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A Literature Review on Breastfeeding, Head Circumference and Leg Length

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A Literature Review on Breastfeeding, Head Circumference and Leg Length

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Report

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Master of Arts

The University of Texas at Austin

May 2012

Acknowledgements

I would like to express my gratitude to my supervisor Dr. Michele R. Forman for her invaluable guidance and insightful advice during my graduate study. Her enthusiasm in research and her broad and in-depth knowledge in epidemiology have inspired me a lot.

I also would like to thank Dr. Steve Hursting for his kind advice and patient encouragement for my graduate study and this master report.

I am indebted to everyone in Dr. Forman's research group for their various help on my research. A special thank to Yeyi Zhu and Lauren Mangini who provide me with kind advice, support and friendship throughout my years in nutritional sciences department.

Finally, I would like to express my deepest gratitude to my family and Fei for their selfless love, profound understanding and consistent encouragement.

Abstract

A Literature Review on Head Circumference, Leg Length and Breastfeeding

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Head circumference and leg length are two important markers for disease outcomes in later life. It has been reported that head circumference values in childhood may be closely related to the brain development and future intellectual functioning. Short leg length in childhood is suggested to have association with an increasing risk of coronary heart disease, diabetes and cancer. Given the potential childhood length and adult disease linkage, it is important to identify the determinants of childhood head circumference and leg length. Breastfeeding is suggested to be a potential postnatal factor that affects head circumference and leg length. However, some studies examining impacts of breastfeeding on leg length and head circumference in childhood reported inconsistent or null findings, indicating that the association between breastfeeding, head circumference and leg length remains controversial. Here we reviewed several studies

that investigated the relationship between breastfeeding, head circumference and leg length, and in some but not all studies there was controlling for the effects of other potential early life influences, including parental height, prenatal factors and other postnatal factors on head circumference and leg length. Collectively, the illustrations on these relationships would be useful in investigating the leg length/head circumference-later disease outcomes associations.

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INTRODUCTION

In 1997, the American Academy of Pediatrics recommended that US infants should be exclusively breast-fed for the first six months of life. Thereafter complementary foods should be introduced with breastfeeding continuing through the first year of life. Breast milk provides nutrients required at this age in a form that is easy to digest. Besides the carbohydrate, protein and fat that are unique to breast milk, it also contains a range of bioactive components, including digestive enzymes, growth factors, hormones and anti-inflammatory factors (Hamosh 2001). Nutrient intake and growth of matched cohorts of infants who were either breastfed (n=73) or formula-fed (n=46) for at least 12 months were examined and compared in the DARLING Study (Heinig et al., 1993). In this study, breast-fed infants had lower intakes of both energy and protein than formula-fed infants: these differences in energy intake might have persisted throughout the first year of life, mainly due to the differences in energy obtained from human milk or formula (Heinig et al., 1993). Breast-fed infants with lower energy intake, at the same time, had significantly lower weight gain compared with formula-fed infants (Heinig et al., 1993). Body length gains, however, were generally not significantly different between breast-fed and formula-fed infants (Dewey et al., 1992).

As an important component of standing height, leg length was proposed to be a more sensitive indicator of childhood circumstances, such as socio-economic and dietary exposures during growth than height five decades ago (Thompson and Duncan, 1954). Poor environmental conditions during early childhood would result in short adult stature as well as relatively short leg length (Gunnell et al., 1998b; Wadsworth et al., 2002). When early environmental conditions are improved, however, increases in adult stature have been demonstrated to be largely due to increases in leg length, rather than the trunk

length (Cole, 2000; Dangour et al., 2002). Leg length is also an important marker for growth before puberty, with more growth observed than that in trunk length (Dangour et al., 2002). Several studies have reported that short leg length in childhood might be associated with an increasing risk of coronary heart disease (Gunnell et al., 1998b), diabetes (Lawlor et al., 2002) and cancer (Strauss 2000), providing evidence for the impact of early life markers of height on later health.

Another important measure in the assessment of growth development and nutrition status in children is head circumference, which is a critical indicator of brain development. Several studies have found that head circumference might be related to specific disorders and diseases, including autism (Nordahl et al., 2011) and Alzheimer's disease (Schofield et al., 1997).

Genetic and environmental factors are important variables that might be related to birth outcomes, childhood growth, and the childhood length-later disease linkage (Rona et al., 1995; Li et al., 2007). For a better understanding of the possible childhood length and adult disease linkage, it is critical to identify the determinants of childhood leg length and head circumference.

In this review, we summarize several studies that examine the effects of breastfeeding on childhood leg length/trunk length and head circumference, and discuss the effects of other potential early life influences, including parental height, prenatal factors and other postnatal factors on leg length/trunk length and head circumference.

METHODOLOGY

IDENTIFICATION OF STUDIES

Because literature that evaluated the effects of breastfeeding on leg length and/or head circumference did not always describe the criteria for exclusivity or duration of breastfeeding, no requirement for exclusively breastfeeding was a set for inclusion in the literature review of the effects of breastfeeding on leg length or head circumference. Specifically, two initial inclusion criteria for literature on the association between breastfeeding and leg length and head circumference were: 1) the primary outcome measure was a widely applied method, that is, either measuring the leg length directly or obtaining the leg length by subtracting sitting height from standing height, 2) a relatively big sample size (i.e. at least 20 infants in each feeding group), given the fact that the smaller the sample size, the higher the risk of statistical insignificance.

Candidate studies were identified by a search of PUBMED database for the period from 1980 to now. [“Head circumference” or “leg length” or “sitting height” AND “breastfeeding”] were used as main search strategy. In total, nine studies met the initial inclusion criteria. All included studies were observational studies, as it is not feasible to randomly assign infants to be breast-fed or formula-fed. For each study, the study design, relevant study attributes and results are summarized and listed in Table 1.

POTENTIAL EARLY LIFE INFLUENCES

The definition of breastfeeding, leg length and head circumference in each study was summarized in Tables 1-2. Besides breastfeeding, other potential early life influences are also discussed to assess their effects on leg length, trunk length and head circumference. These factors include: parental height (paternal height and maternal

height), birth weight, maternal smoking during pregnancy, birth order, gestational age, family size, household crowding and socioeconomic status.

MEASURES

Anthropometry

Of the five studies on breastfeeding and leg length in this review, leg length was either measured directly, as the distance from the heel to the summit of the iliac crest to the nearest 0.1 centimeter (Martin et al., 2002; Whitley et al., 2008), or calculated by subtracting trunk length, which is represented by sitting height, from standing height (Wadsworth et al., 2002; Li et al., 2007; Victora et al., 2003). In the 1946 British national birth cohort, leg length was measured once at a home visit by a well-trained research nurse，when subjects were 43 years old (Wadsworth et al., 2002). In the 1958 British birth cohort, participants' body height and sitting height at 45 years old were measured once by trained medical personnel. Leg length at 45 years old was then calculated as the difference between standing height and sitting height (Li et al., 2007). In the Boyd Orr cohort study, childhood leg length was measured once at the survey clinics when the subjects in the study were aged 2-14 years 9 months. Information regarding whether the measurer was trained was not reported (Martin et al., 2002; Whitley et al., 2008). Adult leg length was self-reported once in the questionnaires as inside leg measurement (Martin et al., 2002). In a birth cohort study from Brazil, a single anthropometrist measured standing height and sitting height once when the subjects were 18 year old. Let length was calculated as the difference between standing and sitting height (Victora et al., 2003).

Of the four studies on breastfeeding and head circumference in this review, head circumference was measured as the distance from above the eyebrows and ears and around the back of the head (Kramer et al., 2003; Kramer et al., 2004; Dewey et al.,

1992; Donma et al., 1997). Two specially trained nurses measured head circumference once at each monthly visit with one person acting as a recorder and the other as a measurer (Donma et al., 1997). In the study reported by Kramer et al., head circumference was measured at birth and then at each polyclinic visit at 1, 2, 3, 6, 9, and 12 months for one time. The measurement techniques were not standardized (Kramer et al., 2003; Kramer et al., 2004). In the DARLING Study, head circumference was measured by four trained assistants once at monthly home visits from 1 to 18 months. The measurement techniques were standardized based on the procedure described by WHO (Dewey et al., 1992).

Prenatal and Postnatal Factors

Information on parental height that served as the markers of genetic factors, if applicable, was obtained by self-report (Wadsworth et al., 2002; Li et al., 2007;). Maternal smoking during pregnancy was recorded as non-smokers, 0-14, or more than 15cigarettes per day (Victora et al., 2003), or smoking more than 1 cigarette per day after the fourth month of pregnancy (Li et al., 2007). Birth order, family size, household crowding, socioeconomic status and parental divorce were obtained from the questionnaires in studies (Martin et al., 2002; Li et al., 2007; Victora et al., 2003; Wadsworth et al., 2002).

RESULTS AND DISCUSSION

BREASTFEEDING AND LEG LENGTH

Study from Brazil

The effect of breastfeeding duration on ratio of leg length to total height was evaluated among 18 year old male Brazilians in the Pelotas birth cohort study (Victora et al., 2003). All 5914 infants born alive during 1982 were recruited. Breastfeeding duration information was collected at the 1983, 1984 and 1986 follow-ups. Two categories of infant feeding were considered: total breastfeeding duration and predominant breastfeeding duration. Total breastfeeding duration was categorized based on months, ranging from less than 1 month to 12 months or more. Given the situation that all recruited subjects also received herbal teas or water since the first week of life and exclusive breastfeeding was rare in this population, it was thus categorized as predominant breastfeeding. Therefore, the age was recorded as the duration of predominant breastfeeding when there was introduction of foods other than breast milk, water or herbal teas, ranging from less than 1 month to 4 months or more. Anthropometric measurements were conducted on 2250 subjects in 2000, when subjects were 18 year. Leg length was obtained by subtracting measured sitting height from measured standing height. Neither the total breastfeeding groups nor the predominant breastfeeding groups were significantly associated with ratio of leg length to total height in 18 years old male subjects after adjustments for family income, maternal education, maternal BMI, maternal smoking during pregnancy, gestational age and birth weight (P value =0.52).

This study has some limitations. First, researchers did not conduct the same study on female subjects. Second, leg length was assessed as the difference between standing

height and sitting height, instead of the direct measurement of leg length. Therefore, given the associated measurement error with both standing height and sitting height, leg length value is likely to have greater error than trunk length, which may influence the possible association between breastfeeding and leg length.

Studies from the United Kingdom

Martin and his colleagues (Martin et al., 2002) examined the relationship between breastfeeding and the components of height and several socioeconomic variables in the Boyd-Orr cohort study, which included a total of 4999 children aged 0-19 years old surveyed between 1937 and 1939 in Britain. There are two infant feeding patterns considered: breastfeeding and bottle-feeding. For breastfed infants, the duration was categorized as: two weeks to less than two months, two months to less than six months, six months to less than 12 months, and 12 months or more. Leg length was measured directly as the distance from the floor to the summit of iliac crest. The information on adult leg length was collected in the follow-up reported anthropometry questionnaire. Breastfeeding seems to be more strongly associated with childhood leg length in boys (mean difference between breast-fed and bottle-fed subjects: 0.23, 95% CI: 0.10 to 0.36) than in girls (mean difference between breast-fed and bottle-fed subjects: 0.13, 95% CI: 0.01 to 0.26) among 2 years to 14 years 9 months age group, but there was no significant gender difference identified (p=0.28). The positive association of breastfeeding with leg length was higher in those over 8 years old than in those under 8 among the 2 years to 14 years 9 months age group. In adult male subjects, the association of breastfeeding with self-reported adult leg length in the fully adjusted models (mean difference between breast-fed and bottle-fed subjects: 1.25, 95% CI: 0.09 to 2.40, p=0.034) was stronger than that in female subjects, which was not significant (mean difference between breast-fed

and bottle-fed subjects: 1.17, 95% CI: -0.08 to 2.42, p=0.067). One limitation of this study is the information on adult anthropometry including height, inside leg measurement and weight was self-reported, which might bring some bias, as people tend to over report their height and inside leg measurement. Researchers suggested that the possible mechanism behind the association between breastfeeding and height above 8 years of age might be the effects of breastfeeding on growth tempo (timing of puberty) throughout childhood, thus breastfed children enter puberty earlier and become taller (Graffar and Corbier., 1972). The findings indicated that leg length was most associated with breastfeeding, as the component of the childhood height, and thus might be more sensitive to impacts of pre-pubertal growth compared with trunk length (Martin et al., 2002).

The relationships between anthropometry variables, such as height, trunk length, leg length, and breastfeeding and other childhood exposures were assessed in 2376 subjects aged 2 to 14 years in the Boyd Orr cohort (Whitley et al., 2008). Breastfeeding was defined as ever or never breastfeeding without specific duration information as 35% of the participants had unknown duration. Leg length was measured as the distance from the floor to the summit of the iliac crest. Breastfeeding was associated with leg length in both sexes (boys: n= 1061, change (95% CI) in anthropometric z-score: 0.23, 95% CI: 0.10 to 0.36, p< 0.01; girls: n=1143, change in anthropometric z-score: 0.19, 95%CI: 0.06 to 0.32, p<0.01), and the gender difference was not significant. Pairwise correlations between the anthropometric z-scores showed that height was most correlated with leg length, with the correlation coefficient of 0.89 in both sexes combined. The associations between childhood anthropometric measures and the breastfeeding were also reported separately for subjects aged less than eight and eight or more years old at the time of anthropometric measurements. Strong association was shown in both age groups in boys

(< 8 group: change (95% CI) in anthropometric z-score: 0.31, 95% CI: 0.12 to 0.50, p< 0.01; ≥ 8 group: change (95% CI) in anthropometric z-score: 0.30, 95% CI: 0.12 to 0.48, p< 0.01), whereas breastfeeding seemed only related to leg length in over eight but not younger than eight years old age group in girls (< 8 group: change (95% CI) in anthropometric z-score: 0.11, 95% CI: -0.07 to 0.30, p> 0.05; ≥ 8 group: change (95% CI) in anthropometric z-score: 0.30, 95% CI: 0.12 to 0.49, p< 0.01). One explanation to characterize this observation might be that breastfeeding does influence the growth tempo in girls but not boys. Therefore, girls who were breastfed might enter puberty earlier between 8 and 14 years and were taller than those bottle-fed, but not taller at earlier ages. Another explanation of these results is that they may occur due to chance. Given the strength of the associations of anthropometric measures and other childhood environment factors, the authors suggested that leg length was most strongly associated with childhood environment in 2 to 14 years age group (Whitley et al., 2008).

The limitations of this study (Whitley et al., 2008) include the anthropometric measurement errors, which might lead to wider confidence intervals. Second, several important confounders, such as the birth weight, gestational age, and birth length were not taken into account. Third, due to the lack of information on breastfeeding duration, the definition of breastfeeding is vague in this study and thus might attenuate the possible association between breastfeeding and anthropometric measures.

The effects of breastfeeding and other environmental factors on adult leg length and trunk length were investigated in the 1946 British national birth cohort (Wadsworth et al., 2002), which included children born in England, Wales and Scotland in one week in March 1946 and followed to 53 years old. The sample size was N=2,879 in this analysis by age 43 years, when outcome variables were measured and recorded. Of the total sample size, 2153 subjects were breastfed. Breastfeeding was categorized in the

study as ever or never breastfeeding. Leg length was obtained as the difference between standing height and trunk length at a home visit when the subjects were 43 years old. The results indicated that ever breastfeeding was related to leg length at age 43 years after adjusting for confounders, including parental heights, birth weight, energy intake at age 4 years, serious illness before 6 years, weight and height at 4 years, and non-manual father's social classes (regression coefficient: 0.10, 95% CI: 0.01 to 0.19, p=0.04), suggesting that leg length might be a marker of early life environment (Wasworth et al., 2002). One limitation of this study is the leg length was calculated as the difference between standing height and sitting height, which led to greater errors compared with direct measurement of leg length. The second limitation is no information regarding breastfeeding duration, which attenuated the strength of the results to some extent.

Li, Dangour and Power (Li et al., 2007) evaluated the influences of prenatal and postnatal factors and parental height on adult leg length at 45 year in the 1958 British birth cohort. This cohort included the population born in England, Scotland and Wale in one week in March 1958 and followed to 45 years old (N=9,377 in the 45 years analysis). Two categories of infant feeding were considered: never and ever breastfeeding, and the latter was further stratified into breastfed less than 1month or longer. Information on exclusivity of breastfeeding was not reported in this study. Leg length at 45 years old was calculated as the difference between standing height and sitting height. Participants' standing and sitting height at 45 years old were measured to the nearest 0.1 cm. After adjusting for parental height, birth weight, family size and social class, breastfeeding was not associated with height, leg length and trunk length at 45 years old. This result was inconsistent with the findings in previous studies showing an effect of breastfeeding on adult leg length (Wadsworth et al., 2002). The authors suggested that the inconsistencies in results might be attributed to the change with constitutions of alternatives to

breastfeeding, as the quality of substitutes to breastfeeding in the 1920s and 1930s may not be relevant change a lot compared to that in the 1950s (Martin et al., 2002; Li et al., 2007).

The limitation of this study includes the measurement error in leg length, which was calculated as the difference between standing height and sitting height. In addition, precise information regarding breastfeeding duration was not reported, and thus the effects of breastfeeding on leg length cannot be fully assessed.

HEAD CIRCUMFERENCE

Study from the United States

The growth patterns of breast-fed infants and formula-fed infants during the first 18 months were all introduced to solid foods at a similar age. Data on head circumference, weight and length were collected monthly over the first 18 months in the DARLING study (Dewey et al., 1992). There were two infant feeding patterns considered: breast-fed group with 46 subjects and formula-fed group with 41 subjects. Those who breast-fed for at least 12 months, and did not feed more than 10mL/d of other milk or formula during the first 12 months were categorized as breast-fed. Comparatively, those who were not breast-fed for more than 3 months (except the ones who stopped breastfeeding due to perceived lactation failure) were considered as formula-fed. Head circumference was measured following standard procedures (Fomon 1977). The results showed, however, that there were no significant differences in head circumference between breast-fed and formula-group from birth to 18 months in both sexes (Dewey et al., 1992).

Study from Turkey

The influence of infant feeding patterns on head circumference among Turkish infants during their first six months of life was investigated in one Turkish study (Donma and Donma, 1997). 172 healthy newborn infants (boys: n=94, girls: n=78) who were all born between 1992 and 1995 and had no problems during the perinatal period were included in the study. No premature newborns, twins and low birth weight infants were included in the study. Three infant feeding patterns were considered: breast-fed group (n=62), with infants exclusively breast fed for the first six months of life, mixed-fed group (n=58), with infants given supplementary foods from the fifteenth day in addition to breast milk, and formula-fed group (n=52), with infants no longer breast-fed for various reasons after 10 days at most and fed formula from birth. Head circumference was measured at each monthly follow-up visit following the standard procedures (Fomon 1977). There was no significant difference in head circumferences among the three groups at birth (boys: BF 35.2 ± 0.1, MF 35.1 ± 0.1, FF 35.0 ± 0.1 cm; girls: BF 35.0 ± 0.1, MF 34.9 ± 0.1, FF 34.8 ± 0.1 cm). Apparently bigger head circumferences for both boys and girls were found in the BF group (38.3 ± 0.1 and 37.9 ± 0.1 cm for boys and girls respectively) than the other two (MF 36.7 ± 0.1, FF 36.6 ± 0.1cm for boys; MF 36.5 ± 0.1,FF 36.4 ± 0.1cm for girls) at the end of first month ($P<0.05$). No significant differences in head circumference were found, however, among the three feeding groups in the subsequent four months. The head circumference value of infants in BF group at the sixth month then (43.7 ± 0.1 and 42.9 ± 0.1 cm for boys and girls respectively) was significantly higher than those of infants in MF and FF groups at the sixth month (MF 42.6 ± 0.1, FF 42.5 ± 0.1cm for boys; MF 41.4 ± 0.1, FF 41.5 ± 0.1cm for girls). The head circumference-for-age values of infants in MF and FF at the sixth month were well below the standard curve as well ($P < 0.05$). The authors suggested that one explanation

for these results might be due to the introduction of supplementary foods early on i.e. from the fifteenth day, and thus infant growth and development was affected by early supplementation (Donma and Donma, 1997).

Studies from Canada

An observational cohort study nested within a large randomized trial compared the effect of 3-months with 6-months of exclusive breastfeeding on growth variables, including head circumference, weight and length (Kramer et al., 2003). 3-months of exclusive breastfeeding was defined as infants who were not given any supplementary foods other than breast milk in the first three months. Infants were classified as 6-months of exclusive breastfeeding if they were not given any supplementary foods other than breast milk in the first six months. Head circumference was measured at birth and then follow- up visits at 3rd, 6th, 9th, 12th months following the standard procedures (Fomon 1977). No significant differences were found in head circumference between 3-month and 6-month of exclusive breastfeeding group at 3, 6, 9 month. Mean head circumference was significantly greater in the 6-mo of exclusive breastfeeding group at 12 month than that in the 3-mo group (47.06 ± 1.49 and 47.25 ± 1.50 cm for 3-mo and 6-mo respectively, the difference was 0.19 cm), but the possibility that this significant difference might occur by chance cannot be excluded (Kramer et al., 2003). Two limitations existed in this study. First, socioeconomic status was not assessed in this study. Second, because the anthropometric measurements were not standardized among study sites, the strength of the results might get attenuated (Kramer et al., 2003).

In 2004, another study working on the same large randomized trial was published (Kramer et al., 2004). The influences of feeding variables on infant head circumferences were analyzed within the intervals 1 to 3, 3 to 6, 6 to 9 and 9 to 12 months throughout the

first year of life in this observational cohort study nested within the same large randomized trial, which included a total of 17,046 infants in the study (Kramer et al., 2004). Breastfeeding only was defined as the reference group. The other feeding variables included mixed-breastfeeding, with breast milk plus formula or other milk, formula/other milk only, water, juice/other liquids, cereal and other solids. Head circumference was measured at birth and then follow- up visits at 3rd, 6th, 9th, 12th months. A strong negative association between cereal intake and head circumference in the 3 to 6 mo interval was observed. The limitations of this study were similar as those mentioned above in another observational study nested within the randomized trial. The authors suggested that long-term follow-up studies might be needed to study the association between exclusive breastfeeding and head circumference (Kramer et al., 2004).

CONCLUSION

Overall, the relationship between breastfeeding and leg length and head circumference is still inconclusive. The nine studies discussed here have markedly different definitions of the breastfeeding, breastfeeding duration, leg length, age group and control for confounding variables. For the association between breastfeeding and leg length, two studies reported a positive association between childhood leg length and breastfeeding (Whitley et al., 2008; Martin et al., 2002; Wadsworth et al., 2002), one study reported that ever breastfeeding was related to adult leg length at 43 years old, while two studies reported no significant effect between leg length and breastfeeding (Li et al., 2007; Victora et al., 2003). For the relationship between breastfeeding and head circumference, except one study conducted in Turkey (Donma and Donma., 1997), none of the other three had significant differences between breast-fed and formula-fed infants (Dewey et al., 1992; Kramer et al., 2003; Kramer et al., 2004).

Breastfeeding provides a good balance of nutrients for infant growth and development, and offers protective effects against human diseases in later life. Head circumference is considered as a parameter of brain growth as well as nutritional sufficiency during infancy (Donma and Donma., 1997). Leg length is an important marker for growth before puberty (Dangour et al., 2002) and childhood leg length was reported to be associated with increasing risk of human diseases. Therefore, it is crucial to characterize the association between breastfeeding, head circumference and leg length. In the future, long term follow-up studies in both sexes with a relatively big sample size, a clear definition of breastfeeding and breastfeeding duration, and standard anthropometric measurement of leg length and head circumference are needed to provide

better understanding of the relationship between breastfeeding, head circumference and leg length.

List of Tables

Table 1. Studies Included in the Review of Breastfeeding and Head Circumference

First Author, Publication Year	Country	Study Design	Sample Size	Definition of Breastfeeding (BF)	Definition of Head Circumference (HC)	Results
Donma, 1997	Turkey	Observational cohort study; Subjects were followed from birth to 6 months.	172	BF group: Exclusively breastfeeding for the first 6 months of life; Mixed-fed group: supplementary foods were introduced from the fifteenth day in addition to breast milk; formula fed group: didn't receive human milk or no longer breast-fed after 10 days at most	Head circumference was measured by laminated tape at each visit. The maximal circumference was measured by placing the tape posteriorly, and anteriorly above the eyebrow, with zero end on the lateral aspect of the head. HC was measured to the nearest millimeter.	At 1st month, head circumference-for-age values of infants in MF and FF group were smaller than that in BF group
Dewey, 1992	USA	Cohort study; Subjects were followed from birth to 18th months	87	BF: breastfeeding throughout 1st year; FF: mothers didn't plan to breastfeed, or to wean the child completely by 3 mo of age. Those who terminated BF due to perceived lactation failure were not eligible.	Head circumference was measured via a paper insertion tape to the nearest millimeter, following the standard procedure.	There was no significant differences in head circumference between breastfeeding group and formula-feeding group from 0 to 18 months

Table 1. Studies Included in the Review of Breastfeeding and Head Circumference

First Author, Publication Year	Country	Study Design	Sample Size	Definition of Breastfeeding(BF)	Definition of Head Circumference (HC)	Results
Kramer, 2003	Canada	Observational cohort study; Subjects were followed from birth to 12 months.	3,483	Exclusively BF at 3 mo: if feeding information obtained at 1, 2, and 3 mo indicated that no liquid or solid foods other breast milk were introduced to the infants; VS exclusively BF at 6 mo: in addition to the above criteria, infants didn't receive any other liquid or solid foods at the 6-mo visit	Standard measurement of head circumference	There is a significantly higher head circumference at 12 month in the 6-mo exclusively BF group
Kramer, 2004	Canada	Observational cohort study nested within a large cluster-randomized trial; Subjects were followed from birth to 12 months	17,046	Breast milk only, mixed BF (breast milk plus formula or other milk), formula only, formula plus whole cow's or other milk, and whole cow's or other milk only, within 1-3, 3-6, 6-9, 9-12 mo;	Standard measurement of head circumference	There were no consistent effects of formula and other milk, cereals, or other solid or liquids on HC.

Table 2. Studies Included in the Review of Breastfeeding and Leg Length

First Author, Publication Year	Country	Study Design	Sample Size	Definition of Breastfeeding(BF)	Definition of Leg Length	Results
Wadsworth, 2002	UK	Longitudinal Study; Subjects were followed from birth to 53 yrs of age.	3,262	Ever Breastfeeding; Never Breastfeeding	Leg length was calculated as the difference between standing and sitting height(= trunk length)	Leg length was associated with BF at 4 years, but this association got weakened by adding the height factor at 4 yrs.
Li, 2007	UK	Longitudinal Study; live birth Subjects were followed at age7 and 45 years old	5,882	BF<1 mo, BF >1 mo or longer, never BF; exclusivity of BF was not recorded	Leg length was calculated as the difference between standing and sitting height(= trunk length)	There was no association between BF and leg length at 7 and 45 years old after adjustment for other factors.
Martin, 2002	UK	Boyd Orr Cohort Study; Subjects were followed between 1937 and 1939.	2,995	BF: 2 wks-2mo, 2mo-6mo, 6-12 mo, more than 12 mo; bottle-feeding	Leg length was measured as the distance from the ground to the summit of the iliac crest.	Leg length was more strongly associated with breastfeeding than trunk length.

Table 2. Studies Included in the Review of Breastfeeding and Leg Length

First Author, Publication Year	Country	Study Design	Sample Size	Definition of Breastfeeding(BF)	Definition of Leg Length	Results
Whitley, 2008	UK	Boyd Orr cohort was cross-sectional study; Subjects were followed during 1937-1939	2,376	Ever BF, Never BF; duration of BF were collected, but 35% of BF had unknown duration	Leg length was measured as the distance from the floor to the summit of the iliac crest.	Leg length was associated with breastfeeding in both sexes.
Victora, 2003	Brazil	Prospective Cohort Study ; Male subjects were followed from birth to 18 years old	2,250	Duration of total BF < 1 mo, 1 -2 mo,3 -5 mo, 6-8 mo, 9-11 mo, 12 mo or more;	Leg length was obtained by subtracting sitting height from standing height	There was no association between BF and leg length at 18 years old in men after adjustment for other factors.

REFERENCES

Birch E, Birch D, Hoffman D, Hale L, Everett M, Uauy R. 1993. Breast feeding and optimal visual development. Journal of Pediatric Ophthalmology & Strabismus 30(1):33-38.

Bronner YL, Paige DM. 1992. Current concepts in infant nutrition. Journal of Nurse-Midwifery 37(2):S43-S58.

Cole TJ. 2000. Secular trends in growth. Proceedings of the Nutrition Society 59(2):317-324.

Dangour AD, Schilg S, Hulse JA, Cole TJ. 2002. Sitting height and subischial leg length centile curves for boys and girls from Southeast England. Annals of Human Biology 29(3):290-305.

Dewey KG. 1998. Cross-cultural patterns of growth and nutritional status of breastfed infants. American Journal of Clinical Nutrition 67(1):10-17.

Dewey KG, Heinig MJ, Nommsen LA, Lonnerdal B. 1991. Adequency of energy-intake among breast-fed infants in the DARLING study-relationships to growth velocity, morbidity, and activity levels. Journal of Pediatrics 119(4):538-547.

Dewey KG, Lonnerdal B. 1986. Infant self-regulation of breast milk intake. Acta Paediatrica Scandinavica 75(6):893-898.

Donma MM, Donma O. 1997. The influence of feeding patterns on head circumference among Turkish infants during the first 6 months of life. Brain & Development 19(6):393-397.

Golding J, Rogers IS, Emmett PM. 1997. Association between breast feeding, child development and behaviour. Early Human Development 49:S175-S184.

Gunnell D. 2002. Commentary: Can adult anthropometry be used as a 'biomarker' for prenatal and childhood exposures? International Journal of Epidemiology 31(2):390-394.

Gunnell DJ, Smith GD, Frankel SJ, Kemp M, Peters TJ. 1998. Socio-economic and dietary influences on leg length and trunk length in childhood: a reanalysis of the Carnegie (Boyd Orr) survey of diet and health in prewar Britain (1937-39). Paediatric and Perinatal Epidemiology 12:96-113.

Hamosh M. 2001. Bioactive factors in human milk. Pediatric Clinics of North America 48(1):69-+.

Harder T, Bergmann R, Kallischnigg G, Plagemann A. 2005. Duration of breastfeeding and risk of overweight: A meta-analysis. American Journal of Epidemiology 162(5):397-403.

Hediger ML, Overpeck MD, Kuczmarski RJ, Ruan WJ. 2001. Association between infant breastfeeding and overweight in young children. Jama-Journal of the American Medical Association 285(19):2453-2460.

Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. 1993. Energy and protein intakes of breast-fed and formula-fed infants during the 1st year of life and their association with growth velocity-the DARLING study. American Journal of Clinical Nutrition 58(2):152-161.

Jain A, Concato J, Leventhal JM. 2002. How good is the evidence linking breastfeeding and intelligence? Pediatrics 109(6):1044-1053.

Koletzko B, von Kries R, Monasterolo RC, Subias JE, Scaglioni S, Giovannini M, Beyer J, Demmelmair H, Anton B, Gruszfeld D and others. 2009. Infant Feeding and Later Obesity Risk. Early Nutrition Programming and Health Outcomes in Later Life: Obesity and Beyond 646:15-29.

Lawlor DA, Ebrahim S, Smith GD. 2002. The association between components of adult height and Type II diabetes and insulin resistance: British Women's Heart and Health Study. Diabetologia 45(8):1097-1106.

Li L, Dangour AD, Power C. 2007. Early life influences on adult leg and trunk length in the 1958 British birth cohort. American Journal of Human Biology 19(6):836-843.

Martin RM, Gunnell D, Smith GD. 2005a. Breastfeeding in infancy and blood pressure in later life: Systematic review and meta-analysis. American Journal of Epidemiology 161(1):15-26.

Martin RM, Middleton N, Gunnell D, Owen CG, Smith GD. 2005b. Breast-feeding and cancer: The Boyd Orr cohort and a systematic review with meta-analysis. Journal of the National Cancer Institute 97(19):1446-1457.

Martin RM, Smith GD, Mangtani P, Frankel S, Gunnell D. 2002. Association between breast feeding and growth: the Boyd-Orr cohort study. Archives of Disease in Childhood 87(3):193-201.

Michels KB, Willett WC, Graubard BI, Vaidya RL, Cantwell MM, Sansbury LB, Forman MR. 2007. A longitudinal study of infant feeding and obesity throughout life course. International Journal of Obesity 31(7):1078-1085.

Morrowtlucak M, Haude RH, Ernhart CB. 1988. Breastfeeding and cognitive-development in the 1st 2 years of life. Social Science & Medicine 26(6):635-639.

Nordahl CW, Lange N, Li DD, Barnett LA, Lee A, Buonocore MH, Simon TJ, Rogers S, Ozonoff S, Amaral DG. 2011. Brain enlargement is associated with regression in preschool-age boys with autism spectrum disorders. Proceedings of the National Academy of Sciences of the United States of America 108(50):20195-20200.

Owen CG, Whincup PH, Odoki K, Gilg JA, Cook DG. 2002. Infant feeding and blood cholesterol: A study in adolescents and a systematic review. Pediatrics 110(3):597-608.

Reynolds A. 2001. Breastfeeding and brain development. Pediatric Clinics of North America 48(1):159-+.

Rogan WJ, Gladen BC. 1993. Breast-feeding and cognitive-development. Early Human Development 31(3):181-193.

Rollandcachera MF, Deheeger M, Akrout M, Bellisle F. 1995. Influence of macronutrients on adiposity development-a follow-up study of nutrition and growth from 10 months to 8 years of age. International Journal of Obesity 19(8):573-578.

Singhal A, Cole TJ, Fewtrell M, Lucas A. 2004. Breastmilk feeding and lipoprotein profile in adolescents born preterm: follow-up of a prospective randomised study. Lancet 363(9421):1571-1578.

Strauss RS. 2000. Adult functional outcome of those born small for gestational age - Twenty-six-year follow-up of the 1970 British Birth Cohort. Jama-Journal of the American Medical Association 283(5):625-632.

Victora CG, Adair L, Fall C, Maternal. 2008. Maternal and child undernutrition: consequences for adult health and human capital (vol 371, pg 340, 2008). Lancet 371(9609):302-302.

Wadsworth MEJ, Hardy RJ, Paul AA, Marshall SF, Cole TJ. 2002. Leg and trunk length at 43 years in relation to childhood health, diet and family circumstances; evidence from the 1946 national birth cohort. International Journal of Epidemiology 31(2):383-390.

Whitley E, Gunnell D, Smith GD, Holly JMP, Martin RM. 2008. Childhood circumstances and anthropometry: The Boyd Orr cohort. Annals of Human Biology 35(5):518-534.