

Original Contribution

Impact of Breastfeeding Duration on Age at Menarche

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The study aims to assess the relation between breastfeeding duration and age at menarche. Analysis was based on a cohort of 994 Filipino girls born in 1983–1984 and followed up from infancy to adulthood by the Cebu Longitudinal Health and Nutrition Survey. The main outcome was self-reported age at menarche. Cox regression was used to investigate the relation between duration of exclusive and any breastfeeding with age at menarche with adjustment sequentially for specific sets of known socioeconomic, maternal, genetic, and prenatal confounders. The estimated median of age at menarche was 13.08 years. After adjustment for potential confounders of the association of breastfeeding with age at menarche, exclusive breastfeeding duration retained an independent and significant association with age at menarche. An increase in 1 month of exclusive breastfeeding decreases the hazard of attaining earlier menarche by 6% (hazard ratio = 0.94, 95% confidence interval: 0.90, 0.98). Any breastfeeding duration was not associated with age at menarche. Although this is the first longitudinal study that reveals a negative association between exclusive breastfeeding and early menarche, the relation is still elusive. Further longitudinal studies within different contexts are warranted to assess the generalizability of these findings.

breast feeding; longitudinal studies; menarche; nutrition; Philippines

Abbreviation: CLHNS, Cebu Longitudinal Health and Nutrition Survey.

Editor's note: A related article by Kramer *et al.* appears on page 978, an invited commentary on both articles is published on page 984, and the response by Kramer *et al.* to the commentary is on page 988. In accordance with Journal policy, Al-Sahab *et al.* were asked if they wanted to respond to the commentary but chose not to do so.

Menarche is a critical biomarker in the reproductive life of females (1, 2). It serves as an intermediate health outcome that affects women's wellbeing at later stages of life (3). Currently, it is gaining more attention as a considerable body of evidence suggests that the age at menarche has declined in the past century (3–7). It has been shown that menarcheal age in the United States, as well as Europe, has decreased at a rate of 2–3 months per decade (5, 7). Early menarche is among the few established risk factors for breast cancer (8–11). It has also been associated with

metabolic syndrome (12), teenage depression (13), and overweight (14, 15).

Only recently have studies begun to investigate the effect of early life events on the timing of puberty, with the majority of studies focusing on birth weight, birth length, gestational age, and ponderal index (1, 3, 4, 16). Although nutrition in early development and childhood has a significant effect on the timing of menarche (17), it is surprising that little attention has been given to the potential role of breastfeeding. Breastfeeding has been shown to be inversely associated with weight gain during childhood (18–20), which in itself is a risk factor for early age at menarche (3, 21).

Although no study has previously investigated the association between breastfeeding and menarcheal age as its primary objective, 3 studies examined this association as part of determining the predictors of menarche (22–24). One of these studies by Novotny *et al.* (22) revealed that

formula-fed girls were 2.7 (95% confidence interval: 1.12, 6.38) times more likely to attain early menarche than breastfed babies. The other 2 studies, however, failed to detect significant associations between breastfeeding and menarcheal timing (23, 24). Several notable limitations such as small sample size, study design, long-term recall, and inconsistency in breastfeeding definitions limit the generalizability of these findings. Addressing these limitations, the present study aims to assess the relation between breastfeeding duration in the first months of life with age at menarche among a cohort of Filipino girls who were followed from infancy to adulthood.

MATERIALS AND METHODS

Sample

The analysis of this study was based on the Cebu Longitudinal Health and Nutrition Survey (CLHNS) conducted by the Carolina Population Center, University of North Carolina at Chapel Hill, the Nutrition Center of the Philippines, and the Office of Population Studies, University of San Carlos. The study was initiated in 1981 with the aim of determining prospectively the feeding patterns of infants in the Metro Cebu Area, Philippines.

CLHNS initially recruited all pregnant women who gave birth in a 12-month span (May 1983–April 1984) from 33 randomly selected communities in Metro Cebu (17 urban and 16 rural). The inclusion criteria for the baseline sample of pregnant women were as follows: 1) residency in one of the 33 sample communities; 2) pregnancy termination between May 1, 1983, and April 30, 1984; and 3) delivery of the sample child in a sample community or any health facility located in the Metro Cebu Area. All pregnant women were interviewed during the second or third trimester of pregnancy and at delivery. Singleton births were subsequently followed, and mothers and infants were assessed bimonthly for 24 months. Follow-up studies were conducted in 1991, 1995, 1998, 2002, and 2005. In this study, data from the first 3 follow-up surveys, when girls were 8–9, 11–12, and 14–15 years of age, were used. Detailed data on the health and wellbeing of the mother and the child, household characteristics, environmental conditions, and community setting were collected by trained personnel. CLHNS has been described previously (25, 26).

Age at menarche

The analysis sample for the present study includes all girls who participated in the 1998 survey and had complete data on breastfeeding. The main outcome of the study was age at menarche, self reported in the 1995 and 1998 surveys as the month and year of the occurrence of the first menstrual cycle. For the purpose of this study, age at menarche was used as a continuous and as a categorical variable. The categorical variable was grouped into early (<12.1 years), average (12.1–14.1 years), and late (>14.1 years) menarche. The age limit for early and late menarche was determined as 1 standard deviation away from the estimated mean age at menarche (3, 4). Premenarcheal girls who were 14 years of

age or older at the time of the 1998 interview were classified in the late menarche group (3, 6, 21).

Breastfeeding

The durations of exclusive breastfeeding and any breastfeeding were the main independent variables in the study. Exclusive breastfeeding was defined as the intake of breast milk alone without any other type of milk, liquid, or food (27). Its duration was calculated as the infant's age when exclusive breastfeeding was terminated. Based on the 7-day recall of feeding patterns, this information was reported bimonthly by the mother. Any breastfeeding, on the other hand, was defined as the intake of breast milk regardless of other type of food or drink intake (18, 28). The duration of any breastfeeding, reported bimonthly by the mother for the first 24 months of life, was defined as the infant's age in days when any breastfeeding had been permanently stopped. Any breastfeeding duration for infants still breastfeeding at 24 months was calculated as the last age when breastfeeding status was known. To ensure the quality of food intake and breastfeeding data, all personnel undertook a 2-week training program in food models and measurement of diets (29).

Covariates

A comprehensive list of covariates that have been found to predict age at menarche was adjusted for in this study. Socioeconomic status was represented through type of residence (urban vs. rural), income, number of household members, and mother's highest educational level as collected from the 1983–1984 baseline questionnaire. Maternal characteristics including age at delivery, history of previous births, skinfold thickness during pregnancy, and postpartum body mass index were also examined from the baseline and birth surveys. Triceps skinfold thickness was measured in triplicate during the third trimester of pregnancy. Baseline data on maternal age at menarche and maternal height were derived from the baseline survey and used as proxy measures of genetic factors (3). Perinatal measures were determined from the birth survey. Birth weight was measured by birth attendants after delivery. Babies missing this information (12.5%) had their birth weight substituted by the weight value measured by the survey staff within the first 8 days of life. Birth length was measured by the survey staff using custom-made measuring boards that complied with the standards of the US Centers for Disease Control and Prevention (25). Gestational age was estimated from the date of the mother's last menstrual period. If this date was missing, if the infant was low birth weight, or if the mother experienced pregnancy complications, the Ballard method performed by trained nurses was used instead to calculate gestational age (3). All anthropometric measures, for both the child and mother, were conducted by well-trained staff.

Statistical analysis

All analyses were performed by using SPSS, version 17.0, statistical software (SPSS, Inc., Chicago, Illinois).

Table 1. Characteristics of Early, Average, and Late Maturers in the Metro Cebu Area, Philippines, 1995–1998^{a,b}

	Early (<12.1 Years)			Average (12.1–14.1 Years)			Late (>14.1 Years)		
	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%
Exclusive breastfeeding, months (<i>n</i> = 974)	2.4 (1.8)			2.6 (1.8)			3.2 (2.0)		
Any breastfeeding, months (<i>n</i> = 974)	11.8 (8.3)			13.8 (7.9)			16.1 (7.3)		
Household income at baseline, per 100 pesos/week (<i>n</i> = 965)	3.1 (3.5)			2.5 (2.5)			2.4 (2.4)		
No. of household members at baseline (<i>n</i> = 974)	5.3 (3.0)			5.7 (2.7)			5.8 (2.8)		
Mother's highest educational level at baseline, years (<i>n</i> = 974)	8.8 (3.9)			7.3 (3.5)			6.3 (3.3)		
Mother's age at menarche, years (<i>n</i> = 973)	13.6 (1.5)			14.0 (1.5)			14.6 (1.6)		
Mother's height, cm (<i>n</i> = 973)	150.8 (4.8)			150.6 (5.0)			151.5 (5.1)		
Mother's age at delivery, years (<i>n</i> = 969)	26.0 (5.2)			26.9 (6.2)			26.5 (5.6)		
Birth weight, kg (<i>n</i> = 956)	3.0 (0.5)			3.0 (0.4)			3.0 (0.4)		
Baby's length at birth, cm (<i>n</i> = 972)	49.3 (1.9)			49.1 (2.1)			48.7 (2.2)		
Gestational age, weeks (<i>n</i> = 919)	38.6 (3.3)			38.7 (2.8)			38.5 (3.1)		
Mother's body mass index after birth, kg/m ² (<i>n</i> = 965)	22.7 (2.6)			22.1 (2.6)			21.4 (2.1)		
Mother's triceps skinfold thickness, mm (<i>n</i> = 974)	13.8 (4.0)			12.7 (3.9)			11.7 (3.6)		
Place of residence (<i>n</i> = 974)									
Urban		124	81.0		473	75.3		113	58.5
Rural		29	19.0		155	24.7		80	41.5
First child (<i>n</i> = 974)									
No		101	66.0		495	78.8		161	83.4
Yes		52	34.0		133	21.2		32	16.6

Abbreviation: SD, standard deviation.

^a Number and frequency for categorical variables.^b Mean and standard deviation for continuous variables.

Initially, Kaplan-Meier analysis was used to estimate the median age at menarche. Accordingly, the distribution of early, average, and late menarche was calculated. This 3-level categorical variable was used only for assessing the characteristics of the population. Differences in the distribution of categorical variables or means of continuous variables were tested by using the chi-square and analysis of variance, respectively. Cox regression was used to investigate the association of breastfeeding with age at menarche while adjusting sequentially for different sets of covariates. Age at menarche was defined in this analysis as a continuous variable taking into consideration girls who did not attain their first menarche at the time of outcome assessment. These observations were treated as censored data. Adjusted hazard ratios with 95% confidence interval were reported for the Cox regression models. Statistical significance for all analyses was set at $P < 0.05$.

RESULTS

Of the 1,447 singleton females born alive in 1983–1984, 994 (68.7%) females were interviewed and completed the 1998 survey. The vast majority of the girls (94.9%) had started menstruating at the time of the follow-up survey. Only 51 girls were premenarcheal. By use of Kaplan-Meier

analysis, the estimated median age at menarche was 13.08 years. Half of the girls attained their menarche between the ages of 12.42 and 13.92 years. The proportions of early, average, and late maturers were 15.5%, 65.0%, and 19.5%, respectively. Of the 994 girls, 974 girls had complete information on breastfeeding. The mean duration of exclusive breastfeeding in this population was 2.72 months (standard deviation = 1.89), while the mean duration of any breastfeeding was 13.91 months (standard deviation = 7.98).

Table 1 presents the characteristics of early, average, and late maturers. The mean duration for exclusive and any breastfeeding was significantly shorter among early maturing girls as compared with average and late maturing girls. Early maturers were also more likely to be firstborns and to live in an urban community. Income and maternal educational level were higher among girls with early menarche in contrast to other girls. Moreover, the mother's age at menarche was significantly lower for girls attaining menarche at a younger age. The mother's postpartum body mass index and triceps skinfold thickness during pregnancy were also higher among early maturers than their counterparts. Finally, birth length was significantly different across the 3 menarche groups.

By use of Cox regression analysis, different model specifications are demonstrated in Table 2 for the impact of

Table 2. Model Specifications for the Impact of Breastfeeding Duration on Age at Menarche^a With Sequential Adjustment for Specific Sets of Known Confounders in the Metro Cebu Area, Philippines, 1995–1998

Variables	Model 1 (Breast Feeding Effect)		Model 2 Model 1 + Socioeconomic and Maternal Related Variables		Model 3 Model 2 + Genetic and Infant Characteristics	
	HR ^b	95% CI	HR	95% CI	HR	95% CI
Exclusive breastfeeding, months	0.93**	0.89, 0.96	0.95*	0.91, 0.99	0.94**	0.90, 0.98
Any breastfeeding, months	0.99*	0.98, 0.99	1.00	0.99, 1.01	1.00	0.99, 1.01
Urban residence at baseline			1.25**	1.07, 1.47	1.24*	1.05, 1.47
Total household income at baseline, 100 pesos/week			0.99	0.96, 1.02	1.00	0.96, 1.03
No. of household members at baseline			0.98	0.96, 1.01	0.97	0.94, 1.00
Mother's education at baseline, years			1.03**	1.01, 1.05	1.02*	1.00, 1.05
First child			1.25*	1.04, 1.49	1.20	0.99, 1.44
Mother's age at delivery, years			1.01	0.99, 1.02	1.01	0.99, 1.02
Mother's body mass index after birth, kg/m ²			1.05**	1.01, 1.09	1.03	0.99, 1.07
Mother's triceps skinfold thickness, mm			1.01	0.99, 1.03	1.02	0.99, 1.04
Mother's age at menarche, years					0.91**	0.87, 0.95
Mother's height, cm					0.99	0.97, 1.00
Birth weight, kg					0.83	0.67, 1.02
Birth length, cm					1.07**	1.02, 1.11
Gestational age, weeks					1.01	0.98, 1.03

Abbreviations: CI, confidence interval; HR, hazard ratio.

* $P < 0.05$; ** $P < 0.01$.

^a Age at menarche was used as a continuous variable whereby premenarcheal girls' data were considered as censored.

^b Hazard ratios greater than 1 and less than 1 signify higher and lower risks of attaining earlier menarche, respectively.

breastfeeding duration on age at menarche, with adjustment for specific sets of known confounders. The sole effect of breastfeeding variables on age at menarche has been assessed in model 1. Shorter durations of both exclusive and any breastfeeding were associated with earlier menarche. In model 2, socioeconomic variables and maternal characteristics were added to the analysis; in this case, only exclusive breastfeeding remained significantly associated with menarcheal timing. Urban residence, mother's educational level, postpartum body mass index, and being the first child were also found to be associated with early age at menarche. Model 3 added variables related to genetic factors and infant characteristics. Urban residence and maternal education sustained their significance. The negative association between exclusive breastfeeding and menarcheal timing was not altered either (hazard ratio = 0.94, 95% confidence interval: 0.90, 0.98). Moreover, mother's age at menarche and birth length emerged as potential predictors for age at menarche, whereby older maternal age at menarche and shorter birth length were associated with lower hazard ratios of menarche. No significant interactions were found between any and exclusive breastfeeding variables in any model.

DISCUSSION

The present study aimed to explore the association of breastfeeding with menarcheal age. The estimated median

age at menarche for the Filipino cohort analyzed in this study was 13.08 years. After adjustment for potential confounders of the association of breastfeeding with age at menarche, exclusive breastfeeding duration retained an independent and significant association with age at menarche. An increase in 1 month of exclusive breastfeeding decreased the hazard of attaining earlier menarche by 6%. This association is a novel finding in the present study. Results suggest that nutrition in early development and childhood plays an important role in determining the timing of menarche.

One of the often cited pathways between breastfeeding and age at menarche is weight gain during childhood. The tempo of growth during infancy and childhood has been associated with breastfeeding and age at menarche. Breastfeeding in early life may prevent or delay weight gain during childhood (18–20). According to a study conducted on a Danish cohort, longer durations of any breastfeeding decreased the weight gain during the first year of life (18). Babies breastfed for less than 20 weeks gained 317.4 g more during the first year of life than those who breastfed for more than 40 weeks (18). As explained by Ong et al. (30), the growth patterns for 3-month-breastfed infants were slower than those for formula-fed infants for the first 5 years of life. Rapid weight gain during infancy has also been shown to increase the risk of attaining earlier menarche (3, 21). Using the same data set as the present study, Adair (3) revealed that faster growth in weight and/or length at 6 months of age also predicted young menarcheal age. Although the mechanism

explaining the link between infant weight gain and age at menarche is still unclear, it has been speculated that a rise in leptin among rapid weight gainers triggers the onset of puberty (31). Similarly, the increased concentration of insulin-like growth factor I due to weight gain during infancy may also promote the initiation of puberty (31).

Until recently, childhood obesity has been thought to be the link as well between menarche and breastfeeding. Childhood obesity has previously been associated with early age at menarche (1, 4, 32, 33). Given that a critical proportion of body fat (17%–22%) may be required to trigger menarche (34–36), it is not surprising that, in multivariable analyses, a lower expected birth weight ratio and higher body mass index at 8 years of age were found to be the strongest predictors of early menarche (4). However, based on the clinical trials by Kramer et al. (37–39), it is suggested that breastfeeding has no impact on childhood weight. According to Kramer, previous findings on the protective role of breastfeeding on childhood weight are attributed mainly to unmeasured confounders (39).

The present study assessed the total effect of exclusive breastfeeding on age at menarche. Although data on postnatal growth, childhood anthropometrics, and childhood energy intake and diet was collected in the CLHNS, it was not considered in the analysis. These variables are believed to lie on the causal pathway between breastfeeding and age at menarche. The direct pathway, therefore, through which breastfeeding can influence age at menarche is still elusive. Because the infant's ability to develop physiologic changes in response to the environment extends to the postnatal period (40), nutritional programming is plausible and may cause long-term consequences in later life (41). In 2004, Singhal et al. (42) provided evidence on the positive programming effect of breast milk on the lipoprotein profile, while the programming of undernutrition in early life may delay the development of insulin resistance for preterm babies (43).

The study findings suggest that girls exclusively breastfed for longer durations had a decreased hazard ratio for menarche than their counterparts. One previous cross-sectional study found that formula-fed girls were 2.7 (95% confidence interval: 1.12, 6.38) times more likely to attain early menarche than breastfed babies (22); however, this study was subject to recall bias, as mothers of the study participants were asked to report their breastfeeding practices 9–14 years prior. Moreover, the sample size was limited ($n = 349$), and exclusive breastfeeding and duration of breastfeeding/bottle feeding were not considered in the analysis (22). Two other longitudinal studies by Karaolis-Danckert et al. (23) and Blell et al. (24) aimed to assess the general predictors of menarche and puberty. As one of the predictors, breastfeeding in both studies was not found to be associated with menarche (23, 24). More specifically, Blell et al. (24) examined the effect of duration of partial breastfeeding on age at menarche that was reported by women aged 49–51 years. Other than the long recall period for age at menarche, only 276 women of the 1,142 original cohort were analyzed in the study (24). The study by Karaolis-Danckert et al. (23), on the other hand, investigated the effect of full breastfeeding at 4 months on age at take-off of the pubertal growth spurt and age at peak height velocity among girls and boys. Similar to the study by

Blell et al. (24), the sample size analyzed ($n = 215$) was at least 5 times less than the original cohort (23).

Interestingly, in the present study, age at menarche was not associated with the duration of any breastfeeding, suggesting that the exclusivity of breastfeeding is more important. However, the reason behind the superiority of exclusive breastfeeding over any breastfeeding in terms of age at menarche is not clear. It can be speculated that the difference in effects between the 2 types of breastfeeding is attributed to the nature of complementary foods, levels of energy intake, weight gain, and health status of the baby. These factors are relatively dependent on geographic areas and cultural variations. This association may be more pronounced in developed countries where complementary foods are more nutritive and energy dense than in developing countries. Understanding this association in different contexts is thus highly warranted.

Several limitations of the current study warrant mention. As expected, the present study lost participants to follow-up. Of the 1,447 singleton girls born alive in 1983–1984, 974 (67.3%) were considered in the analysis. In terms of socioeconomic and maternal related characteristics, girls with missing data were somewhat more likely to be urban residents and to have mothers with a higher educational level. Moreover, girls excluded from the analysis had shorter durations of both, any and exclusive breastfeeding. Therefore, the generalizability of the results to the original cohort must be made with caution. In addition to the above, the study is subject to information bias due to possible measurement errors in the outcome, exposure, and confounding variables. Age at menarche was self-reported by the girls. Menarche data, however, were collected close to the time of the event, reducing the likelihood of recall bias. Errors in reporting breastfeeding practices are also possible as mothers might not remember accurately the timing of liquid or food introduction and/or breastfeeding termination. To ensure the quality of food intake and breastfeeding data, on the other hand, all personnel undertook a 2-week training program in food models and measurement of diets. Residual confounding due to unmeasured variables like diet during pregnancy, intrauterine life, and genetic factors also stands out as another limitation.

Although this is the first longitudinal study that reveals a negative association between exclusive breastfeeding and early menarche, the relation is still elusive. The results suggest that duration of *exclusive* breastfeeding (rather than any breastfeeding) reduces the chances of attaining early menarche. Thus, nutrition during infancy could be an “early window” that might program a child's future growth and development (31, p. 140). It is also among the few childhood modifiable risk factors that might prevent or delay diseases in adulthood. Nevertheless, the potential mechanism for the programming of breastfeeding on age at menarche remains unclear. Further longitudinal studies within different contexts are warranted to assess the generalizability of these findings.

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