

Iron and the Exclusively Breast-Fed Infant from Birth to Six Months

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Summary: This study was designed to determine whether normal, full-term, exclusively breast-fed infants develop iron deficiency anemia, as defined by hemoglobin or red blood cell indices more than two standard deviations below the age-specific mean, or depletion of iron stores, as defined by an abnormally low serum ferritin level. Thirty-three breast-fed infants were followed from birth to 6 months. Maternal blood and cord blood at delivery, and venous blood from the infants at 2, 4, and 6 months were analyzed for anemia as defined above. At 6 months of age, the mean

hemoglobin concentration of these infants was slightly higher than the normal mean; four of 33 infants (12%) had a mean corpuscular volume >2 SD below the reported normal mean; and two of 33 infants (6%) had a serum ferritin level <12 ng protein/ml. These data suggest that the infant who is exclusively breast-fed for the first 6 months of life is not at high risk for the development of iron deficiency anemia or the depletion of iron stores during that time. **Key Words:** Iron deficiency anemia—Breast-feeding—Ferritin level—Hemoglobin.

The recommendation that breast-fed infants receive supplemental iron is based on conflicting data. McMillan et al. (1) reported that breast-fed infants do not need supplemental iron until the birth weight is tripled, which usually occurs at about 12 months of age. Fomon and Strauss (2) noted that (a) human milk contains approximately 0.5 mg per liter and only 49% of this iron is absorbed, and (b) an infant needs to absorb 0.5 mg of iron each day for the first year. If the infant consumes 1 L of milk each day, he or she will absorb only 0.25 mg iron, and hence, Fomon and Strauss (2) recommend iron supplementation for the breast-fed infant. Owen et al. (3) found that infants breast-fed until 20 weeks of age were iron sufficient at 6 months. The American Academy of Pediatrics reviewed these data and recommends iron supplementation for the breast-fed infant during the second half of the first year of life (4).

Thus, there is some controversy as to the need for supplemental iron in the prevention of iron deficiency anemia. In addition, there is some evidence that sup-

plemental iron may be harmful by reducing the bacteriostatic properties of human milk (5,6). Lactoferrin, an iron-binding, bacteriostatic protein, is present in high concentration in human milk. Iron bound to this protein is unavailable for bacterial growth, while unbound or free iron allows rapid bacterial multiplication (5,6). Hence, it is important to establish the age at which iron supplementation is necessary to prevent iron deficiency anemia while preserving as long as possible the bacteriostatic qualities of iron-binding proteins.

This study was designed to determine if normal, full-term, exclusively breast-fed infants need supplemental iron during the first 6 months of life. This need was to be assessed not only in terms of anemia as reflected in the red blood cell indices, but also by the status of the iron stores.

METHODS

Forty mother-infant pairs were enrolled in this study of exclusively breast-fed infants, which had the approval of our institutional review board and of the national review board of the La Leche League. Preg-

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nant women were asked to participate by private physicians, local members of the La Leche League, and midwives. Potential participants were informed about the study by the investigators, and consent was obtained at an interview prior to delivery. Participants agreed to breast-feed their infants for the first 6 months of life without any supplemental formula, solid foods, vitamins, or minerals. Occasional supplemental water was permitted. Mothers agreed to have their infants examined at regularly scheduled well-child visits and to permit us to draw 3 cc of blood at each visit.

All of the women enrolled in the study were well-nourished and healthy and had uncomplicated pregnancies and deliveries. None of the families were indigent. Of the 40 pairs initially recruited for the study, six (15%) dropped out before the first visit at 2 months because of difficulties in establishing breast-feeding or because of abnormalities which developed in the infant. Another dropped out at 5 months when the mother had to return to full-time work and was not able to continue exclusive breast-feeding. A final sample of 33 infants born between July 1980 and June 1982 forms the basis of this report. Thirty-one of the infants were Caucasian, while two were from multiethnic families in which one parent was Caucasian.

The infants in the final sample (21 male and 12 female) had been delivered at term (38–42 weeks) and

were of appropriate size for their gestational age (mean weight 3.5 kg, length 52 cm, and head circumference 35 cm). They had no significant abnormalities and had no excessive bleeding from the cord or with circumcision. None had hemolysis or required treatment for hyperbilirubinemia. All had uncomplicated neonatal courses.

Information collected included maternal age, gravidity, parity, length of gestation, occurrence of infections, use of medications or exposure to radiation during the pregnancy, blood group and Rh, and family history of anemia or of "bleeders." Perinatal information was also obtained as was a history for the interval between each clinic visit. This included maternal infections; maternal iron and vitamin supplementation; infant health; frequency and duration of breast-feeding; supplemental intake of other foods, vitamins, or minerals; history of blood loss; and residence at $\geq 5,000$ ft. The infants were examined at each visit for growth and any evidence of abnormalities.

Laboratory determinations were made on a maternal blood sample taken at the time of delivery, on cord blood, and on samples of the infants' blood taken from a peripheral vein at 2, 4, and 6 months of age. A Coulter counter was used to determine hemoglobin (Hb), hematocrit, red cell count, and indices. Whole

TABLE 1. Means and standard errors for measures of hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, serum ferritin, and reticulocyte count in maternal blood and in exclusively breast-fed infants during the first 6 months of life

	Maternal blood	Cord blood	2 Months	4 Months	6 Months
Hemoglobin (g/dl)					
Mean	12.8	16.3	12.2	12.2	12.12
SE	0.22	0.24	0.22	0.15	0.19
n ^a	32	27	28	29	28
Mean corpuscular volume (fl)					
Mean	92.7	110.3	94.7	81.7	78.7
SE	0.78	0.60	0.77	0.67	0.83
n	32	27	27	29	28
Mean corpuscular hemoglobin (pg)					
Mean	32.0	36.7	33.4	29.1	28.2
SE	0.33	0.37	0.31	0.31	0.30
n	32	27	27	29	28
Serum ferritin (ng/ml)					
Mean	45.1	150.1	247.2	99.1	53.1
SE	15.08	19.07	23.05	15.85	7.08
n	28	29	29	29	28
Reticulocyte count (%)					
Mean	1.6	4.8	1.5	0.7	9.0
SE	0.15	0.35	0.27	0.08	0.15
n	26	24	25	27	27

^aBecause of technical problems in drawing and processing blood for analysis, the entire sample of 33 infant/mother pairs is not represented at any given interval.

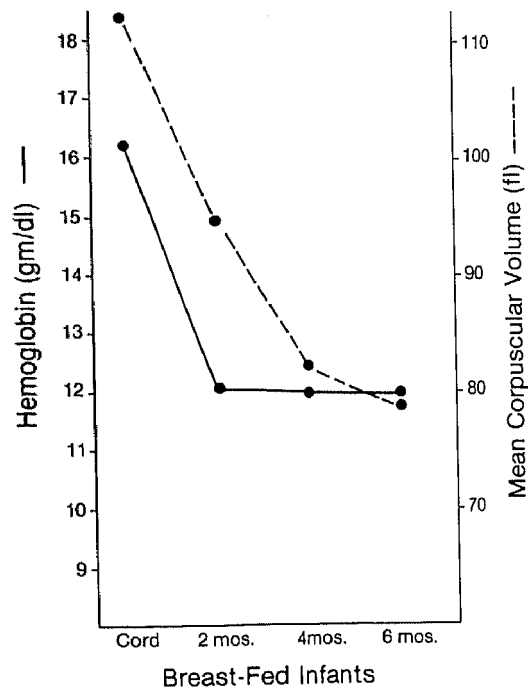


FIG. 1. Changes in mean values of hemoglobin and mean corpuscular volume in breast-fed infants from birth to 6 months.

blood samples were stained with methylene blue for reticulocyte quantitation using standard hematologic technique. Serum ferritin measurements were performed by radioimmunoassay.

RESULTS

Means and standard errors for Hb, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), serum ferritin, and reticulocyte counts from maternal blood, cord blood, and from the infant at 2, 4, and 6 months of age are given in Table 1. Changes in the mean values of these indices for the infant from birth to 6 months of age are shown for Hb and MCV in Fig. 1 and for serum ferritin and MCH in Fig. 2. At 6 months the mean Hb of this group of infants was 12.2 g/dl. At 6 months the mean MCV was 78.7 fl and the mean MCH was 28.2 pg. A serum ferritin level of less than 12 ng/ml was noted in one infant at 4 months and in two infants at 6 months of age. At 6 months the mean reticulocyte count was 0.9%. No infant had a combination of Hb, MCV, MCH, and serum ferritin level less than 2 SD from the reported normal mean values (7).

The age-specific normal values for means and standard deviations used for comparison in this study were those reported by Saarinen and Siimes for a group of

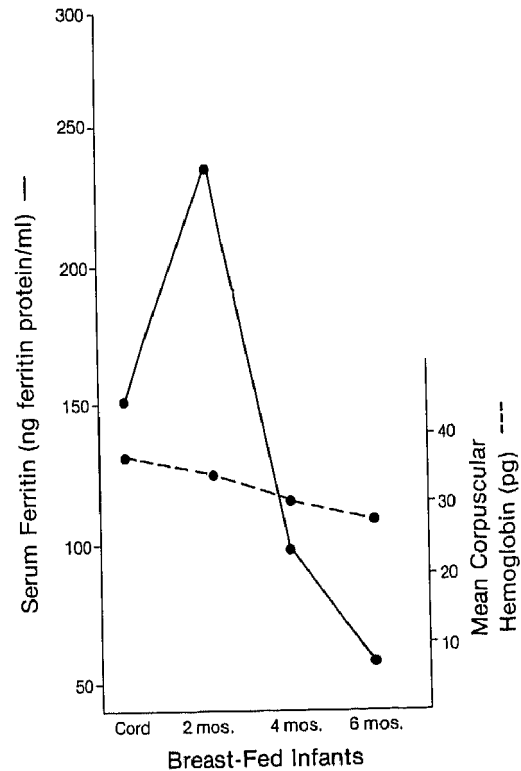


FIG. 2. Changes in mean values of serum ferritin and mean corpuscular hemoglobin in breast-fed infants from birth to 6 months.

infants who were not iron deficient and who were receiving an iron-supplemented milk formula (7). We selected these as standard values because they represented a group of infants with optimal iron status. Normal mean values, values for 2 SD below the mean, and abnormal values observed in this study are shown in Table 2. As reported by Saarinen and Siimes (7), normal mean Hb at 6 months of age is 12.6 g/dl with 2 SD below the mean equal to 11.1 g/dl. The mean Hb of the infants in this study at 6 months was 12.2 g/dl, and four infants had an Hb level less than 11.1 g/dl (10.6–10.9 g/dl). The normal mean for MCV as reported by Saarinen and Siimes (7) is 76.3 fl with 2 SD below the mean being 68 fl. None of the infants in this study had an MCV value less than 68 fl. The normal MCH mean is 26.8 pg and 2 SD below the mean is 24 pg (7). None of the infants in the present study had an MCH value less than 24 pg. Two infants in this study had serum ferritin levels less than 12 ng/ml (4.9 and 8.5 ng/ml), but each had Hb levels greater than 11.1 g/dl (11.9 and 11.7 g/dl, respectively).

Product-moment correlation coefficients were used to assess (a) the extent of association between maternal and infant measures of iron stores, and (b) the

TABLE 2. Normal mean values and abnormal values (<2 SD below normal mean) for measures of hemoglobin, mean corpuscular volume, and serum ferritin in 4- and 6-month-old infants

Laboratory measures	Age of infant	
	4 mo	6 mo
Hemoglobin (g/dl)		
Normal mean value ^a	12.2	12.6
-2 SD ^a	10.3	11.1
Abnormal values	None	10.6, 10.8, 10.8, 10.9
Mean corpuscular volume (fl)		
Normal mean value ^a	86.7	76.3
-2 SD ^a	76	68
Abnormal values	74, 75	None
Mean corpuscular hemoglobin (pg)		
Normal mean value ^a	28.6	26.8
-2 SD ^a	25	24
Abnormal values	None	None
Serum ferritin (ng/ml)		
Normal median value ^b	85	30
Abnormal values	11.2	4.9, 8.5

^aFrom Saarinen and Siimes (7).

^bFrom Siimes et al. (10).

association between measures of physiologic iron stores and measures of iron deficiency anemia in the infant. There were few significant correlations among either set of relationships, and the pattern of results suggested that the correlations might be due to chance alone. One possible exception was a positive correlation between maternal serum ferritin and infant serum ferritin levels at 2 months ($r = 0.39$, $p < 0.05$) and at 6 months ($r = 0.43$, $p < 0.05$). There were no significant associations between laboratory measurements and any portion of the maternal history, infant feeding, or physical examination data.

DISCUSSION

In this study, iron deficiency was defined as values greater than 2 SD below the age-specific mean for physiologic iron stores (serum ferritin), MCV, MCH, and/or Hb. Among the 33 full-term newborns in this sample, all of whom were exclusively breast-fed without supplementation for the first 6 months of life, none developed iron deficiency anemia and only two infants (7%) showed an indication of depleted iron stores as reflected by low ferritin values.

Despite the calculated inadequacy of iron in human milk (2), either the term infant is born with sufficient iron stores or the exclusively breast-fed infant is able to absorb sufficient quantities of iron to preserve an adequate iron status. The enhanced bioavailability of

iron in breast milk does decrease when solids are added to the infant's diet (8,9). This may explain why studies of iron status in breast-fed infants who also received some solid supplementation have found results contrary to those reported here.

The mean serum ferritin values in our infants were greater than the average normal values at each age interval as reported by Siimes and colleagues (10). In part, this may be due to the extremely large values reported for some of the infants. The assay used is a reliable one; however, an acute inflammation process or fever may falsely elevate serum ferritin. None of the infants were overtly ill at the time the blood was drawn, but a nonapparent inflammatory process could have been present.

This study involving infants from the United States corroborates the recent findings of Siimes and colleagues (11), who evaluated the risk of iron deficiency in Scandinavian infants who were breast-fed for 6 months. Using a definition of anemia as a concentration of Hb <10.5 g/dl or an MCV level <70 fl from 6 to 9 months of age, none of their 36 infants developed anemia. Four additional laboratory criteria were used to define iron deficiency in their study: serum iron concentration <55 mg/dl, total iron-binding capacity >375 mg/dl, transferrin iron saturation <30%, and serum ferritin <10 mg/L. At 6 months, 8% (nine of 116) of their infants met three of these six laboratory criteria. A control group of infants who received iron-fortified formula and solids after 3½ months had fewer laboratory values below the established criteria.

Our study involved a unique set of mothers who were adamant about the importance of exclusive breastfeeding for at least the first 6 months. Many were involved with the "return-to-nature" philosophy as reflected by the fact that 13 (39%) delivered their infants at home by licensed midwives or naturopaths and 29% used herbal medications. However, these same qualities probably minimized the dropout rate and assured their adherence to exclusive breast-feeding. Reported dietary indiscretions were almost nonexistent. The lack of solid food supplementation may have been partially responsible for these infants not developing anemia. It is our conclusion that the full-term infant who is exclusively breast-fed for the first 6 months of life is not at high risk of developing iron deficiency anemia or depleted iron stores during that time.

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REFERENCES

1. McMillan JA, Landaw SA, Oski FA. Iron sufficiency in breast-fed infants and the availability of iron from human milk. *Pediatrics* 1976;58:686-91.
2. Fomon SJ, Strauss RG. Nutrient deficiencies in breast-fed infants. *N Engl J Med* 1978;299:355-7.
3. Owen GM, Garry PJ, Hooper EM, Gilbert BA, Pathak D. Iron nutriture of infants exclusively breast-fed the first five months. *J Pediatr* 1981;99:237-40.
4. American Academy of Pediatrics, Committee on Nutrition. Nutrition and lactation. *Pediatrics* 1981;68:435-43.
5. Bullen JJ, Rogers HJ, Leigh L. Iron-binding proteins in milk and resistance to *Escherichia coli* infections in infants. *Br Med J* 1972;1:69-75.
6. Spok G, Cheron A, Mantrevil J, Dolby JM. Bacteriostasis of milk-sensitive strain of *Escherichia coli* by immunoglobulins and iron-binding proteins in association. *Immunology* 1978;35:663-71.
7. Saarinen UM, Siimes MA. Developmental changes in red blood cell counts and indices of infants after exclusion of iron deficiency by laboratory criteria and continuous iron supplementation. *J Pediatr* 1978;92:412-6.
8. Saarinen UM, Siimes MA. Iron absorption from breast milk, cow's milk, and iron supplemented formula: an opportunistic use of changes in total body iron determined by hemoglobin, ferritin, and body weight in 132 infants. *Pediatr Res* 1979;13:143-7.
9. Oski FA, Landaw SA. Inhibition of iron absorption from human milk by baby food. *Am J Dis Child* 1980;134:459-60.
10. Siimes MA, Addiego JE Jr, Dallman PR. Ferritin in serum: diagnosis of iron deficiency and iron overload in infants and children. *Blood* 1974;43:581-90.
11. Siimes MA, Salmenpera L, Perheentopa J. Exclusive breast-feeding for 9 months: risk of iron deficiency. *J Pediatr* 1984;104:196-9.