and Obesity by Duration of Breastfeeding in Preschool Age Children 33

Table 5: Crude and Adjusted Odds Ratios of the Duration of Breastfeeding and Childhood Weight Status 34

Table 6: Adjusted Odds Ratios of the Duration of Breastfeeding and Childhood Weight Status, Stratified by Sex 35

Table 7: Adjusted Odds Ratios of the Duration of Breastfeeding and Childhood Weight Status, Stratified by SGA 36

Table 8: Adjusted Odds Ratios of the Duration of Breastfeeding and Childhood Weight Status, Stratified by Delivery Hospital 37

INTRODUCTION

In recent years, researchers have suggested a potential protective effect of breastfeeding against subsequent childhood overweight and obesity. Although the literature remains mixed, this association deserves continued attention, as obesity rates continue to rise in the United States. The purpose of this study is to evaluate existing literature on the topic, and contribute further epidemiological analysis of the association among a diverse population of children.

The Obesity Epidemic in the United States

Obesity is a serious health concern for children and adolescents.[1] Childhood weight status can be practically measured using body mass index (BMI).[2, 3] For children and adolescents (ages 2-19 years), the BMI value is plotted on the Centers for Disease Control (CDC) growth charts to determine the corresponding BMI-for-age percentile.[2] Overweight is defined by the CDC as a BMI at or above the 85th percentile and lower than the 95th percentile, adjusted for age and sex, while obesity is defined as a BMI at or above the 95th percentile.[4] The 2007 National Health and Nutrition Examination Survey (NHANES) estimates that 17% of children and adolescents ages 2-19 are obese.[5] National trends indicate that the prevalence of obesity is rising, as there is a relatively greater increase in the upper BMI percentiles compared with the lower. Between 1976 and 2007, obesity increased from 5% to 10.4% among children ages 2-5, from 6.5% to 19.6% among 6-11 year olds, and from 5% to 18.1% among adolescents ages 12-19.[5]

Childhood overweight and obesity can result from the influences and interactions of a number of factors, including genetic, behavioral, and environmental causes.[1] Known risk factors for childhood obesity include genetic predisposition and excessive energy intake.[1] Factors that lead to this energy imbalance include unhealthy dietary habits, sedentary behavior, and low physical activity levels.[1]

Obese children are at risk for health problems during their youth and as adults. Health consequences of overweight and obesity include, but are not limited to: coronary heart disease, type 2 diabetes, hypertension, high cholesterol, stroke, cancer, depression, liver disease, sleep apnea, infertility, and osteoarthritis.[4] These associated health problems have a significant economic impact on the U.S. healthcare system. Direct medical costs include preventive, diagnostic, and treatment services related to obesity, while indirect costs relate to morbidity and mortality.[4] In 1998, medical costs of obesity were estimated to be as high as $78.5 billion per year, with roughly half financed by Medicare and Medicaid.[6] By 2006, costs had nearly doubled to $147 billion per year.[7] Across all payers, obese people had annual medical spending that was $1,429 greater than spending for normal-weight individuals.[7] Because of the steep health and economic costs of obesity, behaviors that protect against childhood overweight and obesity could have a significant public health impact.

Breastfeeding Practices in the United States

The American College of Obstetricians and Gynecologists recommends six months of exclusive breastfeeding for all infants, defined as feeding of breast milk only, without complementary nutrition.[8] The American Academy of Pediatrics and the American Academy of Family Physicians similarly recommend exclusive breastfeeding for the first six months of life, continuing at least through the infant's first birthday[9, 10], while the World Health Organization (WHO) recommends at least two years of breastfeeding for all infants.[11] In the United States, breastfeeding durations fall far short of these guidelines.[12]

In 2007, *Healthy People 2010 (HP2010)* objectives for breastfeeding initiation and duration were updated to include two new objectives on exclusive breastfeeding: to increase the proportion of mothers who exclusively breastfeed their infants through age 3 months to 60% and through age 6 months to 25%.[12] To monitor the progress toward reaching these objectives, CDC analyzed data from the National Immunization Survey (NIS). Among infants born in 2000, breastfeeding rates for the early postpartum period, 6 months, and 12 months were 70.9%, 34.2%, and 15.7%, respectively.[12] For infants born in 2004, these rates had consistently increased to 73.8%, 41.5%, and 20.9%, respectively.[12] The revised 2004 questions also enabled researchers to inquire about exclusive breastfeeding rates. Rates for exclusive breastfeeding through ages 3 months and 6 months among infants born in 2004 were 30.5% and 11.3%, respectively.[12] While rates of breastfeeding increased over this four-year period, rates of exclusive breastfeeding are still well below the targets set forth by *HP2010*. The authors also examined maternal factors related to exclusive breastfeeding and found that rates were significantly lower among black infants (compared with white infants) and infants born to unmarried mothers (compared with married mothers).[12] Additionally, older age, urban residence, higher education, and higher incomes of mothers were all positively associated with exclusive breastfeeding.[12]

Shealy et al. also examined the characteristics of breastfeeding practices among U.S. mothers by analyzing the 2005-2007 Infant Feeding Practices Study.[13] Participants received monthly questionnaires during their infants' first year of life. For the first 3 months, exclusive breastfeeding was the most prevalent type of breastfeeding.[13] After 3 months, exclusive breastfeeding declined greatly; slightly more than one third of the breastfeeding mothers supplemented with infant formula from 3 to 7 months.[13] In addition, the median frequency of breast milk feedings per day and the average reported length of individual breastfeeding sessions declined gradually throughout the year.[13]

In addition to providing essential nutrients to infants, benefits of breastfeeding for both children and their mothers have been reported. Health outcomes differ substantially for mothers and infants who formula feed compared with those who breastfeed.[14] Mothers who don't breastfeed have an increased incidence of premenopausal breast cancer, ovarian cancer, retained gestational weight gain, type 2 diabetes, postpartum depression, myocardial infarction, and metabolic syndrome.[14, 15] Infants who aren't breastfed have an increased risk of infectious morbidity (including acute ottis media, nonspecific gastroenteritis, severe lower respiratory tract infections, atopic dermatitis, and asthma), as well as elevated risks of type 1 and type 2 diabetes, leukemia, sudden infant death syndrome (SIDS), and childhood obesity.[14, 15]

The suboptimal breastfeeding rates in the U.S. result in significant excess healthcare costs and preventable infant deaths. Bartick and Reinhold computed current costs and compared them with projected costs if an increasing proportion of U.S. families complied with the recommendation to exclusively breastfeed for 6 months.[16] The cost analysis included all pediatric diseases for which the Agency for Healthcare Research and Quality reported risk ratios that favored breastfeeding. If the *HP2010* goals regarding exclusive breastfeeding were met, savings were estimated to be $2.2 billion/year, with 142 deaths prevented. Increasing exclusive breastfeeding rates to 80% and 90% among U.S. families was estimated to increase savings to $10.5 and $13 billion/year and prevent 741 and 911 deaths annually, respectively.

The Association between Breastfeeding and Childhood Obesity

The protective effect of breastfeeding against childhood obesity was initially proposed by Kramer in 1981.[17] In the last three decades, dozens of papers have examined this relationship, with conflicting results. A large proportion of the literature has reported a significant protective effect of breastfeeding against childhood overweight and obesity[18-29], while several studies have reported a modest, non-significant protective effect.[30-41] In contrast, a few studies have concluded that breastfeeding actually increases the risk of childhood overweight and obesity[42-47]; however, only one of these studies[42] presented a significant adjusted odds ratio. Finally, several studies have reached mixed conclusions, depending on the definition of the dependent variable (overweight,

overweight and obese, or obese).[48-50] As a majority of the research regarding breastfeeding and childhood overweight and obesity is observational, several methodological issues affect the internal validity of individual studies and the heterogeneity among studies.

Factors affecting the internal validity of individual studies:

Potential sources of bias in observational cohort studies include selection bias, misclassification, and inadequate control for confounding. Selection bias relates to the need for follow-up of individuals for a period of time after breastfeeding exposure in order to assess the occurrence of the outcome of interest, childhood overweight or obesity. Breastfeeding status and other baseline characteristics should be examined to determine whether there are systematic differences between those who complete the study and those lost to follow-up, in order to assess the possibility of selection bias.

Misclassification of breastfeeding status or duration is a potential source of bias, particularly in retrospective studies. Huttly et al. compared actual breastfeeding duration with that reported retrospectively by mothers.[51] They observed a systematic bias towards reporting longer durations of breastfeeding among wealthier and more educated mothers, while those from low socioeconomic status families did not tend to err more in one direction than another.[51] While misclassification of breastfeeding status is less likely, it remains a possibility, particularly in studies with long recall periods. Appropriate characterization of feeding exposures may also be hindered by inability to define and quantify mixed feeding. The timing, amount, and quality of complementary foods may vary substantially between breast- and formula-fed infants in the same study and within studies.[52]

Inaccurate measurement of confounders, as well as incorrect specification of multivariable models may prevent full adjustment for confounding. Commonly considered confounders in studies of the relationship between breastfeeding and overweight or obesity include birthweight, parental BMI, parental smoking, dietary factors, physical activity, socioeconomic status (SES), age, sex, birth order, and number of siblings.[53] A number of studies fail to control for these factors appropriately, leading to residual confounding.

Factors affecting heterogeneity among studies

As studies have addressed the relationship between breastfeeding and childhood overweight or obesity for decades, the parameters used in individual studies vary widely. This heterogeneity among studies may undermine the conclusions being drawn.

Studies on the effect of breastfeeding have included subjects born during several decades in the last century. During this period, the diets of non-breastfed infants have changed markedly. In the first decades of the 20th century, most non-breastfed infants received formula based on whole cow's milk or top milk, with a high sodium concentration and levels of cholesterol and fatty acids that are similar to those in mature breast milk.[54] By the 1950s, commercially prepared formulas became increasingly popular. At this time, formulas tended to have a high sodium concentration and low levels of iron and essential fatty acids.[54] Since 1980, the composition of infant formulas has evolved to more closely emulate the nutrient composition of breast milk.[54] This variation in formula content may affect the long-term effects of breastfeeding, depending on the study cohorts' birth year.

Studies also vary in the length of recall of breastfeeding and the source of information on breastfeeding duration. Misclassification of breastfeeding duration increases with the time elapsed since weaning.[51] While the vast majority of studies assessed infant feeding by maternal recall, others relied on information from health workers or medical records; studies that rely on recall may be more prone to bias.

Studies also vary in their categorization of breastfeeding duration and definition of breastfeeding. Most studies compared ever-breastfed subjects to those that were never-breastfed. However, other studies compared subjects who were breastfed for less than a given number of months to those breastfed for longer periods. Few studies treated breastfeeding duration as a continuous or ordinal variable with several categories, which would allow for dose-response analysis. Furthermore, studies differ in their definitions of breastfeeding, with some limiting the analysis to exclusive breastfeeding, while others examined predominant or partial breastfeeding patterns. In addition, most studies did not differentiate between breastfeeding and feeding of expressed breast milk.

Finally, studies differ in whether they use mean BMI or prevalence of overweight/obesity as a dependent variable. Grummer-Strawn suggested that breastfeeding is protective against underweight as well as overweight[29]; therefore, one would not expect to see an effect on the mean BMI but only on the extremes. This may explain the observation that the protective effect of breastfeeding has been reported for binary outcomes (obese vs. not obese), but not for mean BMI.[55] It is possible that breastfeeding reduces the extremes at both ends, resulting in a reduced prevalence of overweight/obesity, but no difference in mean BMI.[56]

Meta-Analyses

In order to address the mixed results and frequently small sample sizes of recent studies, four meta-analyses were conducted from 2004-2007. The methods and results of these studies are described below.

In 2004, Arenz et al. were the first to publish a meta-analysis of studies from 1966 to 2003, investigating the relationship between breastfeeding and childhood obesity.[57] In order to be included in the meta-analysis, studies had to adjust for at least three of the following confounders: birthweight, parental overweight, parental smoking, dietary factors, physical activity, and socioeconomic status. In addition, odds ratios or relative risks had to be reported, age at last follow-up had to be between 5 and 18 years, feeding mode had to be assessed and reported, and obesity as outcome had to be defined by BMI percentiles ≥90, 95, or 97. Nine studies comprising more than 69,000 children were included in the meta-analysis.

The adjusted odds ratio for the nine studies was 0.78 (95% CI, 0.71-0.85) for both the fixed and random-effects models, suggesting that there was no heterogeneity between the studies. Sensitivity analysis was performed, and the protective effect of breastfeeding was found to be independent of the following study characteristics: study design (cohort or cross-sectional), definition of breastfeeding (never-ever or other definition), definition of obesity (≥95^{th} percentile or ≥97^{th} percentile), and age group (≤6 years or >6 years). In contrast, the protective effect of breastfeeding was more pronounced in studies with adjustment for less than seven potential confounders compared with adjustment for seven or more potential confounders (AOR, 0.69 and 0.78, respectively).

In 2005, Owen et al. published a meta-analysis which included 28 studies and 298,000 subjects.[58] The authors were less stringent in their inclusion criteria than Arenz et al. and included studies which only presented crude odds ratios, and allowed for a variety of definitions for BMI percentiles, obesity, and breastfeeding. Meta-regression analysis was used to investigate differences in the pooled odds ratio according to study size, age group at outcome measurement, year of birth, response rate, length of recall of feeding status, and definition of obesity.

In the fixed-effects model including all studies, breastfed subjects were less likely to be defined as obese than formula-fed subjects (OR, 0.87; 95% CI, 0.85-0.89). Small studies reported the strongest relationships between breastfeeding and reduced risk of obesity. An odds ratio of 0.43 (95% CI, 0.33-0.55) was reported for 11 small studies (<500 subjects), in comparison with an odds ratio of 0.78 (95% CI, 0.69-0.89) in 7 studies of intermediate size (500-2500 subjects), and an odds ratio of 0.88 (95% CI, 0.86-0.90) in 10 large studies (>2500 subjects). The authors were also able to examine the effect of adjustment for three confounders (SES, parental BMI, and maternal smoking) in six studies. The pooled odds ratio in these studies was reduced from 0.86 (95% CI, 0.81-0.91) before adjustment to 0.93 (95% CI, 0.88-0.99) after adjustment, underscoring the importance of adjusting for potential confounders in observational studies.

Unlike the previous two analyses, the 2005 meta-analysis by Harder et al. attempted to assess the effect of duration of breastfeeding on the risk of overweight, in search of a possible dose-response mechanism.[59] To be eligible, studies had to fulfill the following three criteria: be an original report comparing breastfed subjects with exclusively formula-fed subjects (referent group) at any given age, report the odds ratio and 95% confidence interval of overweight or obesity associated with breastfeeding, and report the duration of breastfeeding for at least one exposure group. Any definition of overweight or obesity was allowed, and some effect estimates were not adjusted for potential confounders. Seventeen studies, with a total of 120,831 subjects, were selected for inclusion in the meta-analysis. From these studies, 14 gave data for more than one category of breastfeeding duration, leading to the inclusion of 52 estimates in the meta-regression analysis.

From one month of breastfeeding onward, the risk of subsequent overweight continuously decreased up to a reduction of more than 30%, reaching a plateau at 9 months of breastfeeding. Categorical analysis confirmed this dose-response relationship (<1 month of breastfeeding: OR, 1.0; 95% CI, 0.65-1.55; 1-3 months: OR, 0.81; 95% CI, 0.74-0.88; 4-6 months: OR, 0.76; 95% CI, 0.67-0.86; 7-9 months: OR, 0.67; 95% CI, 0.55-0.82; >9 months: OR, 0.68; 95% CI, 0.50-0.91). Trend analysis found that each month of breastfeeding was associated with a 4% decrease in risk of overweight (OR, 0.96/month of breastfeeding; 95% CI, 0.94-0.98).

In 2007, the WHO conducted a meta-analysis including recently published studies, all of the papers included in the previously published meta-analyses, and those identified by two independent literature searches at the WHO and the University of Pelotas.[54] The authors included 33 studies with 39 estimates on the effect of breastfeeding on prevalence of overweight/obesity. In a random-effects model including all studies, breastfed individuals were less likely to be overweight/obese (OR, 0.78; 95% CI, 0.72-0.84). There was no marked effect modification by age group, birth year, control of confounding, categories of breastfeeding duration, study setting, study design, or length of recall of breastfeeding. In contrast, the effect of breastfeeding varied by study size, with small studies reporting a more significant association. However, intermediate and large studies had similar protective effects, which were comparable to the pooled effect estimate for all studies. Eight studies provided odds ratios for more than one outcome (i.e. overweight only, overweight plus obesity, obesity only). Six of these eight studies reported a more marked protective effect against obesity than overweight or overweight plus obesity.

As the literature remains divided, the purpose of this study was to further investigate the relationship between breastfeeding and the prevalence of overweight and obesity among a population of racially and economically diverse preschool children.

METHODS

Study Design

The present research is derived from the Fetal Growth and Development Study (FGDS) birth cohort. The study sample includes infants born from February 1, 1993 through December 31, 1994 at two large delivery hospitals in Atlanta, Georgia. The two hospitals deliver nearly half of the births in Atlanta, and serve distinct populations. Grady Memorial Hospital, a public hospital in downtown Atlanta, serves a primarily African American population of low socioeconomic status. In contrast, Northside Hospital, a private hospital in suburban Atlanta, serves a primarily White, middle-class population. During the recruitment period, study staff were randomly assigned to one of the two hospitals each week. To ensure a random, seasonal distribution of births, hospital assignments were conducted in four-week blocks. The final cohort from each hospital included deliveries for 50 weeks over the two-year period.

Black or White singleton infants, born 32 to 42 weeks gestation, were eligible for inclusion in the study. A total of 24,860 eligible births occurred at the two hospitals during the study period. Each infant was classified as either small-for-gestational-age (SGA) or appropriate-for-gestational-age (AGA). SGA was defined as birthweight-for-gestational-age below the 10^{th} percentile. Birthweight-for-gestational-age was related to the analytical questions posed by the FGDS, for which the sample was originally recruited. Therefore, 100% of SGA infants (n=830) and a 3% simple random sample of AGA infants (n=425) were included in the study.

Data Collection

Each mother was interviewed in the hospital within 48 hours of delivery. Study questions related to demographics, as well as behavioral, reproductive, and medical factors of interest. Written, informed consent was obtained from the mothers. In cases where the mother was younger than 18 years of age, the maternal grandmother also provided informed consent for her daughter to participate. Participation rates were 88% for Grady and 69% for Northside. Reasons for non-participation included refusal (n=153), maternal medical reasons (n=22), maternal discharge prior to consent (n=78), and inability to communicate with the mother due to a language barrier or a mental or hearing disability (n=16). Due to the disparity in participation rates, the potential for selection bias was evaluated by comparing the study sample to all singleton infant deliveries during the recruitment period. No statistically significant differences were found among the two populations with respect to sex, gestational age, maternal education, or maternal smoking.

A sub-sample of the study population was selected for the Follow-Up Development and Growth Experiences (FUDGE) Study at preschool age. A principal interest of the study investigators was the potential effect of maternal alcohol consumption during pregnancy on fetal growth and subsequent childhood development. Therefore, the sub-sample included: 1) all of the randomly-sampled AGA children whose mothers had been interviewed in the neonatal period (n=252), 2) all of the SGA children whose mothers reported any alcohol use during pregnancy (n=266), and 3) a 50% random sample of the remaining SGA children whose mothers reported abstaining from alcohol during pregnancy (n=188). Of the 706 children selected for the study, follow-up was completed on 511 (72%). Mean age of the sample was 55 months at follow-up. The mother was re-interviewed regarding breastfeeding duration, infant and preschool nutrition, and home environment factors. In addition, anthropometric data was obtained for each child. Height was measured twice using a portable or digital stadiometer; a third replicate was obtained if the first two measurements differed by more than 0.5 cm. Weight was measured twice using an electronic scale; a third replicate was obtained if the first two measurements differed by more than 0.2 kg. For the analysis, the two anthropometric measurements were averaged; when the two observations were outside the predetermined standard, the measurement closest to the third replicate was used.

Strict protocols for interviews, measurements, and data entry were observed to ensure the accuracy and quality of the data. Reliability interviews were conducted over the telephone by a project coordinator on a 10% random sample of subjects. In addition, all data forms were edited for consistency and completeness immediately after the hospital interview, and again by the project coordinator. All potential errors were reviewed with the interviewer and the data was verified by the respondent, if necessary. A data entry clerk utilized double key data entry, and all records were reviewed by the project coordinator.

Statistical Analysis

Our exposures of interest were predominance and duration of breastfeeding. Questions on infant feeding practices related to whether the child was ever breastfed and the age at which the child completely stopped breastfeeding. Infant feeding was defined based on the duration (in months) that the children were breastfed. For predominance of breastfeeding, our primary analysis compared subjects who were ever vs. never breastfed. For duration of breastfeeding, our primary analysis compared subjects in the following feeding groups: never breastfed, breastfed for >0 and <6 months, and breastfed for ≥ 6 months.

The outcomes of interest were prevalence of overweight and obesity at follow-up. Body mass index was calculated from the anthropometric data, and weight status was defined using BMI-for-age-and-gender percentiles from the revised NCHS/CDC growth charts.[60] Following current guidelines for children and adolescents, a BMI between the 85^{th} and 95^{th} percentile was defined as “overweight” and at or above the 95^{th} percentile as “obese”.[2]

The effect of infant feeding mode on early childhood BMI was examined by multiple logistic regression. For the outcome of overweight, we compared odds of being between the 85^{th} and 95^{th} BMI percentile with odds of being less than the 85^{th} percentile. For obesity, we compared odds of being equal to or greater than the 95^{th} percentile with odds of being less than the 95^{th} percentile. Possible confounding variables were selected for model inclusion based on stepwise backward elimination, and included small-for-gestational age, birthweight, delivery hospital, sex, maternal age, pre-pregnancy maternal BMI, parity, and maternal smoking and drinking during pregnancy. All analyses were conducted using SAS statistical software (version 9.1).

RESULTS

Characteristics of the Sample

Sample sizes and characteristics of the study population are given in Table 1. A total of 10% of the children were overweight and 7.6% were obese at follow-up. The sample characteristics differ greatly by hospital of delivery. The total sample was evenly divided by sex (48.3% male, 51.7% female) and race (47.3% White, 52.7% African-American). However, Grady deliveries were nearly exclusively African-American (96.3%) and Northside deliveries were mostly White (86.2%). In terms of feeding mode, 50% of infants were never breastfed, 28% were breastfed for less than 6 months, and 22% were breastfed for at least 6 months. Breastfeeding prevalence differed greatly by hospital, as Northside infants were three times more likely to have ever been breastfed than Grady infants (74.6% and 22.6%, respectively). In addition, Northside mothers were three times more likely to breastfeed for at least 6 months, per recommended pediatric guidelines. Maternal characteristics also varied greatly by hospital, with Grady mothers having significantly higher prevalence of overweight/obesity, single marital status, lower education level, young age at child's birth, and smoking during pregnancy.

There were differences in breastfeeding prevalence by key demographic, maternal, and perinatal characteristics (Table 2). Married mothers were significantly more likely to have ever breastfed (74.2%) compared with single mothers (22.8%). Breastfeeding prevalence was also positively associated with higher maternal education, older maternal age at child's birth, non-smoking status during pregnancy, and nulliparity. Finally, birthweight-for-gestational-age was associated with breastfeeding prevalence, with SGA infants less likely to have ever been breastfed.

One of the strongest predictors of child BMI status was mother's concurrent BMI (Table 3). Children were at moderately increased risk of overweight/obesity with an overweight mother, but at a much higher increased risk of overweight/obesity with an obese mother. Furthermore, the prevalence of childhood overweight was 2-fold greater with maternal obesity compared with normal maternal BMI, and the prevalence of childhood obesity was nearly 4-fold greater with maternal obesity.

Feeding Mode and Early Growth

Table 4a shows mean childhood BMI and proportions of subjects who were overweight and obese, by duration of breastfeeding. Ever vs. never breastfeeding was associated with a decrease in the prevalence of obesity, but not overweight. This trend was replicated when comparing children breastfed for >0 and <6 months to those breastfed for ≥6 months. Interestingly, when the sample was stratified by sex, boys who were ever breastfed had lower mean BMI and lower risk of obesity, but the trend was not replicated for girls (Table 4b). The prevalence of overweight and obesity by duration of breastfeeding in the three populations (total, boys only, and girls only) is shown in Figure 1.

Multiple logistic regression was used to compare the odds of overweight and obesity in three models: 1) never vs. ever breastfed children, 2) never breastfed vs. children breastfed for >0 and <6 months vs. children breastfed for ≥6 months, and 3) children breastfed for less than 6 months (including never) vs. children breastfed for at least 6 months (Table 5). There was no significant reduction in being overweight among ever breastfed children either in unadjusted (OR, 1.09; 95% CI, 0.60-1.97) or adjusted analyses (AOR, 0.72; 95% CI, 0.35-1.50). Similarly, being ever breastfed did not significantly decrease the odds of obesity in unadjusted (OR, 0.61; 95% CI, 0.30-1.21) or adjusted (AOR, 0.76; 95% CI, 0.32-1.82) models.

Breastfeeding for >0 and <6 months did not significantly decrease the odds of overweight (AOR, 0.62; 95% CI, 0.25-1.53) or obesity (AOR, 1.26; 95% CI, 0.47-3.36) compared with never breastfed children. Likewise, breastfeeding for ≥6 months did not significantly reduce the odds of overweight (AOR, 0.83; 95% CI, 0.35-1.98). The odds of obesity was significantly reduced in this group in the crude analysis (OR, 0.28; 95% CI, 0.08-0.96); however, when the model was adjusted for relevant confounders, the reduction in risk was no longer significant (AOR, 0.34; 95% CI, 0.09-1.34).

When breastfeeding was dichotomized by duration, there was a reduction in the risk of obesity among children breastfed for at least 6 months compared with those breastfed for less than 6 months, including never (AOR, 0.32; 95% CI, 0.09-0.99), but no reduction in the risk of childhood overweight (AOR, 0.97; 95% CI, 0.45-2.10).

Although none of the single-order interaction terms were significant confounders, the models were run with stratification by sex, SGA, and hospital of birth. Breastfed boys had a much greater reduction in obesity risk than breastfed girls; however, the reduction in risk did not reach statistical significance (Table 6). Stratification by SGA and hospital of birth did not yield any significant differences between the populations (Tables 7 and 8).

DISCUSSION

Our findings indicate that infants who were breastfed for at least 6 months had a lower risk of obesity in early childhood. Compared with infants breastfed for less than 6 months (including never), the estimated reduction in risk was approximately 70%. In contrast, breastfeeding for at least 6 months did not significantly reduce the risk of childhood overweight.

Strengths and Weaknesses

A strength of the present study is its capacity to account for differences in a number of potential confounders, including race, maternal BMI, marital status, educational attainment, age, and smoking during pregnancy. This study also represents an ethnically and economically diverse group, in contrast to studies with homogenous populations. This study also includes information about duration of breastfeeding, rather than prevalence only, which allowed for the identification of a potential threshold effect of breastfeeding on childhood BMI. This threshold suggests that the categorization scheme of breastfeeding duration may be critical in such studies, and may explain why some studies on breastfeeding and childhood BMI failed to find a significant association.

A unique feature of our study was the inclusion of a large proportion of small-for-gestational-age (SGA) infants. We were able to adjust for birthweight and birthweight-for-gestational-age, as both have been shown to be associated with early childhood growth.

One factor that strengthens confidence in the validity of our findings is that stronger associations were evident for obesity than for overweight. In addition, a substantial association between breastfeeding duration and childhood obesity remained after adjustment for relevant confounding variables.

Weaknesses of the study include a limited sample size (n=511), which could account for the wide confidence intervals and inadequate power to find a significant association between breastfeeding and childhood overweight. A larger sample would have also allowed for a more robust examination of the dose-response relationship between breastfeeding duration and childhood BMI. Additional factors that may have affected the study power include a low prevalence of childhood overweight and obesity, given the earlier timeframe and high proportion of SGA infants included in the sample population. The analysis could also be subject to selection bias due to missing data, as childhood BMI category and/or breastfeeding duration were unknown for 25 subjects. This accounts for 4.9% of the study sample.

The data also lacks information on formula supplementation and the timing of solid food introduction. The subjects were asked only how long they breastfed, but not whether they supplemented with formula or other foods during this period. Therefore, we were unable to control for additional feeding modes during the first year of life. In addition, the breastfed population was not limited to exclusively breastfed infants, and survey questions did not account for whether infants were fed expressed milk in a bottle. Recall bias of breastfeeding duration is also a possibility; however, several studies have addressed the validity of maternal recall of their children's infant feeding habits and found the information to be highly reliable.[61-64]

Residual confounding is always a concern in an observational study. Unmeasured potential confounders include attributes of the parents and family environment, such as child feeding practices, parental control of feeding during childhood, and physical activity. Parents who choose to breastfeed may have a healthier lifestyle in general; therefore, it is possible that these families practice better dietary habits and higher levels of physical activity. These lifestyle differences may explain the link between breastfeeding and childhood obesity.

Potential Biological Mechanisms

The notion that early life exposures can have lifetime consequences is well established in developmental biology and has been described as the "developmental origins of health and disease."[65] According to this hypothesis, early life exposures such as nutrition can have a lasting effect on subsequent growth patterns. Possible explanations for the inverse relationship between breastfeeding and childhood obesity include differences in macronutrient intake, hormonal responses, and behavioral mechanisms.

Differences in protein intake and energy metabolism may be one of the biological mechanisms linking breastfeeding to later obesity. Higher protein intake in early life is associated with an increase risk of later obesity.[66] Formula-fed infants consume up to double the amount of protein than breastfed infants at 3 to 6 months, and by 12 months their intake may be 5 to 6 times what is needed.[56] In a double-blind, randomized clinical trial, the European Childhood Obesity Trial Study Group randomly assigned formula with differing protein concentrations to healthy infants.[67] The follow-up data at age two indicated that feeding formula with reduced protein content normalizes early growth relative to a breastfed reference group. Finally, in contrast to the linear intake of milk during formula feeding, 80% to 90% of breast milk is consumed in the first 4 minutes of feeding. As the energy dense hind milk is consumed in only small amounts, infants may absorb less energy per volume of breast milk compared with formula.

Another possible mechanism is that breastfed and formula-fed infants have different hormonal responses to feeding. Lucas et al. found lower serum concentrations of insulin, which stimulates adipose tissue and fat storage, in breastfed infants than in formula-fed infants.[68] Another hormone of great importance in the etiology of obesity is leptin, which reduces appetite and increases energy expenditure.[69] It has been suggested that breastfeeding may affect metabolism by causing the leptin-dependent feedback loop to be less sensitive later in life, leading to greater leptin resistance.[56]

Behavioral mechanisms, such as learned self-regulation of energy intake, could also explain how breastfeeding protects against childhood obesity. One of the advantages of breastfeeding is that it allows the infant to control the amount of milk consumed, based on internal satiety cues. In contrast, bottle-feeding promotes more parental control. Parents often bottle-feed on a regular schedule, rather than in response to the infant's signals for frequency and volume of feedings. In addition, bottle-fed infants may be encouraged to finish the bottle, even when satiated.

Future Directions

Observational studies will likely continue to be the main method utilized for researching the association between breastfeeding and childhood overweight and obesity. These studies can be improved by implementing the following: clear subject selection criteria, a common definition of "exclusive breastfeeding", reliable collection of feeding data, specific and quantifiable outcomes of interest, and increased control of potential confounders. Prospective studies are particularly useful since they decrease the potential for recall bias and allow for follow-up at multiple, clinically relevant ages, thus allowing researchers to examine growth trajectories over time.

Almost all of the evidence to date on the association between infant feeding and childhood weight status relies on BMI, a surrogate measure of adiposity, rather than on a more direct measure of excess fat mass, such as dual-energy X-ray absorptiometry (DXA), hydodensitometry weighing, bioelectrical impedance, and skinfold measurements. However, adiposity rather than weight is thought to explain the major health comorbidities associated with obesity. Thus, studies that use BMI as an outcome may be misleading due to the potential misclassification of overweight and obese children. The use of BMI as a proxy for adiposity may be an explanation for the conflicting results in the literature, and future studies should utilize these alternative techniques to further explore the relationship.

In addition to observational studies, several study designs are suitable for this research. Sibling difference studies are particularly useful because they implicitly control for several major predictors of childhood obesity shared by siblings, such as parental obesity, socioeconomic status, and family eating habits. Clinical trials with random assignment of mothers to breastfeeding or formula feeding are unethical and unfeasible; however, community-level or cluster randomized controlled studies allow for the evaluation of the effectiveness of breastfeeding promotion interventions with long-term follow-up. In addition, the causal effect of the various components of human milk could be tested in randomized trials with formulas of different nutrient compositions.

Recommendations for Intervention

The current epidemic of overweight and obesity cannot solely be explained by breastfeeding trends, as the incidence of breastfeeding has increased in recent years. However, efforts to increase duration and exclusivity of breastfeeding may help reduce rates in the future. A number of approaches have been pursued in order to support mothers who wish to breastfeed, including state and federal legislation, support in the workplace, public health campaigns, and improvements to the Women, Infants, and Children (WIC) program.

The breastfeeding-obesity link is now recognized by key government agencies and professional groups. The White House Task Force on Childhood Obesity, the U.S. Department of Health and Human Services, and the CDC have recently advocated increased support for breastfeeding.[70,71] In order to overcome cultural, social, and structural challenges, communities are advised to implement programs in hospitals, workplaces, and maternity care settings. Examples of potential interventions include: clear hospital policies that promote and support breastfeeding; community-based peer counseling programs aimed at increasing breastfeeding rates among low-income women; and well-designed workplace programs such as established breastfeeding facilities, onsite childcare services, and expanded maternity leave.

The percentage of obesity cases preventable by breastfeeding may be small; however, the rapid spread of the obesity epidemic and its implications for public health emphasizes the urgency with which potentially effective strategies should be implemented. Promoting the initiation and increased duration of breastfeeding provides a low-cost, readily available strategy to help attenuate childhood overweight and obesity in the United States and elsewhere.

REFERENCES

1. Centers for Disease Control and Prevention. Childhood Overweight and Obesity. Atlanta, GA; 2010. (http://www.cdc.gov/obesity/childhood/index.html). (Accessed November 1, 2010).

2. Centers for Disease Control and Prevention. About BMI for Children and Teens. Atlanta, GA; 2010. (http://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html). (Accessed March 29, 2011).

3. Mei Z, Grummer-Strawn LM, Pietrobelli A, et al. Validity of body mass index compared with other body-composition screening indexes for the assessment of body fatness in children and adolescents. *Am J Clin Nutr*. 2002; 75(6): 978-85.

4. Centers for Disease Control and Prevention. Overweight and Obesity. Atlanta, GA; 2010. (http://www.cdc.gov/obesity/index.html). (Accessed November 1, 2010).

5. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of high body mass index in US children and adolescents, 2007-2008. *JAMA*. 2010; 303(3): 242-9.

6. Finkelstein EA, Fiebelkorn IC, Wang G. National medical spending attributable to overweight and obesity: how much, and who's paying? *Health Aff*. 2003; Suppl Web Exclusives: W3-219-26.

7. Finkelstein EA, Trogdon JG, Cohen JW, et al. Annual medical spending attributable to obesity: payer-and service-specific estimates. *Health Aff*. 2009; 28(5): w822-31.

8. American College of Obstetricians and Gynecologists. Breastfeeding: maternal and infant aspects. *Int J Gynaecol Obstet*. 2001; 74(2): 217-32.

9. Gartner LM, Morton J, Lawrence RA, et al. Breastfeeding and the use of human milk. *Pediatrics*. 2005; 115(2): 496-506.

10. American Academy of Family Physicians. Breastfeeding, family physicians supporting (Position Paper). 2009. (http://www.aafp.org/online/en/home/policy/policies/b/breastfeedingpositionpaper.html). (Accessed November 15, 2010).

11. World Health Organization. *Infant and young child nutrition: Global strategy on infant and young child feeding*. Geneva, Switzerland; 2002.

12. Scanlon KS, Grummer-Strawn LM, Shealy KR, et al. Breastfeeding Trends and Updated National Health Objectives for Exclusive Breastfeeding - United States, Birth Years 2000-2004. *Morbidity and Mortality Weekly Report*. 2007; 56(30): 760-3.

13. Shealy KR, Scanlon KS, Labiner-Wolfe J, et al. Characteristics of breastfeeding practices among US mothers. *Pediatrics*. 2008; 122 Suppl 2: S50-5.

14. Stuebe A. The risks of not breastfeeding for mothers and infants. *Rev Obstet Gynecol*. 2009; 2(4): 222-31.

15. Ip S, Chung M, Raman G, et al. A summary of the Agency for Healthcare Research and Quality's evidence report on breastfeeding in developed countries. *Breastfeed Med*. 2009; 4 Suppl 1: S17-30.

16. Bartick M, Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-56.

17. Kramer MS. Do breast-feeding and delayed introduction of solid foods protect against subsequent obesity? *J Pediatr*. 1981; 98(6): 883-7.

18. Armstrong J, Reilly JJ. Breastfeeding and lowering the risk of childhood obesity. *Lancet*. 2002; 359(9322): 2003-4.

19. Von Kries R, Koletzko B, Sauerwald T, et al. Breast feeding and obesity: cross sectional study. *BMJ*. 1999; 319(7203): 147-50.

20. Thorsdottir I, Gunnarsdottir I, Palsson GI. Association of birth weight and breast-feeding with coronary heart disease risk factors at the age of 6 years. *Nutr Metab Cardiovasc Dis*. 2003; 13(5): 267-72.

21. Bergmann KE, Bergmann RL, Von Kries R, et al. Early determinants of childhood overweight and adiposity in a birth cohort study: role of breast-feeding. *Int J Obes Relat Metab Disord*. 2003; 27(2): 162-72.

22. Liese AD, Hirsch T, von Mutius E, et al. Inverse association of overweight and breast feeding in 9 to 10-y-old children in Germany. *Int J Obes Relat Metab Disord*. 2001; 25(11): 1644-50.

23. Sung RY, Tong PC, Yu CW, et al. High prevalence of insulin resistance and metabolic syndrome in overweight/obese preadolescent Hong Kong Chinese children aged 9-12 years. *Diabetes Care*. 2003; 26(1): 250-1.

24. Toschke AM, Vignerova J, Lhotska L, et al. Overweight and obesity in 6- to 14-year-old Czech children in 1991: protective effect of breast-feeding. *J Pediatr*. 2002; 141(6): 764-9.

25. Tulldahl J, Pettersson K, Andersson SW, et al. Mode of infant feeding and achieved growth in adolescence: early feeding patterns in relation to growth and body composition in adolescence. *Obes Res*. 1999; 7(5): 431-7.

26. Czajka-Narins D, Jung E. Physical growth of breast-fed and formula-fed infants from birth to age two years. *Nutrition Research*. 1986; 6: 753-62.

27. Langnase K, Mast M, Danielzik S, et al. Socioeconomic gradients in body weight of German children reverse direction between the ages of 2 and 6 years. *J Nutr*. 2003; 133(3): 789-96.

28. Simon VG, Souza JM, Souza SB. Breastfeeding, complementary feeding, overweight and obesity in pre-school children. *Rev Saude Publica*. 2009; 43(1): 60-9.

29. Grummer-Strawn LM, Mei Z. Does breastfeeding protect against pediatric overweight? Analysis of longitudinal data from the Centers for Disease Control and Prevention Pediatric Nutrition Surveillance System. *Pediatrics*. 2004; 113(2): e81-6.

30. Li C, Kaur H, Choi WS, et al. Additive interactions of maternal prepregnancy BMI and breast-feeding on childhood overweight. *Obes Res*. 2005; 13(2): 362-71.

31. Li L, Parsons TJ, Power C. Breast feeding and obesity in childhood: cross sectional study. *BMJ*. 2003; 327(7420): 904-5.

32. O'Callaghan MJ, Williams GM, Andersen MJ, et al. Prediction of obesity in children at 5 years: a cohort study. *J Paediatr Child Health*. 1997; 33(4): 311-6.

33. Poulton R, Williams S. Breastfeeding and risk of overweight. *JAMA*. 2001; 286(12): 1449-50.

34. Scaglioni S, Agostoni C, Notaris RD, et al. Early macronutrient intake and overweight at five years of age. *Int J Obes Relat Metab Disord*. 2000; 24(6): 777-81.

35. Strbak V, Skultetyova M, Hromadova M, et al. Late effects of breast-feeding and early weaning: seven-year prospective study in children. *Endocr Regul*. 1991; 25(1-2): 53-7.

36. Burdette HL, Whitaker RC, Hall WC, et al. Breastfeeding, introduction of complementary foods, and adiposity at 5 y of age. *Am J Clin Nutr*. 2006; 83(3): 550-8.

37. Dewey KG, Heinig MJ, Nommsen LA, et al. Breast-fed infants are leaner than formula-fed infants at 1 y of age: the DARLING study. *Am J Clin Nutr*. 1993; 57(2): 140-5.

38. Elliott KG, Kjolhede CL, Gournis E, et al. Duration of breastfeeding associated with obesity during adolescence. *Obes Res*. 1997; 5(6): 538-41.

39. Neyzi G, Binyildiz P, Gunoz H. Influence of feeding pattern in early infancy on ponderal index and relative weight. In: Borms J, ed. *Human Growth and Development*. New York, NY: Plenum; 1984. p. 603-11.

40. Victora CG, Barros F, Lima RC, et al. Anthropometry and body composition of 18 year old men according to duration of breast feeding: birth cohort study from Brazil. *BMJ*. 2003; 327(7420): 901.

41. Wadsworth M, Marshall S, Hardy R, et al. Breast feeding and obesity. Relation may be accounted for by social factors. *BMJ*. 1999; 319(7224): 1576.

42. Agras WS, Kraemer HC, Berkowitz RI, et al. Influence of early feeding style on adiposity at 6 years of age. *J Pediatr*. 1990; 116(5): 805-9.

43. Araujo CL, Victora CG, Hallal PC, et al. Breastfeeding and overweight in childhood: evidence from the Pelotas 1993 birth cohort study. *Int J Obes*. 2006; 30(3): 500-6.

44. He Q, Ding ZY, Fong DY, et al. Risk factors of obesity in preschool children in China: a population-based case-control study. *Int J Obes Relat Metab Disord*. 2000; 24(11): 1528-36.

45. Huus K, Ludvigsson JF, Enskar K, et al. Exclusive breastfeeding of Swedish children and its possible influence on the development of obesity: a prospective cohort study. *BMC Pediatr*. 2008; 8: 42.

46. Reilly JJ, Armstrong J, Dorosty AR, et al. Early life risk factors for obesity in childhood: cohort study. *BMJ*. 2005; 330(7504): 1357.

47. Yeung DL, Pennell MD, Leung M, et al. Infant fatness and feeding practices: a longitudinal assessment. *J Am Diet Assoc*. 1981; 79(5): 531-5.

48. Hediger ML, Overpeck MD, Kuczmarski RJ, et al. Association between infant breastfeeding and overweight in young children. *JAMA*. 2001; 285(19): 2453-60.

49. Frye C, Heinrich J. Trends and predictors of overweight and obesity in East German children. *Int J Obes Relat Metab Disord*. 2003; 27(8): 963-9.

50. Gillman MW, Rifas-Shiman SL, Camargo CA, Jr., et al. Risk of overweight among adolescents who were breastfed as infants. *JAMA*. 2001; 285(19): 2461-7.

51. Huttly SR, Barros FC, Victora CG, et al. Do mothers overestimate breast feeding duration? An example of recall bias from a study in southern Brazil. *Am J Epidemiol*. 1990; 132(3): 572-5.

52. Adair LS. Methods appropriate for studying the relationship of breast-feeding to obesity. *J Nutr*. 2009; 139(2): 408S-11S.

53. Ip S, Chung M, Raman G, et al. Breastfeeding and maternal and infant health outcomes in developed countries. *Evid Rep Technol Assess*. 2007; (153): 1-186.

54. Horta BL, Bahl R, Martines JC, et al. *Evidence on the long-term effects of breastfeeding : systematic review and meta-analyses*. Geneva, Switzerland: World Health Organization Press; 2007.

55. Beyerlein A, Toschke AM, von Kries R. Breastfeeding and childhood obesity: shift of the entire BMI distribution or only the upper parts? *Obesity*. 2008; 16(12): 2730-3.

56. Dewey KG. Is breastfeeding protective against child obesity? *J Hum Lact*. 2003; 19(1): 9-18.

57. Arenz S, Ruckerl R, Koletzko B, et al. Breast-feeding and childhood obesity-a systematic review. *Int J Obes Relat Metab Disord*. 2004; 28(10): 1247-56.

58. Owen CG, Martin RM, Whincup PH, et al. Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. *Pediatrics*. 2005; 115(5): 1367-77.

59. Harder T, Bergmann R, Kallischnigg G, et al. Duration of breastfeeding and risk of overweight: a meta-analysis. *Am J Epidemiol*. 2005; 162(5): 397-403.

60. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC growth charts: United States. *Adv Data*. 2000; (314): 1-27.

61. Vobecky JS, Vobecky J, Froda S. The reliability of the maternal memory in a retrospective assessment of nutritional status. *J Clin Epidemiol*. 1988; 41(3): 261-5.

62. Kark JD, Troya G, Friedlander Y, et al. Validity of maternal reporting of breast feeding history and the association with blood lipids in 17 year olds in Jerusalem. *J Epidemiol Community Health*. 1984; 38(3): 218-25.

63. Haaga JG. Reliability of retrospective survey data on infant feeding. *Demography*. 1988; 25(2): 307-14.

64. Tomeo CA, Rich-Edwards JW, Michels KB, et al. Reproducibility and validity of maternal recall of pregnancy-related events. *Epidemiology*. 1999; 10(6): 774-7.

65. Gluckman PD, Hanson MA. *Developmental Origins of Health and Disease*. Cambridge, United Kingdom: Cambridge University Press; 2006.

66. Rolland-Cachera MF, Deheeger M, Akrout M, et al. Influence of macronutrients on adiposity development: a follow up study of nutrition and growth from 10 months to 8 years of age. *Int J Obes Relat Metab Disord*. 1995; 19(8): 573-8.

67. Koletzko B, von Kries R, Closa R, et al. Can infant feeding choices modulate later obesity risk? *Am J Clin Nutr*. 2009; 89(5): 1502S-8S.

68. Lucas A, Sarson DL, Blackburn AM, et al. Breast vs bottle: endocrine responses are different with formula feeding. *Lancet*. 1980; 1(8181): 1267-9.

69. Savino F, Liguori SA, Fissore MF, et al. Breast milk hormones and their protective effect on obesity. *Int J Pediatr Endocrinol*. 2009; 327505.

70. White House Task Force on Childhood Obesity. *Solving the Problem of Childhood Obesity Within a Generation: Report to the President*. Washington, DC; 2010.

71. Kettel Khan L, Sobush K, Keener D, et al. Recommended Community Strategies and Measurements to Prevent Obesity in the United States. *Morbidity and Mortality Weekly Report*. 2009; 58(RR07): 1-26.

Table 1. Characteristics of Preschool Age Children by Delivery Hospital, Atlanta, Georgia, 1993-1994

	Total Sample*		Grady		Northside	
Child Characteristics	**n=511**	**%**	**n=240**	**%**	**n=261**	**%**
Sex						
Male	242	48.3	101	42.1	141	54.0
Female	259	51.7	139	57.9	120	46.0
Missing	*10*					
Race						
White	241	47.3	9	3.7	225	86.2
Black	268	52.7	231	96.3	36	13.8
Missing	*2*					
Weight category (BMI)						
Underweight/Normal (<85th percentile)	403	82.4	190	82.2	205	82.7
Overweight (85th to <95th percentile)	49	10.0	20	8.7	28	11.3
Obese (≥95th percentile)	37	7.6	21	9.1	15	6.0
Missing	*22*		*9*		*13*	
Breastfeeding duration, mo						
Never	253	49.9	184	77.4	66	25.4
>0 - <6	142	28.0	27	11.3	111	42.9
≥6	112	22.1	27	11.3	82	31.7
Missing	*4*		*2*		*2*	
Birthweight for gestational age						
Small (<10th percentile)	295	58.9	160	66.7	135	51.7
Appropriate/Large (>10th percentile)	206	41.1	80	33.3	126	48.3
Missing	10					
Maternal Characteristics						
Pre-pregnancy weight category (BMI, kg/m^2)						
Underweight (<18.5)	48	9.5	28	11.7	20	7.8
Normal (18.5 - 24.9)	319	62.9	134	56.1	177	68.6
Overweight (25.0 - 29.9)	87	17.2	48	20.1	39	15.1
Obese (≥30.0)	53	10.4	29	12.1	22	8.5
Missing	*4*		*1*		*3*	
Marital Status						
Single	238	46.6	214	89.2	23	8.8
Married	273	53.4	26	10.8	238	91.2
Education of mother						
≤9th grade	41	8.0	39	16.3	2	0.8
10th-11th grade	82	16.1	77	32.1	5	1.9
High school graduate or equivalent	112	21.9	83	34.6	29	11.1
Some college or technical school	111	21.7	37	15.4	68	26.0
Junior college graduate	10	2.0	1	0.4	9	3.5
College graduate	108	21.1	3	1.2	102	39.1
Any post-graduate work	47	9.2	0	0.0	46	17.6
Mother's age at child's birth, y						
<20	75	15.0	70	29.3	5	1.9
20-34	358	71.6	155	64.8	203	77.8
≥35	67	13.4	14	5.9	53	20.3
Missing	*11*		*1*			
Mother's smoking during pregnancy						
Yes	137	26.8	89	37.1	47	18.0
No	374	73.2	151	62.9	214	82.0

* 10 missing values for hospital of birth

Table 2. Characteristics of Preschool Age Children by Infant Feeding Mode, Atlanta, Georgia, 1993-1994

	Breastfeeding Duration*				
	Ever (n=255)		Never (n=253)		*p-value*
Characteristics	**n**	**%**	**n**	**%**	
Hospital					*<.0001*
Northside	194	74.6	66	25.4	
Grady	54	22.7	184	77.3	
Missing	*7*		*3*		
Mother's pre-pregnancy BMI (kg/m²)					*0.7832*
Underweight (<18.5)	20	43.5	26	56.5	
Normal (18.5 - 24.9)	163	51.3	155	48.7	
Overweight (25.0 - 29.9)	45	51.7	42	48.3	
Obese (≥30.0)	26	49.1	27	50.9	
Missing	*1*		*3*		
Marital Status					*<.0001*
Single	54	22.8	183	77.2	
Married	201	74.2	70	25.8	
Parity†					*<.0001*
0	145	65.6	76	34.4	
1	77	49.7	78	50.3	
2	19	38.8	30	61.2	
3	6	16.7	30	83.3	
4+	8	17.0	39	83.0	
Education of mother					*<.0001*
≤9th grade	7	17.5	33	82.5	
10th-11th grade	13	16.0	68	84.0	
High school graduate or equivalent	34	30.4	78	69.6	
Some college or technical school	62	56.4	48	43.6	
Junior college graduate	8	80.0	2	20.0	
College graduate	95	88.0	13	12.0	
Any post-graduate work	36	76.6	11	23.4	
Mother's age at child's birth, y					*<.0001*
<20	21	28.0	54	72.0	
20-34	182	51.1	174	48.9	
≥35	45	68.2	21	31.8	
Missing	*7*		*4*		
Mother's smoking during pregnancy					*<.0001*
Yes	42	31.1	93	68.9	
No	213	57.1	160	42.9	
Birthweight for gestational age					*0.0059*
Small (<10th percentile)	132	45.0	161	55.0	
Appropriate/Large (>10th percentile)	116	56.6	89	43.4	
Missing	*7*		*3*		

* 3 missing values for breastfeeding duration

† Parity - number of times mother has given birth

Table 3. Weight Status of Preschool Age Children by Mother's Weight Status*

	Child BMI Category					
	Underweight/Normal (<85th Percentile)		**Overweight (85th - <95th Percentile)**		**Obese (≥95th Percentile)**	
Mother's BMI Category	**n**	**%**	**n**	**%**	**n**	**%**
Total†	401	82.7	48	9.9	36	7.4
Underweight (<18.5)	44	95.6	1	2.2	1	2.2
Normal (18.5 - 24.9)	261	85.6	29	9.5	15	4.9
Overweight (25.0 - 29.9)	65	76.5	9	10.6	11	12.9
Obese (≥30.0)	31	63.2	9	18.4	9	18.4

† Sample size (n=485) excludes those with missing data for mother's BMI and/or child's BMI.

* Spearman correlation coefficient=0.29 ($p < 0.0001$)

BMI - body mass index (kg/m^2). Child's BMI adjusted for age and sex. Criteria for mother's BMI from Centers for Disease Control and Prevention guidelines.

Table 4a. Duration of Breastfeeding and Prevalence of Overweight and Obesity Among Preschool Age Children

Duration of breastfeeding	n	Mean BMI, kg/m^2	Overweight, n (%)	Obese, n (%)
Never	242	15.6	23 (9.5)	22 (9.1)
Ever	244	15.6	25 (10.3)	14 (5.7)
>0 and <6 months	134	15.8	13 (9.7)	11 (8.2)
≥6 months	110	15.3	12 (10.9)	3 (2.7)

* Sample size (n=486) excludes those with missing data for breastfeeding duration and/or child's BMI
Overweight (BMI 85^{th} - $<95^{th}$ percentile); Obese (BMI ≥95th percentile)

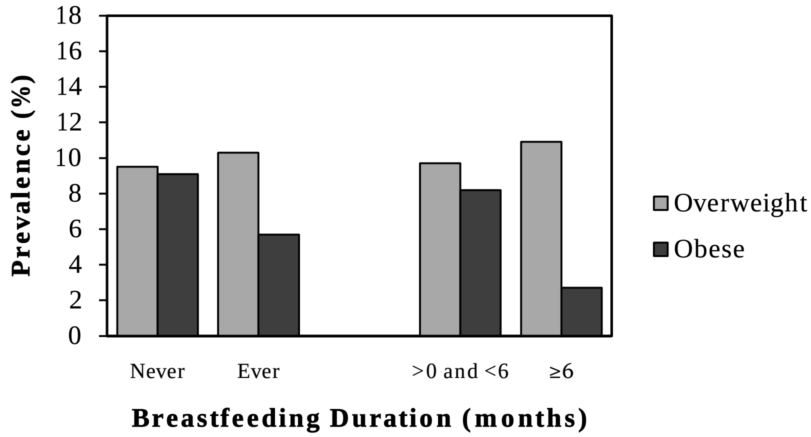
Table 4b. Duration of Breastfeeding and Prevalence of Overweight and Obesity Among Preschool Age Children, Stratified by Sex

	Boys (n=232)				Girls (n=244)			
Duration of breastfeeding	n	Mean BMI, kg/m^2	Overweight, n (%)	Obese, n (%)	n	Mean BMI, kg/m^2	Overweight, n %)	Obese, n (%)
Never	112	15.8	6 (5.4)	18 (16.1)	127	15.4	17 (13.4)	3 (2.4)
Ever	120	15.5	5 (4.2)	8 (6.7)	117	15.7	19 (16.2)	6 (5.1)
>0 and <6 months	61	15.8	1 (1.6)	7 (11.5)	69	15.8	11 (15.9)	4 (5.8)
≥6 months	59	15.2	4 (6.8)	1 (1.7)	48	15.5	8 (16.7)	2 (4.2)

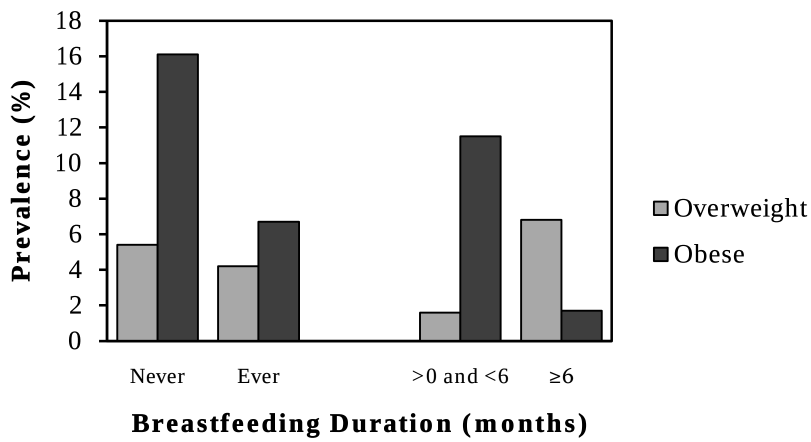
* Sample size (n=476) excludes those with missing data for sex, breastfeeding duration, and/or child's BMI
Overweight (BMI 85^{th} - $<95^{th}$ percentile); Obese (BMI ≥95th percentile)

Figure 1. Prevalence of Overweight and Obesity by Duration of Breastfeeding in Preschool Age Children

A. Total study population



B. Boys only



C. Girls only

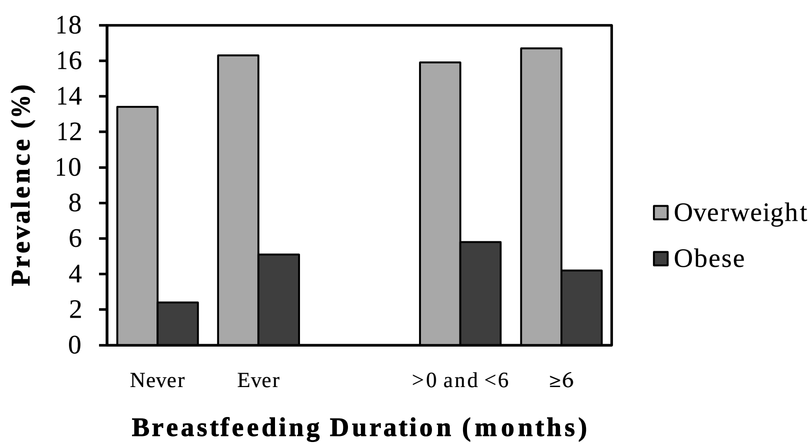


Table 5. Crude and Adjusted Odds Ratios of the Duration of Breastfeeding and Childhood Weight Status

	Overweight (BMI 85th - <95th Percentile)		**Obese (BMI ≥ 95th Percentile)**	
Duration of Breastfeeding	**Crude OR (95% CI)**	**Adjusted OR* (95% CI)**	**Crude OR (95% CI)**	**Adjusted OR* (95% CI)**
Model 1:				
Never (referent)	-	-	-	-
Ever	1.09 (0.60-1.97)	0.72 (0.35-1.50)	0.61 (0.30-1.21)	0.76 (0.32-1.82)
Model 2:				
Never (referent)	-	-	-	-
>0 and <6 months	1.01 (0.49-2.08)	0.62 (0.25-1.53)	0.89 (0.42-1.91)	1.26 (0.47-3.36)
≥6 months	1.08 (0.52-2.27)	0.83 (0.35-1.98)	0.28 (0.08-0.96)	0.34 (0.09-1.34)
Model 3:				
<6 months (referent)	-	-	-	-
≥6 months	1.08 (0.54-2.15)	0.97 (0.45-2.10)	0.29 (0.09-0.95)	0.32 (0.09-0.99)

* Adjusted for small-for-gestational-age (SGA), sex, hospital, maternal pre-pregnancy BMI, smoking during pregnancy

OR - odds ratio

CI - confidence interval

Table 6. Adjusted Odds Ratios* of the Duration of Breastfeeding and Childhood Weight Status, Stratified by Sex

Duration of Breastfeeding	Overweight (BMI 85th - <95th Percentile)		Obese (BMI ≥ 95th Percentile)	
	Boys	Girls	Boys	Girls
Model 1:				
Never (referent)	-	-	-	-
Ever	0.59 (0.15-2.37)	0.77 (0.32-1.82)	0.67 (0.22-2.01)	1.09 (0.22-5.32)
Model 2:				
Never (referent)	-	-	-	-
>0 and <6 months	0.20 (0.02-2.08)	0.79 (0.29-2.18)	1.37 (0.41-4.64)	1.19 (0.21-6.91)
≥6 months	0.84 (0.17-4.20)	0.77 (0.26-2.31)	0.18 (0.02-1.57)	0.65 (0.09-4.73)
Model 3:				
<6 months (referent)	-	-	-	-
≥6 months	1.67 (0.43-6.55)	0.76 (0.29-1.99)	0.16 (0.02-1.22)	0.75 (0.14-3.87)

* Adjusted for SGA, hospital, maternal pre-pregnancy BMI, smoking during pregnancy

Table 7. Adjusted Odds Ratios* of the Duration of Breastfeeding and Childhood Weight Status, Stratified by SGA

Duration of Breastfeeding	Overweight (BMI 85th - <95th Percentile)		Obese (BMI ≥ 95th Percentile)	
	SGA	**AGA and LGA**	**SGA**	**AGA and LGA**
Model 1:				
Never (referent)	-	-	-	-
Ever	0.85 (0.24-3.01)	0.67 (0.28-1.65)	0.72 (0.18-2.95)	0.71 (0.24-2.11)
Model 2:				
Never (referent)	-	-	-	-
>0 and <6 months	0.54 (0.12-2.48)	0.67 (0.22-2.06)	1.56 (0.36-6.76)	1.00 (0.28-3.60)
≥6 months	1.05 (0.18-6.23)	0.81 (0.29-2.23)	†	0.48 (0.11-2.07)
Model 3:				
<6 months (referent)	-	-	-	-
≥6 months	0.91 (0.18-4.65)	1.02 (0.42-2.47)	†	0.49 (0.13-1.82)

* Adjusted for sex, hospital, maternal pre-pregnancy BMI, smoking during pregnancy
† Unable to run logistic model, as so few SGA infants were obese at preschool age

Table 8. Adjusted Odds Ratios* of the Duration of Breastfeeding and Childhood Weight Status, Stratified by Delivery Hospital

Duration of Breastfeeding	Overweight (BMI 85th - <95th Percentile)		Obese (BMI ≥ 95th Percentile)	
	Grady	**Northside**	**Grady**	**Northside**
Model 1:				
Never (referent)				
Ever	0.53 (0.15-1.86)	0.92 (0.35-2.46)	0.83 (0.23-3.05)	0.84 (0.24-2.89)
Model 2:				
Never (referent)				
>0 and <6 months	0.27 (0.03-2.52)	0.86 (0.29-2.59)	1.55 (0.32-7.48)	1.12 (0.31-4.02)
≥6 months	0.86 (0.21-3.44)	0.89 (0.27-2.95)	0.40 (0.05-3.58)	0.37 (0.06-2.20)
Model 3:				
<6 months (referent)				
≥6 months	0.95 (0.24-3.81)	1.04 (0.40-2.68)	0.41 (0.05-3.45)	0.34 (0.07-1.59)

* Adjusted for SGA, sex, maternal pre-pregnancy BMI, smoking during pregnancy