Infant milk feeding and bone health in later life: findings from the Hertfordshire Cohort Study

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Abstract

Purpose

Using data from the Hertfordshire Cohort Study (HCS), this study aims to examine the effect of infant milk feeding on bone health in later life by comparing the effect of breastfeeding and bottle feeding on lumbar spine and femoral neck bone mineral content (BMC) and bone mineral density (BMD).

Methods

Information about infant milk feeding, birth weight (kg) and weight at 1 (kg) was collected by health visitors between 1931 and 1939 in Hertfordshire. BMC and BMD measurements were taken by DXA scan between 1998-2004. Linear regression models adjusted for conditional weight at 1, age at DXA scan, sex, adult BMI, smoking behaviour, alcohol consumption, physical activity, dietary calcium, and prudent diet score.

Results

Infant milk feeding was significantly associated with lumbar spine BMD (b=-0.028, 95% CI -0.055, -0.000, p-value: 0.047) in males. On average, males who consumed breastmilk alternatives in infancy had lower lumbar spine BMD measurements than those who were fed only breastmilk.These associations remained significant in fully adjusted models. There were no significant associations between infant milk feeding and bone health for females.

Conclusions

Significant associations between infant milk feeding and lumbar spine BMD in males indicate that breastmilk may be protective for the bone health of male babies. The evidence presented here underscores the potential lifelong benefits of breastfeeding and may highlight the differences between osteoporotic risk factors for males and females.

Keywords

Breastfeeding; bottle feeding; osteoporosis; bone and bones

Mini abstract

Using data from the Hertfordshire Cohort Study, this study examined the effect of breastfeeding and bottle feeding on adult lumbar spine and femoral neck bone mineral content (BMC) and bone mineral density (BMD). Type of infant milk feeding was significantly associated with lumbar spine BMD in males.

Introduction

As evidence in support of the developmental origins hypothesis of health grows, particular attention has been given to how adult bone health and its associated outcomes are related to childhood diet and environment, as early childhood is a period during which bone growth patterns are established. Infant nutrition is a potential mediator of adult bone health, because type of infant feeding has been shown to influence early growth, and rate of early growth sets the stage for peak attainment of bone mass[1]. Indeed, increased weight gain over the first year of life has been associated with better bone health in adulthood[2-4]. In a study of the bone phenotypes of the 1946 British birth cohort, faster growth (in both weight and height) in childhood was associated with greater bone strength in the sixth decade of life[4], meaning that breast or bottle feeding practices may have implications for bone health in childhood and beyond[20].

Research into the relationship between infant feeding and infant growth has linked cow's milk to faster weight gain over the first year of life[5-8] and breastfeeding with longer leg length in childhood[9, 10] and adulthood[9, 11]. While modern formula milk has also been associated with faster weight gain over the first year[8], breastfeeding has been positively related to infant length[9, 10] and with potential changes to bone cell programming which could result in higher bone mass in adulthood[12]. Infant feeding practices have been linked to height[11, 13], bone mineral density[14, 15], bone mass[16-18], and body composition[6, 8, 10, 19] in children and adolescents, with associations between breastfeeding and bone health outcomes differing in direction depending on the age and cohort membership of the children studied. Breastfeeding was found to be positively associated with bone mass in children at both 8 years old and 16 years old in Tasmania[17, 18], and negatively associated with lumbar spine bone area and bone mineral content (BMC) and total body bone mineral density (BMD) in Finnish males at 32 years old[15]. In one study of adult bone health, the influence of early life indicators, such as infant feeding and birth weight, was attenuated by adult body size[14], further indicating the need to examine infant milk feeding and bone health in later life, as this association could vary with body size throughout the lifecourse.

Despite the relationships between type of infant milk consumed, weight gain in infancy, adult BMI, and bone health across the lifecourse, there has been little research utilizing these measures in later life. Very few studies have examined the relationship between infant milk feeding and adult BMC and BMD, and to our knowledge, none have investigated this link in the sixth and seventh decades of life. This study aims to examine the effect of infant milk feeding on bone health in later life by comparing the effects of breast milk feeding and bottle feeding on lumbar spine and femoral neck BMC and BMD in an older age cohort.

Methods

The Hertfordshire Cohort Study (HCS) includes 2997 males and females who were born in Hertfordshire County between 1931 and 1939. Cohort members were recruited if their births were recorded in health visitor ledgers in the 1930s and if they were still resident in Hertfordshire from 1998-2004, when these ledgers were discovered and individuals were invited to participate in the study. The construction of this cohort study has previously been described in greater detail[20, 21].

Data on feeding during the first year of life (breastmilk fed, breast and bottle fed, or bottle fed), in addition to birth weights (kg) and weights at one year (kg), were collected contemporaneously by health visitors between 1931 and 1939 in Hertfordshire. As the infant milk feeding information included in these analyses was extracted from health visitor ledgers recorded in the 1930s, the definition of breastmilk fed in this study does not align with the WHO definition of exclusive breastfeeding, in which only breastmilk is consumed and cereals and other solids are avoided for the first six months[22]. Historical records indicate that in Hertfordshire in the 1930s, babies were fed either breastmilk or cow's milk preparations; there was little, if any, use of commercial infant formula milk[23]. While infant milk information was recorded in the ledgers, specific infant weaning data is unavailable in the HCS. Therefore, in the analyses presented here, the term breastmilk fed refers to no other milk but breastmilk for the first twelve months and does not make inferences about which early infant foods were consumed.

In addition to infant health and feeding variables drawn from the ledgers, demographic and health variables collected from the HCS participants in adulthood via postal questionnaire are utilized. These questionnaire variables include whether or not a participant had ever smoked regularly, levels of alcohol consumption, prudent diet score, age at clinic visit, adult height, physical activity score, dietary calcium, adult BMI, and the use of hormone replacement therapy in females. Alcohol consumption was measured in sex-specific recommended units per week, as per recommendations at the time of data collection, with the variable including three categories: Non-drinker; <=recommended units per week (21 for males and 14 for females); >=recommended units per week (21 for males and 14 for females). Prudent diet score is a marker of overall diet quality wherein a high score denotes a diet rich in fruits, vegetables, fatty fish and whole cereals, and a low score indicates a diet more defined by white carbohydrates, sugar, chips, and dairy. The calculation of this score has been described previously[23]. Physical activity score, calculated using HCS activity questionnaire data, is a continuous score from 0-100, in which a higher score indicates greater physical activity. Amount of dietary calcium was estimated from weekly nutrient intakes obtained by Food Frequency Questionnaires. Sex-specific adult BMI (Low: <25.2 for males, <24.9 for females;

Normal: 25.2-28 for males, 24.9-29 for females; and High: >=28 for males, >=29 for females) was included in models as a body size adjustment. Lumbar spine and femoral neck BMC (g) and BMD (g/cm^2) measurements for 996 participants (498 males and 498 females) were taken using dual-energy X-ray absorptiometry (DXA) at clinic visits from 1998-2004 (Hologic QDR 4500). Each participant attended one DXA clinic over the course of these years. Age at DXA scan, adult height, and adult BMI were recorded at the participant's clinic visit.

Statistical methods

Using these data from the HCS, linear regression models were run to examine the relationship between type of infant milk feeding and lumbar spine and femoral neck BMC and BMD. For the purposes of this study, the three-category infant feeding variable (breastfed, breast and bottle fed, or bottle fed) was collapsed into a two-category, binary variable: breastmilk fed or any other infant milk feeding combination, including breast and bottle fed or exclusively bottle fed any amount of breastmilk substitute. A sex-standardized z-score measure of conditional weight gain in infancy was created using birth weight and weight at one year, and this weight gain measure was included in models as a potential confounder.

Models adjusted for sex, age at DXA clinic visit, adult height, adult BMI, weight gain in infancy, smoking behaviour, alcohol consumption (in sex-specific recommended units per week), prudent diet score, physical activity score, and dietary calcium. Inclusion of these confounders was based on a review of literature regarding the biological indicators of bone health. The sample was stratified by sex after significant results of t-tests examining bone outcomes by sex and a large effect size of the interactions by outcome indicated effect modification by sex. Once the sample was split by sex, the association between bone health outcomes and infant feeding was examined in fully adjusted models, with the use of hormone replacement therapy included for females. After stratification by sex, there were 498 participants in the male sample and 498 participants in the female sample. Descriptive statistics are presented as mean (standard deviation) or as number counts and percentages. Significance levels were set to $p \leq 0.05$.

All analyses were performed using STATA 14 (College Station, TX).

Results

Descriptive statistics are detailed in Table 1 below. While the males and females in this sample had similar mean ages (Male: 64.182 (2.518) years; Female: 65.624 (2.546) years), and did not differ

substantially in their infant feeding experience, males had higher weights at one year of age (Male: 10.188 (1.108) kg; Female: 9.727 (1.038) kg) and poorer adult diets (Male: -0.370 (1.245); Female: 0.402 (1.140)) than females. Additionally, more males reported smoking (Male: 66.47%; Female: 37.95%) and consuming more than the recommended units of alcohol per week (Male: 24.70%; Female: 2.41%) than females in this sample at the time of DXA measurement.

Table 1 Descriptive statistics for HCS participants with DXA measurements from 1998-2004

	Total (max n=996)		**Males (max n = 498)**		**Females (max n = 498)**	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age at clinic (years)	64.903	2.631	64.182	2.518	65.624	2.546
Birthweight (kg)	3.452	0.544	3.523	0.562	3.381	0.516
Weight at 1 year (kg)	9.957	1.100	10.188	1.108	9.727	1.038
Height at clinic (cm)	167.654	9.161	174.271	6.759	161.038	5.881
Prudent diet score	0.016	1.253	-0.370	1.245	0.402	1.140
Dietary calcium	8350.733	2335.654	8822.677	2330.301	7878.789	2246.079
Physical activity score	62.598	14.920	63.952	14.773	61.245	14.959
Lumbar spine BMC (g)	67.503	17.662	77.385	15.607	57.117	13.171
Lumbar spine BMD (g/cm^2)	1.018	0.176	1.076	0.159	0.960	0.173
Femoral neck BMC (g)	4.442	0.925	5.004	0.796	3.882	0.669
Femoral neck BMD (g/cm^2)	0.803	0.130	0.850	0.121	0.757	0.121
	N	**%**	**N**	**%**	**N**	**%**
Infant feeding						
Breastmilk fed	566	57.17	278	56.28	288	58.06
Bottle +/- breastfed	424	42.83	216	43.72	208	41.94
Ever smoked regularly						
No	476	47.79	167	33.53	309	62.05
Yes	520	52.21	331	66.47	189	37.95
BMI (kg/m^2)[1]						
Low	349	35.04	171	34.34	178	35.74
Normal	335	33.63	176	35.34	159	31.93
High	312	31.33	151	30.32	161	32.33
Alcohol use[2]						
Non-drinker	113	11.35	20	4.02	93	18.67
Less than or equal to recommended units per week	748	75.10	355	71.29	393	78.92
More than recommended units per week	135	13.55	123	24.70	12	2.41

[1]Sex-specific BMI categories: Low (<25.2 in males, <24.9 in females); Normal (25.5-28 in males, 24.9-29 in females); and High (>=28 in males, >=29 in females)

[2]Sex-specific alcohol consumption categories: <=recommended units per week (21 units for males, 14 units for females); >recommended units per week (21 units for males, 14 units for females)

Table 2 below displays the results of models run to illuminate any differences in the relationship between infant milk feeding and bone health between males and females. Infant milk feeding was a significant predictor of bone health in later life for males: bottle feeding was negatively associated with lumbar spine BMD (b=-0.028, 95% CI -0.055, -0.000, p-value: 0.047). On average, males who were bottle fed in infancy had lower lumbar spine BMD measurements than those who were breastmilk fed. Type of infant milk feeding had no significant association with lumbar spine or femoral neck BMC and BMD for females in this sample.

Table 2 Adjusted models of relationship between infant feeding and lumbar spine and femoral neck BMC and BMD, by sex[1]

		Lumbar spine BMC (g)	Lumbar spine BMD (g/cm^2)	Femoral neck BMC (g)	Femoral neck BMD (g/cm^2)
Males	β[2]	-2.383	-0.028*	-0.088	-0.014
	CI (95%)	[-4.940, 0.175]	[-0.055, -0.000]	[-0.219, 0.042]	[-0.035, 0.006]
	p-value	0.068	0.047	0.183	0.171
Females					
	β[2]	-0.565	-0.017	-0.059	-0.000
	CI (95%)	[-2.783, 1.654]	[-0.046, 0.012]	[-0.113, 0.101]	[-0.020, 0.020]
	p-value	0.617	0.259	0.914	0.981

*P<0.05 **P<0.01 ***P<0.001

[1] Models control for age at baseline clinic visit, adult height, smoking behaviour, alcohol consumption, prudent diet score, physical activity score, dietary calcium, conditional weight gain over first year of life, adult BMI, and hormone replacement therapy in females.

[2]Reference category: breastmilk fed

Discussion

The results of this study suggest that in the HCS, males who were bottle fed (predominantly cow's milk preparations) in infancy had lower lumbar spine BMD measurements than those who were breast milk fed, indicating that breastmilk is positively associated with lumbar spine BMD in males in later life. This is a novel finding, as to our knowledge, this is the first paper to examine the relationship between infant milk feeding and bone health outcomes in older age.

There is little previous literature examining infant milk feeding and bone health in adulthood and later life, perhaps due to a lack of datasets in which prospective infant milk feeding data were collected in infancy. One study of Finnish adults born in 1975 found that type of infant milk was significantly associated with adult bone health in males aged 32 years, with shorter breastfeeding duration (and therefore greater infant formula exposure) being associated with higher spinal BMC and whole body BMD than prolonged breastfeeding[15]. It is difficult to compare the results of the

Finnish study to the results presented in this paper, as the two studies utilized different infant feeding measures. The Finnish study examined the relationship between infant feeding and adult bone health by investigating duration of breastfeeding and the use of commercial infant formula milk, diluted cow's milk, and commercial cow's milk. The present study examines the differences between those fed breast milk and those fed breast milk alternatives, a majority of which were cow's milk preparations. A major difference between the Finnish study conducted in 1975 and the present study utilizing data from the 1930s is the availability and use of commercial infant formula milks.

However, while the results of the Finnish cohort study differ from those of the present study, it is important to note that like the present study, it reported significant associations between infant milk feeding and bone health outcomes in males, while finding no effect in females. These differences in bone health outcomes between the sexes echo a report from the Newcastle Thousand Families Cohort Study, which found that indicators of early life health (including birth weight, breastfeeding duration, age at menarche, and childhood growth) explained more variation in adult BMD for males than for females[14]. Bone health in females may be more influenced by hormonal and postmenopausal lifestyle indicators such as diet[24] than by early life factors.

Other studies, exploring bone health in children and adolescents, have reported positive, negative, and no relationship between breastfeeding and BMD. Breastfeeding was associated with higher spinal, femoral, and total body BMD at both 8 years of age and 16 years of age in a Tasmanian birth cohort[17, 18] and with higher total body BMD in children at 6 years old in the Generation R Study in the Netherlands[16]. Research also indicates that there may be a positive relationship between breastfeeding and fracture prevention in children[18]. Future studies are needed to determine whether breastfeeding is associated with reductions in osteoporotic fractures in older age[18].

Conversely, infant milk feeding was not associated with bone health at 4 years of age for children participating in the Southampton Women's Survey[25], and infants and children who were breastfed had lower BMD z-scores than those who were not breastfed in a study conducted in Ohio, USA[26]. This lack of consensus in the literature is reflected in a systematic review conducted in 2014, which determined that the direction of association between infant milk feeding and bone mass varies according to the age of study participants and the cohort analysed[27].

Given the equivocal results of previous studies, further study of the association between breast milk and infant formula milk and bone health across the lifecourse is an avenue for future research. Specifically, analyses using data collected from older cohorts fed more modern formula milks during

infancy would help determine how contemporary infant milk feeding practice is associated with bone health in later life.

The biggest limitation of this study in informing contemporary feeding practice is that the breast milk substitutes utilized in the 1930s are not comparable to the formula milks used to feed infants today, as the composition of infant formula has changed over time. According to a history of parenting in Hertfordshire in the 1920s and 1930s, the majority of parents utilizing bottles at the time used cow's milk or condensed or dried milk preparations, which would not be the case today[23, 28] (although cow's milk preparations were still in use in Finland in 1975, as per the study discussed above). However, the aim of this study was to compare the influence of breast milk feeding to that of any cow's milk alternative to breastfeeding, and the information contained in the HCS allowed this comparison. Further research into the influence of modern formula milks on bone health in older age is needed.

The significant associations between infant milk feeding and lumbar spine BMD in males indicate that breastmilk may be protective for the bone health of male babies as they age. The evidence presented here underscores the potential lifelong benefits of breastfeeding and highlights the differences between osteoporotic risk factors for males and females.

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