A Longitudinal Analysis of Infant Morbidity and the Extent of Breastfeeding in the United States

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ABSTRACT. ***Background.*** **Studies on the health benefits of breastfeeding in developed countries have shown conflicting results. These studies often fail to account for confounding, reverse causality, and dose-response effects. We addressed these issues in analyzing longitudinal data to determine if breastfeeding protects US infants from developing diarrhea and ear infections.**

Methods. **Mothers participating in a mail panel provided information on their infants at ages 2, 3, 4, 5, 6, and 7 months. Infants were classified as exclusively breastfed; high, middle, or low mixed breast- and formula-fed; or exclusively formula-fed. Diarrhea and ear infection diagnoses were based on mothers' reports. Infant age and gender; other liquid and solid intake; maternal education, occupation, and smoking; household size; family income; and day care use were adjusted for in the full models.**

Results. **The risk of developing either diarrhea or ear infection increased as the amount of breast milk an infant received decreased. In the full models, the risk for diarrhea remained significant only in infants who received no breast milk compared with those who received only breast milk (odds ratio = 1.8); the risk for ear infection remained significant in the low mixed feeding group (odds ratio = 1.6) and among infants receiving no breast milk compared with those who received only breast milk (odds ratio = 1.7).**

Conclusions. **Breastfeeding protects US infants against the development of diarrhea and ear infection. Breastfeeding does not have to be exclusive to confer this benefit. In fact, protection is afforded in a dose-response manner. The more breast milk an infant receives in the first 6 months of life, the less likely that he or she will develop diarrhea or ear infection.** ***Pediatrics*** **1997;99(6). URL: http://www.pediatrics.org/cgi/content/full/99/6/e5;** ***longitudinal analysis, diarrhea, ear infection, breastfeeding.***

Does breastfeeding protect against infection? In developing countries, the answer clearly is yes.[1–4] However, in industrialized countries the findings are mixed. Numerous nonprospective studies of industrialized populations in the literature examine the association between breastfeeding and infectious disease; many report a protective effect[5–12] whereas others report little or no effect at all.[13,14] Prospective studies show similarly conflicting findings.[15–25] A 1986 review of the literature concluded that breastfeeding "has at most a minimal protective effect [against infection] in industrialized countries."[26]

The conflicting results have been attributed to flawed methodologies.[20,23,26–30] Specific criticisms include failure to (1) collect data prospectively at frequent intervals; (2) control for known confounding variables such as day care, infant age, and indicators of socioeconomic status; (3) clearly define feeding and outcome variables; (4) apply appropriate statistical strategies to a population in which both feeding and exposure to infectious agents change over time; and (5) account for small samples with the potential for unspecified biases.

The objective of our study was to determine if breastfeeding protects US infants against the development of diarrhea and ear infection. If the answer was affirmative, we also wanted to know whether the breastfeeding has to be exclusive to confer these benefits.

METHODS

Sampling Frame

The Infant Feeding Practices Study was a panel study of US mother-infant pairs followed from late pregnancy through the infant's first year. The Food and Drug Administration conducted the study between 1993 and 1994. The agency used as the sampling frame a consumer mail panel which yielded a set of households in which someone had agreed to respond to questionnaires. The panel included approximately 500 000 households, and the contractors attempted to maintain (compared with US Census data) representativeness on five characteristics: geographic region, annual income, population density, household size, and age. Members of the panel were recruited in a variety of ways: recommendation from other panel members, notices in places likely to attract the type of people needed, and lists compiled by companies who specialize in finding particular types of people. Prenatal intake questionnaires were sent to 3155 households identified as including a pregnant women. All infants enrolled in this study were born between March and October 1993.

Exclusion Criteria

Subjects were considered ineligible for the study at the time of the prenatal questionnaire if the expected due date was more than 3 months away. After the prenatal questionnaire was administered, subjects were ineligible for the study if the infant weighed less than 5 pounds at birth, there were multiple infants, medical problems prevented the mother from feeding her infant for more than 1 week, the infant stayed in the intensive care unit for more than 3 days, the infant had medical problems that affected feeding, the mother or infant died at any time during the data collection

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TABLE 1. Sample Size by Age of Child and Feeding Category in the Preceding Month

Feeding Category (% Breast Milk)	Month*					
	2 (%)	3 (%)	4 (%)	5 (%)	6 (%)	Sum of infant-mo (%)
Breast milk only (100)	468 (28.9)	396 (26.6)	354 (24.3)	334 (23.7)	299 (21.2)	1851 (25.1)
High mixed (89–99)	150 (9.3)	114 (7.7)	95 (6.5)	58 (4.1)	59 (4.2)	476 (6.4)
Middle mixed (58–88)	161 (10.0)	130 (8.7)	109 (7.5)	89 (6.3)	80 (5.7)	569 (7.7)
Low mixed (1–57)	116 (7.2)	116 (7.8)	91 (6.2)	90 (6.4)	81 (5.7)	494 (6.7)
Formula only (0)	722 (44.7)	733 (49.2)	809 (55.5)	840 (59.5)	891 (63.2)	3995 (54.1)
Total	1617	1489	1458	1411	1410	7385

* Due to the lagged nature of the analysis, feeding category was not defined for month 7.

period, or the infant was born too early for the neonatal questionnaire to be administered on time. Five hundred forty women were ineligible, yielding a sample base of 2615 mother-infant pairs.

Data Collection

The Infant Feeding Practices Study was a series of 11 questionnaires administered by mail beginning when the mother was approximately 6 months pregnant and continuing until the infant was 1 year old. Infant feeding and health status information were collected at months 2, 3, 4, 5, 6, and 7 (ie, when the infant was 2, 3, 4, 5, 6, and 7 months old). Information on smoking status and day care use was collected at months 3 and 6. An additional demographic questionnaire collected information on education, employment, household size, and income.

Nonresponse

A woman was considered a nonrespondent if she failed to complete the first (prenatal) or second (birth screener) questionnaire or if she failed to complete at least one of the first two questionnaires sent after the infant's birth (n = 812). We did not eliminate a mother from the study for failure to complete a subsequent questionnaire. The response rate was 69% (1803/2615).

For this analysis, we excluded women who failed to complete the demographic questionnaire (n = 60), which left 1743 mother-infant pairs. In any given month, we also excluded infants who received neither breast milk nor formula.

There was a slight attrition in the number of questionnaires completed at each successive month. We compared the demographic characteristics of mothers completing all the questionnaires between months 2 and 7 with those missing at least one questionnaire. The two groups were similar regarding household size, infant gender, and income. They were different concerning education and employment. Mothers with a higher level of education were more likely than less educated mothers to complete all the questionnaires. Similarly, homemakers and professional women were more likely to complete all the questionnaires.

Population Characteristics

To better understand the characteristics of our sample, we compared them with a nationally representative population of mothers participating in the National Maternal and Infant Health Survey.[31] In comparison, our cohort of mothers was more likely to belong to middle- and upper-income groups; to be older, white, and married; and to have taken a prenatal class. They were also less likely to drink alcohol or smoke.

Classification of Predictor and Outcome Variables

Each month, the mother reported the number of times over the past 7 days that her infant received breast milk, formula, or both. Using this information, we created five feeding categories based on the percentage of breastfeedings an infant received: breast milk only (100% of feedings were breast milk), high mixed (89% to 99% of feedings were breast milk), middle mixed (58% to 88% of feedings were breast milk), low mixed (1% to 57% of feedings were breast milk), and formula only (0% of feedings were breast milk). The cutoffs for the mixed feeding categories (ie, high, middle, and low) were defined by dividing the mixed-feeding group into terciles. Table 1 lists the sample size for each breastfeeding group and the infant's age in months.

Each month, the mother also reported whether her infant had experienced diarrhea or an ear infection in the preceding 2 weeks. Diarrhea was defined for the mother as three or more watery or semiwatery stools in a 24-hour period. Before answering this question, the mother was asked to describe the infant's usual stool. We believe this gave her a reference by which to distinguish between normally loose stools and diarrhea. Ear infection was not predefined.

Confounding Variables

Each month, the mother reported the number of times in the past 7 days her infant received other liquids (cow's milk, other milk, other dairy products, and fruit juice) or solids (baby cereal, other cereals, fruit, vegetables, meat, peanut butter, eggs, and sweets). All analyses, including the crude models, were adjusted for whether or not the infant received in the previous month any other liquids and any solids.[a] The infant's intake of other liquids and solids was adjusted separately to allow us to examine the formula-breast milk differential independent of any other intake the infant received. We also adjusted all models for the infant's age as a categorical variable.

In the full models, we also adjusted for infant gender; maternal education, occupation, and smoking pattern; household size and income; and day care use (Table 2). Maternal education, maternal occupation, household size, and household income are socioeconomic indicators that have known associations with both breastfeeding and infectious disease. Day care use increases the risk of infection because it increases exposure to infectious agents, and it decreases breastfeeding because the infant is physically separated from its mother. Maternal smoking is associated with increased risk of infectious disease as well as decreased lactational capacity,[32] and it may be a marker of maternal health behaviors. Data on day care and maternal smoking were collected only in months 3 and 6. Therefore, for outcomes in month 4, the day care and smoking data were imputed from responses given in month 3; for outcomes in months 5 and 7, the day care and smoking data were imputed from responses given in month 6.

Analysis

We linked infection in any given month with feeding for the preceding month. Thus, infection in month 3 was linked to feeding in month 2; infection in month 4 was linked to feeding in month 3, and so on. This lagged association allowed us to rule out the possibility of reverse causality (ie, the type of milk given to an infant changes in response to illness rather than the illness results from the type of milk given) by ensuring that a reported illness

[a] Additional analyses controlling for the number of feedings of liquids or solids did not substantively alter our results.

TABLE 2. Confounding Variables Used in Multivariate Analysis

Infants's age*	
	3, 4, 5, 6, and 7 months
Other liquid intake last month	
Solid intake last month	
Infant's gender	
	Female
	Male
Maternal education	
	0–11 y of school
	12 y of school
	1–4 y of college
	More than 4 y of college
Maternal occupation	
	Full-time homemaker
	Unemployed, student or retired
	Professional or executive
	Clerical or sales
	Craftsperson, fabricator, technician, farmer, service worker, etc
Maternal smoking	
	No smoking
	10 or fewer cigarettes/day
	11–20 cigarettes/day
	More than 20 cigarettes/day
Household size	
	1–2 people
	3 people
	4–8 people
Household income	
	Less than $22 500
	$22 500–$34 999
	$35 000–$50 000
	More than $50 000
Day care	
	None
	In the home, any amount of time
	With other children 1–2 days/wk
	With other children 3–5 days/wk
	With other children 6–7 days/wk

* Adjusted at months 3 through 7 due to the lagged nature of the analysis.

occurred after a specified type of feeding. This information then was aggregated across all the groups so we could examine the effect of the previous month's feeding on diarrhea and ear infection.

We used logistic regression to model the effects of covariates on the odds of experiencing diarrhea and ear infections. Because several months of data were included for each child, it was necessary to account for the correlation of the data from 1 month to the next in the estimation of the regression models. To do this, we used the Generalized Estimating Equations approach[33,34] and assumed that the correlation structure of the data was best captured by stationary 1-dependence. This correlation structure assumes that there is a constant degree of correlation between any two adjacent months of data for a single child (eg, outcomes in month 3 are correlated with outcomes in month 4 to the same extent that outcomes in month 4 are correlated with outcomes in month 5, and so on). We experimented with other correlation structures and found little change in the parameter estimates or standard errors. We performed the analysis using the Statistical Package for Interactive Data Analysis (SPIDA), version 6 (Statistical Computing Laboratory, New South Whales, Australia).

RESULTS

An analysis of our baseline data indicated that anywhere from 5.4% to 11.4% of our infants reportedly experienced diarrhea between 2 and 7 months of age; 6.8% to 13.2% experienced an ear infection (Table 3). In the crude model, the association between the percentage of breastfeedings and the development of diarrhea showed a dose-response effect (Fig 1). Specifically, when each feeding group was compared with infants who received breast milk only (referent), there was a small but steady increase in the risk of developing diarrhea as the amount of breast milk an infant received decreased. This was significant among low mixed ($P = .02$) and formula only ($P < .001$) infants. When we adjusted this model for confounders, the dose-response remained apparent, although its magnitude diminished and the effect remained significant only among infants receiving no breast milk ($P < .001$).

TABLE 3. Percentage of Infants 2 to 7 Months of Age Reported as Experiencing Diarrhea or Ear Infection, by Feeding Category in the Preceding Month

Feeding Category (% Breast Milk)	Diarrhea	Ear Infection
Breast milk only (100)	5.4	6.8
High mixed (89–99)	4.8	6.6
Middle mixed (58–88)	6.4	9.4
Low mixed (1–57)	8.5	11.1
Formula only (0)	11.4	13.2

A dose-response relationship also emerged when we assessed the effect of feeding on ear infections (Fig 2). Again, as the amount of breast milk an infant received decreased, relative to the referent group, the risk of developing an ear infection steadily increased, up to an 80% increased risk among low mixed ($P = .003$) or formula only ($P < .001$) infants. When we adjusted the model, the magnitude of the effect diminished but the associations in both the low mixed ($P = .02$) and formula only ($P < .001$) groups remained significant.

DISCUSSION

We conclude that breastfeeding protects US infants against the development of diarrhea and ear infection. Exclusive breastfeeding is not crucial to confer this benefit. In fact, protection is afforded in a dose-response manner.

In looking at the relationship between feeding and diarrhea (after accounting for confounders), we found the odds ratios across feeding groups showed a steadily increasing risk of diarrhea as the relative amount of breast milk decreased. A similar pattern of protection was seen for ear infections. When compared with exclusively breastfed infants, infants who received formula only had an 80% increase in their risk of developing diarrhea and a 70% increase in their risk of developing an ear infection.

We view these findings in light of the limitations of this study. Because mothers responded via a mailed survey, some misclassification of diarrhea or ear infections may have occurred. Furthermore, the normally loose stools of breastfed infants may have been misreported as diarrhea. Under both of these circumstances, the bias created would weaken the strength of our association. Thus, our results may underestimate the true magnitude of the relationship between infant feeding and diarrhea or ear infections. Second, feeding choices reflect inherent differences between mothers. We addressed this limitation by controlling for a wide variety of sociodemographic characteristics, but other characteristics that were not measured

Association between diarrhea and feeding in preceding 1 month.

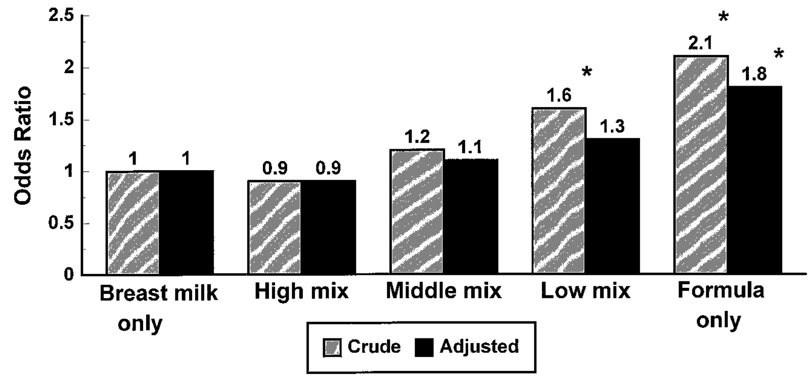
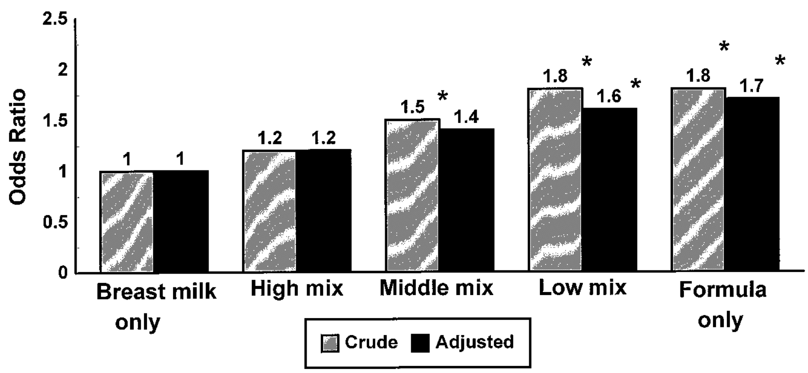


Fig 1. Asterisks indicate $P < .05$ relative to breast-milk-only group. Crude analyses takes into account infant's age and intake of other liquids and solids for the preceding month. Adjusted analyses take into account infant's age, gender, and intake of other liquids and solids the previous month; maternal education, occupation, and smoking pattern; household size and income; and day care use.

Association between ear infection and feeding in preceding 1 month.



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could confound our results. Third, mothers who participate in mail panel surveys may differ from the general population. As we noted earlier, our study population was of a higher socioeconomic status than the general population. This difference should have also weakened the strength of our association, because we expected the benefits of breastfeeding to be harder to demonstrate in high-socioeconomic status groups. Finally, the sample size of this study did not allow us to examine the effect of feeding infants a small proportion of breast milk relative to formula (eg, <20%). This group was small because it is physiologically difficult for a mother to maintain small numbers of breastfeedings over prolonged periods.

A notable strength of this study is its methodology. By using longitudinal data, we were able to examine infectious disease outcomes in relation to the feeding pattern that immediately preceded them. Because the data were collected month by month, it was possible to obtain specific data on supplemental foods as well as the number of formula feedings and breastfeedings, thus allowing a very precise definition of feeding patterns unaffected by recall bias. Appropriate statistical methods were used to account for the longitudinal nature of the data.

It is our hope that the three main points of this study will serve as tools for the education of pregnant and lactating women in the US. First, breast milk provides protection against selected diseases. This adage is by no means new, but past evidence for protection against infectious disease in developed countries has been less than adequate.[13,14,18,20,24] In the US, where only 53% of women initiate breastfeeding,[35] it is a message that deserves renewed attention and support. Second, supplementing breastfeedings with small amounts of formula does not eliminate the protection afforded by breast milk. Clearly, this is not meant to discourage mothers from practicing exclusive breastfeeding, but, in a society where the mother has to meet many responsibilities in addition to feeding her infant, exclusive breastfeeding may not always be practical. Finally, breastfeeding is not an all-or-none phenomenon; the more breast milk an infant receives in the first 6 months of life, the better.

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