Predominant Breast-Feeding from Birth to Six Months Is Associated with Fewer Gastrointestinal Infections and Increased Risk for Iron Deficiency among Infants¹,²

Eva C. Monterrosa,³,⁴ Edward A. Frongillo,⁵ Edgar M. Vásquez-Garibay,⁶ Enrique Romero-Velarde,⁶ Linda M. Casey,⁷ and Noreen D. Willows³,⁸

³Department of Agricultural, Food, and Nutritional Sciences, University of Alberta, T6G 2P5 Edmonton, Canada; ⁴Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853; ⁵Department of Health Promotion, Education, and Behavior, University of South Carolina, Columbia, SC 29208; ⁶Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico 44340; and ⁷Department of Pediatrics, University of Alberta, T6G 2J3 Edmonton, Canada

Abstract
Iron deficiency (ID) is prevalent among infants world-wide and may be more likely among infants born to women living in disadvantaged environments. A strategy to address ID in this context is to feed iron-fortified formula, but this may create risk for gastrointestinal (GI) infection. Our objective was to investigate the relationship between infant feeding practices, iron status, and likelihood of a GI infection in the first 6 mo of life. We conducted a prospective study at a public hospital in Guadalajara, Mexico. Healthy women who gave birth to a healthy term infant were eligible to participate. Each month, mothers (n = 154) provided information on infant feeding methods and symptoms of GI infection. At 6 mo of age, infants’ iron status was assessed [hemoglobin (Hb) and serum ferritin concentration]. When compared with nonpredominantly breast-fed [partially breast-feeding (PBF) and formula feeding (FF) combined], predominantly breast-fed (PRBF) infants to 6 mo had a lower incidence of GI infection from 0–6 mo [18 vs. 33%; P = 0.04; adjusted odds ratio (OR) = 0.4; 95% CI = 0.2, 1.0] but a higher risk for ID (serum ferritin < 12 μg/L) at 6 mo (22 vs. 4%; P = 0.001; adjusted OR = 9.2; 95% CI = 2.3, 37.0). Anemia (Hb < 110 g/L) prevalence did not differ among feeding groups (13% for PRBF, 19% for PBF, and 4% for FF; P = 0.09). In this low-income population, our results suggest that PRBF should be promoted and the risk for ID managed using public health and nutrition strategies. J. Nutr. 138: 1499–1504, 2008.

Introduction
Exclusive breast-feeding (EBF)⁹ to 6 mo of age is recommended because it protects against infectious morbidity, mortality, and promotes adequate growth and development (1). For some infants, particularly those born with suboptimal iron stores, EBF to 6 mo may increase the risk for iron deficiency (ID) (1), because total iron concentration in human milk is low (2). In healthy term infants, factors associated with low iron stores at 6 mo of age include poor maternal iron status during pregnancy, consumption of cow milk, rapid growth, and low socioeconomic status (3). In Mexico, 28% of pregnant women have anemia (4), cow milk is a common breast milk substitute particularly among the low-income households (5), weaning foods are low in bioavailable iron (6), and 50% of children 1–2 y of age are anemic (7). These facts suggest that the risk of ID among Mexican infants and children is a public health concern. ID in infancy has been associated with altered cognitive functions that may be irreversible (8).

Although some breast-fed infants may be at risk for ID, full breast-feeding (i.e. exclusive and predominant) protects against gastrointestinal (GI) morbidity (1). This is extremely important in low-income populations where hygienic preparation of foods may be compromised and frequent GI infections can contribute to malnutrition, which adversely affects infant growth and development (9). The confluence of food security, child care practices, maternal health and education, sanitation and health services, and social, political, and economic structures act to influence the relationship between infant feeding and infant health (9). It is therefore possible that infants born to women in disadvantaged environments are more likely to experience deficits in nutrients in the postnatal period than infants born to women in more advantaged environments (10). As such,
context-specific data of the health consequences associated with particular feeding regimens need to be assessed (10). This facilitates the development of feasible, local public health recommendations for best breast-feeding practice (10,11).

The objective of this research was to provide needed information about the health consequences for infants born to low-income women in Guadalajara, Mexico, who receive standard health care services and feed according to local breast-feeding practices. In Mexico, qualitative studies have shown that mothers have a positive attitude toward breast-feeding but consider that water and teas are important for infant health (12,13). In this context, we proposed that those infants who were predominantly breast-fed (PRBF) throughout the first 6 mo of life would experience fewer GI infections during this period but would be at increased risk for ID or anemia at 6 mo of age compared with infants who were regularly fed iron-fortified formula.

Methods

Study setting. The greater metropolitan area of Guadalajara, with a population of ~4.5 million people, is one of Mexico’s most populous cities. The study took place at the Hospital Civil Dr. Juan I Menchaca, a certified Baby Friendly Hospital. It is 1 of 2 public, tertiary care hospitals that serve the city of Guadalajara and the state of Jalisco. In general, patients of the hospital are low income. In 2004, a Mexican family of 4 whose monthly income was below 1–2 minimum salaries, $125–250 U.S. dollars (USD), was considered unable to meet their basic food needs.

Study design. Mother-infant pairs were recruited from the hospital following birth and were followed for 6 mo. Infants were followed monthly at the hospital outpatient clinic and at each well-baby visit, infants received standard care and mothers received timely information about appropriate feeding and care practices. Ethical approval for the study was granted by the Research Ethics Board of the Faculty of Agriculture, Forestry, and Home Economics, University of Alberta (Edmonton, Canada) and by the Ethics Committee of the Hospital Civil Dr. Juan I Menchaca. All women gave written informed consent to participate.

Participants, recruitment, and follow-up. From May to August 2004, all mother-infant pairs were screened for eligibility following delivery. Healthy mothers ≥18 y of age who had delivered their first or 2nd child were eligible to participate. Women with HIV/AIDS, gestational diabetes, morbid obesity, eclampsia or preeclampsia, or anemia (Hb < 100 g/L) during pregnancy were ineligible. Healthy singletons born at term (≥37 wk) with a birth weight of ≥2.5 kg who did not require medical observation in the nursery were eligible. Baseline data were collected while mother-infant pairs were in the hospital: infant weight and length, maternal prenatal care, and household sociodemographics. Before discharge, mothers were given an appointment to return for a well-baby clinic visit after 1 mo. Follow-up visits were conducted at infants’ monthly birthdays (≥1 wk) until they were 6 mo old. At each follow-up visit, infant’s length and weight were measured and the study pediatrician conducted a physical assessment of the infant. Mothers reported symptoms of infants’ GI infections, infant feeding since the previous visit, maternal employment, and smoking status.

We enrolled 230 of the 357 eligible mother-child pairs. At the 1-mo visit, 165 mothers returned and 134 completed the study. Of the women who did not return at 1 mo, 64 could not be reached because they lacked phone service and 21 did not return for follow-up despite numerous telephone reminders. After the 1-mo visit, 11 women did not return; 2 moved away, 2 were seeing another pediatrician, and 7 stated that the commute was too long. Of the 134 that completed the study, 8 infants had symptoms of infection at the 6-mo visit and did not return later to have blood drawn.

Anthropometric assessment. To ensure the adequacy of feeding practices and the general health of the infants, anthropometry was assessed at each follow-up visit. Trained researchers obtained infant weight to the nearest 20 g using a pediatric beam scale (Health-o-meter) and length to the nearest 0.1 cm using a locally made length board (14). Weight and length at 6 mo of age were converted to Z-scores using the WHO Child Growth Standards (15).

Illness assessment. The criteria specified by Rubin et al. (16) were used to diagnose a GI infection episode as the presence of at least 2 symptoms with a duration of 2–20 d: fever (≥38.5°C), decreased stool consistency, increased stool frequency, or vomiting. At each follow-up, we asked the mother if in the previous month the infant had any of those symptoms and the duration of each reported symptom. If no duration was reported, a minimum of 3 symptoms were necessary to identify a GI infection (16) or a diagnosis of a GI infection by the study pediatrician was required.

Biochemical assessments. At the 6-mo birthday, a pediatric nurse obtained a 6-mL nonfasting venous blood sample. If infants had symptoms of infection, the blood draw was deferred until the following week or until the infant was convalescent to mitigate the influence of inflammation on hemoglobin (Hb) and serum ferritin concentrations (17). Three milliliters were deposited into a blood collection vial for analysis of serum C-reactive protein (CRP) and serum ferritin using immunosorbent assay (Beckman Immage). Three milliliters were collected into a vial with EDTA to determine Hb concentration using an automated blood cell counter (Cell Dyne Beckman Coulter). Anemia was defined as a Hb concentration <110 g/L and ID was considered a serum ferritin concentration <12 μg/L (18). Infants with both Hb <110 g/L and serum ferritin <12 μg/L were considered to have ID anemia. CRP >0.8 mg/L was considered a marker for acute inflammation.

Assessment of infant feeding. At each follow-up visit, we asked mothers to report infant feeding practices in the previous day using a 24-h dietary recall and a monthly report of usual feeding practices. Mothers reported the number of times the child had been breast-fed (day and night feeds) and the amount of infant formula, nutritious and nonnutritive liquids, and solid foods provided to the child. Throughout follow-up, almost all infants received water, tea, juices, and/or "tastes" of foods (defined as less than a tablespoon or ~15 g of solid food given to the infant at weekly or monthly intervals). In Mexico, all infant formulas are iron fortified (8–12 mg/L).

Grouping of infant feeding. We created 3 mutually exclusive feeding groups based on the amount of human milk received throughout the 6-mo period. The formula-fed (FF) group received very little breast milk; no human milk by 3 mo of age and continued use of formula to at least 5 mo. The partially breast-fed (PBF) group received a moderate amount of breast milk along with formula: human milk and regular use of formula by 3 mo. We used the 3-mo cut-off because Mexican mothers typically transition their infants to formula at about this time (19). The PRBF group received substantial amounts of human milk: human milk for at least 5 mo with small and inconsistent amounts of formula at various times during the 6 mo. Grouping infant feeding this way resulted in PRBF having the highest exposure to human milk, PBF an intermediate exposure, and FF lowest exposure.

Statistical analyses. To detect a clinically significant difference of 20% in GI infection, assuming a baseline prevalence of 20% at an α of 0.05 and 80% power, using a 1-tailed test, 49 infants were required for each group. This sample size would allow us to detect a difference of 20% in ID considering a baseline proportion of 13% of anemia in children 6–11 mo (7). Anemia was considered a proxy for ID, because we could not find data on prevalence of ID at 6 mo in Mexican infants. Data were analyzed using SPSS Version 13 (SPSS).

Continuous variables were analyzed using ANOVA with a Tukey’s post hoc test. Interval data that were not normally distributed were analyzed using the Mann-Whitney or the Kruskal-Wallis test. Categorical variables were tested using Pearson’s χ² or a 1-sided Fisher’s exact test. We used regression analyses to assess the strength of the relationship between infant feeding practices and continuous outcome variables while controlling for confounding variables. Serum ferritin was posi-
tively skewed and was transformed using the natural logarithm of ferritin; serum ferritin concentrations were reported as geometric means. We also report the concentration ratio for serum ferritin, which is the exponentiated, unstandardized coefficient, because the outcome is on the log scale.

To test the hypothesis that frequent breast-feeding from 0–6 mo would protect against GI infections but not against ID or anemia, we dichotomized the exposure variable into predominant breast-feeding vs. not predominant breast-feeding (PBF and FF combined). To ensure that dichotomization of the exposure variable was adequate, we ran the analyses using both duration of breast-feeding and average formula intake as continuous variables. We obtained similar results with all 3 analyses. Therefore, we present risk for disease outcomes where infant feeding was dichotomous.

Logistic regression was used to test the association between PRBF and ID, anemia, and GI infection. We selected potentially confounding factors based on theoretical considerations of iron status (birth weight, infant sex, people in the home as proxy for crowding, maternal education, and parity) and GI infection (infant sex, people in the home, maternal education, and parity). Maternal education was associated with drop-out status and, thus, adjusting for education mitigated the effect of selection bias due to drop-out. Income was considered as categories of minimum salaries. Because participants were low-income, there was little difference in this variable. Therefore, income was not considered in the models, because it provided unstable estimates; maternal education can be considered a proxy variable for income. Similarly, there was little variation in hygiene (use of boiled water, ownership of a refrigerator, sewage disposal) and hygiene variables were not included in the models. The fit of logistic regression models was assessed with the Hosmer-Lemeshow test. A

### Results

**Sociodemographic characteristics of participants and women lost to follow-up.** The only variable to differ between participants and drop-outs was education, with drop-outs more likely to report <9 y of schooling (Table 1). Participants lived in relatively hygienic environments (88% had a refrigerator and 97% had sewage disposal). The majority of the women who reported using a bottle also reported hygienic preparation practices such as using boiled water and boiled teats (data not shown). The median number of people in the home was 5 (range, 2–18) and the groups did not differ ($P = 0.435$). Modal income was in the range of $251–496 USD and only 18% reported earning the minimum salary of $250 USD/mo. Household income (above vs. at or below the minimum salary) did not differ among feeding groups ($P = 0.09$) or between PRBF vs. non-PRBF group ($P = 0.40$). Compared with the PBF or FF groups, women in the PRBF group were least likely to have smoked before pregnancy (Table 1) and ≥3 mo during follow-up (PRBF 4% vs. PBF 18% vs. FF 24%; $P = 0.019$). Attained infant growth (weight, length, or Z-scores at 6 mo) did not differ among the feeding groups even after adjusting for potential confounders (data not shown).

**Breast-feeding frequency and duration.** Of the 154 participating mothers, 91% ($n = 141$) initiated breast-feeding in the hospital. At 6 mo, 50% ($n = 76$) of the mothers reported continued breast-feeding of their infant. The majority of infants (82%, $n = 117$) were never EBF. Some mothers (18%, $n = 34$) exclusively breast-fed for at least 1 mo; the longest duration of EBF was 5 mo (1.9%, $n = 3$). The use of powdered cow milk was minimal and inconsistent (7%, $n = 11$).

Of the 154 infants of participating women, 32% ($n = 49$) were PRBF, 37% ($n = 55$) were PBF, and 32% ($n = 50$) were FF from 0 to 6 mo. Our grouping of infant feeding practices captured exposure to human milk such that PRBF had the highest, PBF had less, and FF the lowest exposure. In the PRBF group, all except 1 infant continued to be breastfed at 6 mo and only 7 infants received some amount of formula (2 received ≤120 mL of formula/d and 5 infants received 150–360 mL of formula/d during the first or 2nd mo of life only). In the PBF group, between 4–6 mo visit 27 infants were no longer breastfed, 2 of whom were weaned to cow milk and the remainder to formula and 28 infants continued to be breast-fed at 6-mo visit. The number of months that breast-feeding was practiced was significantly greater for PRBF infants (median, 6 mo; range, 5–6 mo) than for PBF (median, 5 mo; range, 3–6 mo) or FF infants (median, 1 mo; range, 0–2 mo) ($P < 0.005$). For the months in which breast-feeding was practiced, PRBF infants were breastfed (mean ± SD) 10.5 ± 2.8 times/d (includes day and night

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**Table 1** Baseline characteristics of participants stratified by feeding group and of drop-outs

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PRBF</th>
<th>PBF</th>
<th>FF</th>
<th>Total</th>
<th>Drop-outs</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>49</td>
<td>55</td>
<td>50</td>
<td>154</td>
<td>96</td>
</tr>
</tbody>
</table>
| Infant
| Boys, n (%)  | 25 (51) | 29 (53) | 28 (56) | 82 (53) | 49 (51) |
| Birth weight, g | 3040 ± 300 | 3120 ± 360 | 3140 ± 340 | 3100 ± 340 | 3120 ± 360 |
| Length, cm     | 48.6 ± 1.5 | 48.6 ± 1.7 | 48.8 ± 1.5 | 48.7 ± 1.6 | 48.5 ± 2.3 |
| Birth2 WAZ     | −0.48 ± 0.65 | −0.31 ± 0.77 | −0.30 ± 0.80 | −0.37 ± 0.74 | −0.44 ± 1.10 |
| LAZ            | −0.58 ± 0.83 | −0.54 ± 1.20 | −0.48 ± 0.77 | −0.53 ± 0.94 | −0.73 ± 1.68 |
| WLZ            | −0.11 ± 0.77 | −0.07 ± 1.02 | 0.04 ± 0.83 | −0.05 ± 0.88 | −0.04 ± 0.93 |
| Maternal
| Age, y        | 22 ± 3 | 22 ± 3 | 22 ± 3 | 22 ± 3 | 22 ± 3 |
| Height, cm     | 157.1 ± 6.3 | 158.7 ± 6.5 | 156.8 ± 5.3 | 157.6 ± 6.1 | 157.4 ± 6.7 |
| Primipara, n (%) | 26 (53) | 27 (49) | 32 (64) | 85 (55) | 45 (47) |
| Education, ≥9 y, n (%) | 27 (55) | 32 (58) | 38 (76) | 97 (63) | 40 (41) |
| People in the home, >5 people, n (%) | 18 (37) | 32 (58) | 17 (34) | 67 (44) | 42 (44) |
| Prepregnancy smoking, yes, n (%) | 6 (13) | 17 (30) | 17 (36) | 40 (27) | 17 (20) |

1 Values are means ± SD, unless otherwise noted, n = 147 (participants) and 70 (drop-outs). 2 Different from participants, Pearson’s $χ^2 < 0.05$, 3 different from PRBF and FF, Pearson’s $χ^2 < 0.05$. 4 WHO 2006 growth standards (15): WAZ, Weight-for-age Z-score; LAZ, length-for-age Z-score; WLZ, weight-for-length Z-score.
Acute inflammation and iron status. Despite only drawing blood from infants when they did not appear to have an infection, 10 infants had elevated CRP (3 PRBF, 3 PBF, 4 FF). The serum ferritin concentrations of those infants did not differ from infants with normal concentrations of CRP (P = 0.56). For this reason, we did not exclude infants who had elevated CRP from the analysis of iron status.

GI infection and iron status. The majority (71.4%, n = 110) of infants never had a GI infection. Of the 44 cases of GI infection in the study period, 35 (80%) were single episodes and 9 were recurrent (2 or 3 GI infections). Because few infants had more than 1 infection, GI infection in the entire 6-mo period was dichotomized into never sick vs. ever sick. PRBF infants compared with non-PRBF infants (PBF + FF combined) were almost one-half as likely to have a GI infection [18% vs. 33%; Fisher’s 1-sided test, P = 0.04; unadjusted odds ratio (OR) = 0.5, 95% CI = 0.2, 1.0] (Table 2).

Mean Hb concentration was lower in PRBF infants than PBF and FF infants (P = 0.005) (Table 2). Even after adjusting for confounding, Hb concentration was 6 g/L lower in the PRBF infants than in FF infants (P = 0.003). Anemia prevalence did not differ among infant feeding groups (Table 2) nor was it significantly different between PRBF and non-PRBF infants (13 vs. 12%; Fisher’s 1-sided test, P = 0.50). For completeness, we ran an anemia model with the same predictors used for ID except that infant feeding was categorical instead of dichotomous. Feeding practices categorized this way remained unrelated to anemia (data not shown).

PRBF group had a lower serum ferritin concentration than the PBF and FF groups (Table 2). The PRBF group had one-half the mean serum ferritin concentration of the FF group even after controlling for confounding. In this model, serum ferritin at 6 mo was lower in primipara (concentration ratio = 0.7; P < 0.001) and in boys (concentration ratio = 0.6; P < 0.001) but was positively affected by birth weight (concentration ratio = 1.8; P < 0.001). ID was most prevalent in PRBF infants, less prevalent in PBF infants, and was absent in FF infants (P = 0.02) (Table 2). PRBF infants compared with non-PRBF infants had higher odds of ID [22 vs. 4%, Fischer’s 1-sided test, P = 0.001; unadjusted OR = 5.6; 95% CI = 1.8, 16.8]. Controlling for other variables, the PRBF group compared with the non-PRBF group still had higher odds of ID (Table 3). Only 1 infant, a PRBF baby, had ID anemia (Hb = 106 g/L, ferritin = 7.9 µg/L).

### Discussion

There are very few prospective studies in Mexico that examine infant feeding practices and a health benefit-vulnerability relationship. Our findings suggest that PRBF and feeding with ID formula each offer infants born to low-income women in Mexico a health benefit and health vulnerability. Iron-fortified formula protected infants from ID at 6 mo but increased infants’ risk for GI infection from 0 to 6 mo, whereas the reverse was true for PRBF infants throughout the first 6 mo of life. The overall prevalence of ID was low (10%), but when stratified by feeding group, 22% of PRBF infants were iron deficient, whereas ID was absent in FF. After controlling for confounding, PRBF infants had 9 times the odds for ID compared with infants who regularly received iron-fortified formula; however, only a single infant had ID anemia, a severe form of ID. PRBF infants who were breast-fed for 6 mo were one-half as likely to have a GI infection from 0 to 6 mo as infants who consumed more formula in the same time period (18 vs. 33%). This is an important consideration when taking feeding practices into account in this context, because GI infections are a cause of morbidity and mortality in infancy (20).

Iron status in the postnatal period is dependent on iron stores at birth (2) and on maternal iron status during pregnancy (3). Although we excluded low birth weight babies and mothers with severe anemia during pregnancy, we cannot say with certainty that all infants were born with sufficient iron stores, because no measures of iron status were obtained at birth. In their sample of lower-middle class mother-child pairs in Mexico City, Chaparro et al. (21) reported that ~29% of the pregnant women had ID anemia and mean newborn serum ferritin concentrations were 131 µg/L. Normally, serum ferritin concentrations at birth average 160 µg/L (22). It is likely that among socioeconomically disadvantaged populations, neonatal iron stores may be less than adequate. Also, low-income women in Mexico are more

### TABLE 2

Bivariate analysis of growth, GI infection, and iron status at 6 mo of age by feeding group

<table>
<thead>
<tr>
<th>Characteristic, 6 mo</th>
<th>PRBF</th>
<th>PBF</th>
<th>FF</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>49</td>
<td>55</td>
<td>50</td>
<td>154</td>
<td>0.642</td>
</tr>
<tr>
<td>Weight, g</td>
<td>7300 ± 920</td>
<td>7440 ± 900</td>
<td>7480 ± 840</td>
<td>7400 ± 900</td>
<td>0.02</td>
</tr>
<tr>
<td>Length, cm</td>
<td>65.1 ± 2.2</td>
<td>65.6 ± 2.5</td>
<td>65.7 ± 2.2</td>
<td>65.5 ± 2.3</td>
<td>0.74</td>
</tr>
<tr>
<td>WA2</td>
<td>−0.43 ± 1.0</td>
<td>−0.28 ± 0.96</td>
<td>−0.28 ± 0.95</td>
<td>−0.33 ± 0.96</td>
<td>0.683</td>
</tr>
<tr>
<td>LA2</td>
<td>−0.74 ± 1.0</td>
<td>−0.54 ± 0.92</td>
<td>−0.52 ± 0.89</td>
<td>−0.60 ± 0.94</td>
<td>0.494</td>
</tr>
<tr>
<td>WL2</td>
<td>0.12 ± 1.0</td>
<td>0.15 ± 0.98</td>
<td>0.14 ± 1.09</td>
<td>0.14 ± 1.01</td>
<td>0.993</td>
</tr>
<tr>
<td>GI infection, n (%)</td>
<td>9 (18)</td>
<td>18 (33)</td>
<td>17 (34)</td>
<td>44 (29)</td>
<td>0.158</td>
</tr>
<tr>
<td>Hb, g/L</td>
<td>116 ± 9 a</td>
<td>119 ± 9</td>
<td>122 ± 10</td>
<td>119 ± 9</td>
<td>0.005</td>
</tr>
<tr>
<td>Anemia, n (%)</td>
<td>6 (13)</td>
<td>10 (19)</td>
<td>2 (4)</td>
<td>18 (12)</td>
<td>0.091</td>
</tr>
<tr>
<td>Serum ferritin, µg/L</td>
<td>26.1 (19.3, 34.6)</td>
<td>45.5 (38.3, 56.9)</td>
<td>52.3 (43.3, 63.2)</td>
<td>40.1 (34.9, 46.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ID, n (%)</td>
<td>10 (22)</td>
<td>4 (8)</td>
<td>0 (0)</td>
<td>14 (10)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

1 P-values are expressed as means ± SD or mean (95% CI), unless otherwise noted. nPRBF significantly different from PBF and FF groups, P < 0.005.
2 P-values for group differences: Pearson χ² for categorical variables, ANOVA with Tukey’s post hoc test for continuous variables.
3 WHO 2006 growth standards (15). WAZ, Weight-for-age Z-score; LAZ, length-for-age Z-score; WLZ, weight-for-length Z-score.
4 Defined as ever sick with a GI infection.
5 n = 145: PRBF (n = 45), PBF (n = 53), FF (n = 47).
6 Anemia defined as Hb < 110 g/L; ID defined as serum ferritin <12 µg/L.
likely to EBF (19). Thus, the effects attributed to PRBF may be partially due to poor iron status at birth. Despite this limitation, our results highlight that among healthy term infants, PRBF from 0 to 6 mo of life may increase their risk for ID. The elevated risk for ID at 6 mo is a concern given that weaning foods in Mexico are low in bioavailable iron (6). ID in infancy has been linked with poor cognitive outcomes in adolescence (8). Although comparisons across populations are difficult because the degree of EBF varies, the mean serum ferritin of PRBF infants reported here at 6 mo are comparable to values reported in other studies of healthy breast-fed Latin American infants (23,24).

Our findings add to a small body of literature of the negative association of full (i.e. EBF and PRBF) breastfeeding to 6 mo and infant iron status. In their longitudinal study of Mexican infants (n = 184), Meinzen-Derr et al. (25) reported that EBF >6 mo of age was associated with increased risk of anemia at 9 mo (OR = 18.4, 95% CI = 1.9, 174.0) compared with EBF infants <4 mo. Similarly, in their cross-sectional survey, Chantry et al. (26) reported that among U.S. children 12–24 mo (n = 502) full breastfeeding >6 mo of age was associated with low serum ferritin (OR = 5.2, 95% CI = 1.8, 16.7) and a history of anemia (OR = 5.0, 95% CI = 1.6, 16.6) compared with infants fully breast-fed 4–5 mo.

Anemia at 6 mo was unrelated to feeding status even though FF infants had the highest Hb concentrations. The 12% prevalence of anemia at 6 mo was comparable to the national prevalence in Mexico for this age group (7). There has been considerable debate on the appropriate Hb cut-off to estimate the true prevalence of anemia, because the Hb concentrations between the anemic and nonanemic infants overlap considerably (27). The prevalence reported here may be an artifact of the cut-off used to define anemia (110 g/L). We adhered to WHO definition for anemia in infancy (18), but had we used a more conservative cut-off of 105 g/L, as suggested by Domellof et al. (27), the prevalence of anemia in the cohort would have dropped from 12 to 4% (n = 2 PRBF, n = 3 PBF, and n = 1 FF). More studies are needed to address the appropriate cut-off for anemia in a healthy infant population and its implications on functional outcomes.

We found that the PRBF group had a significantly lower risk for GI infection at 0–6 mo than the non-PRBF group, which is an important finding for health care providers. Full breastfeeding protects against GI infection, because breast milk contains numerous immunological components, and these components cannot be obtained in other foods or supplements (28). This is particularly significant during infancy when the immune system is still developing (28). Moreover, the antibodies present in breast milk are specific to the mother’s infectious environment (20). Long et al. (29) suggested that the secretory antibodies may help prevent the development of symptomatic diarrhea. Researchers have shown that both full breastfeeding (30) and EBF offer protection against GI infections (1). However, in our study, lower rates of GI infection would be anticipated if women exclusively breast-feed. Prior research has also shown that improved EBF rates to at least 3 mo result in a 40 (31) to 50% (32) reduction in the risk of GI infections even when EBF to 6 mo is not achieved. The variability in the duration and frequency of breastfeeding in our PBF group may have left many infants in this group with inadequate protection.

A methodological issue to consider was the reliance on maternal recall for morbidity. A 1-mo recall period for morbidity data might result in some women failing to recall symptoms that occurred early in the month. Before conducting this study, however, all pediatricians we consulted agreed that in this population (women having their first or 2nd child), the mother could recall well when her young child was sick, how long the illness lasted, and the symptoms. If recall bias did occur for GI symptoms, it would bias our results toward the null. We attempted to minimize detection bias through active surveillance of all study infants.

Our 3 feeding categories depict an overall pattern from 0 to 6 mo. These categories capture the degree of infant exposure to human milk, which is an important consideration in the biological relationship among breastfeeding, iron status, and GI infection. The infant feeding practices reported here such as initiation of breastfeeding, early weaning (regular use of formula and nutritive liquids), and ubiquitous use of nonnutritive liquids have also been documented previously by others in Mexico (12,13,19,33). Given that our study was conducted under standard care conditions, we chose breastfeeding frequency to approximate the amount of human milk consumed by the infant. Piwoz et al. (34) noted that Peruvian women tended to overreport the amount of formula used by 30% and underreport breast-feeding frequency by 25%. The presence of a dose-response relationship among degree of breastfeeding, GI infection, and serum ferritin values suggests that recall and reporting bias in our sample of Mexican women were probably small and distributed evenly among the 3 groups.

Because of our high refusal rate and drop-out rate, we cannot exclude the possibility of selection bias or confounding. Women who participated in this study may have differed from the low-income population of Mexican women. Compared with the national average, a greater proportion of our participants reported an education of ≥9 y (63 vs. 52%) and a smaller proportion reported a household income <$250 USD/mo (18 vs. 32%) (35). Also, drop-outs were less educated than participants. As such, participants may have had different health-seeking behaviors and care practices, which may have reduced the incidence of GI infection, although the adjustment in the analysis for education should have mitigated this potential bias. We noted, however, that the majority of women recruited into our study sought prenatal care and took prenatal vitamins (data not shown). It is plausible that eligible nonparticipants and drop-outs had less than adequate iron status during pregnancy (4), breast-fed more frequently (19), and had different health-seeking behaviors. In this case, our results are conservative estimates of the effects that we would expect to see in low-income population.

In our study, PRBF to 6 mo was the best feeding practice for infants, because it protected against GI infections. All women, and especially those who predominantly breast-fed (which indicates the motivation to breast-feed), should be considered

TABLE 3  Adjusted OR and 95% CI for ID and GI infections in infants1,2

<table>
<thead>
<tr>
<th>Variable</th>
<th>ID (OR CI)</th>
<th>P-value</th>
<th>GI infection4</th>
<th>OR CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBF3</td>
<td>9.2 (2.3, 37.0)</td>
<td>0.002</td>
<td>0.4 (0.2, 1.0)</td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td>Education, ≥9 y</td>
<td>1.2 (0.3, 4.7)</td>
<td>0.766</td>
<td>0.6 (0.3, 1.3)</td>
<td>0.178</td>
<td></td>
</tr>
<tr>
<td>People in the home</td>
<td>1.2 (0.9, 1.4)</td>
<td>0.148</td>
<td>1.0 (0.8, 1.1)</td>
<td>0.556</td>
<td></td>
</tr>
<tr>
<td>Primiparas</td>
<td>3.5 (0.7, 1.1)</td>
<td>0.074</td>
<td>1.1 (0.6, 2.3)</td>
<td>0.751</td>
<td></td>
</tr>
<tr>
<td>Sex, boys</td>
<td>4.0 (1.03, 15.8)</td>
<td>0.046</td>
<td>0.9 (0.6, 2.2)</td>
<td>0.824</td>
<td></td>
</tr>
<tr>
<td>Birth weight, kg</td>
<td>0.18 (0.02, 1.8)</td>
<td>0.148</td>
<td>–</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 All variables included in the model are shown.
2 ID defined as serum ferritin <12 μg/L, n = 145; GI infections defined as ever had a GI infection, n = 154.
3 Modeled as PRBF vs. non-PRBF (PBF + FF combined).
4 Birth weight was not included in the GI infection model.
for interventions and public policies that support and encourage EBF. If women are unable or choose not to breast-feed exclusively, then PRBF, which confers significant benefits to the child, should be supported. To reduce the risk for ID in a low-income population, it is crucial that prenatal, perinatal, and postnatal strategies be used in parallel with breast-feeding promotion. Such strategies include iron supplementation in pregnancy, delaying the clamping of the umbilical cord (21), introducing iron-rich or iron-fortified foods at ~6 mo, and universal screening for ID at well-baby clinics prior to 12 mo of age. Universal iron supplementation may be a preventative measure for ID (36), although the safety of this method has been questioned (37). Multifaceted maternal and child healthy public policies may adequately address the complex and context specific nature of infant feeding and health outcomes.

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Literature Cited