Failure of Hematocrit to Detect Iron Deficiency in Infants

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Background. Infants of low-income families have three times the risk of iron deficiency as those of families above the poverty level. Psychomotor deficits have been associated with iron deficiency once it produces anemia. High-risk infants are usually screened for iron deficiency between 9 and 12 months of age with a hematocrit measurement. This type of screening may miss iron-deficient infants who are not yet anemic.

Methods. In the well-child clinics for low-income families in Houston, Texas, a hematocrit (Hct) ≤33% is the standard screening criterion for iron deficiency. Three hundred twenty-one infants between the ages of 9 and 18 months had capillary blood drawn for Hct testing. Serum ferritin levels were simultaneously measured.

Results. Six (1.9%) of the 321 infants were anemic, but none because of iron deficiency. Fifty-one infants (15.9%) were iron deficient (ferritin <10 μg/L), none of whom were anemic. Hematocrit and ferritin levels did not correlate statistically.

Conclusions. The Hct is not an adequate screening test for iron deficiency in this population of infants. Although this population is usually considered high-risk, iron deficiency was mild. Selective screening of high-risk infants in this population may be appropriate, but a more sensitive screening test is required. Further studies are needed to determine the prevalences of iron deficiency in this and other high-risk populations.

Key words. Anemia, iron deficiency; medical indigency; poverty; infant; prevalence.
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Iron deficiency is the most common nutritional deficiency in the United States.[1(pp19-36)] It is routinely screened for in infants about 1 year of age by using a hemoglobin or hematocrit (Hct) measurement. Historically, there has been little impetus to identify iron deficiency during the pre-anemic stage because the hematologic consequences of iron deficiency anemia (IDA) are typically asymptomatic and easily reversible.

In the past decade, studies have linked IDA to behavioral, cognitive, and developmental deficits.[2,3] These deficits do not occur until the iron deficiency has resulted in anemia; however, it is uncertain whether these impairments can be reversed with correction of the iron deficiency and the anemia.[2,4] Therefore, the standard practice of screening for iron deficiency by measuring hematocrit may miss iron-deficient infants at a stage during which correction of the deficiency would prevent these psychomotor deficits.

The purpose of this study was to prospectively evaluate a population of infants traditionally at high risk for IDA to determine the number of healthy infants in whom iron deficiency goes undetected using the current screening technique.

Methods

Infants aged 9 to 18 months who were brought voluntarily to any of four well-child clinics in Houston, Texas, between April and August 1990 were potential candidates for this study. These clinics provide service exclusively to low-income families. Infants were excluded from the study if they had not been entirely well 2 weeks before screening or if there was evidence of an infectious disease process, as determined by the examining physician. These infants were excluded because infection can transiently

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lower the Hct or elevate the serum ferritin level, or both.[5,6] Chronically ill infants, those previously diagnosed as anemic, including infants with sickle cell anemia, and those receiving medicinal iron were also excluded. Causes of anemia other than iron deficiency, such as thalassemia, were not determined.

Clinic staff members reviewed with the guardian or parent of each of the eligible infants a 2-page informed consent form written in English or Spanish. Age, sex, and race were recorded. Capillary blood samples were drawn and sent to the city's central laboratory, where all Hcts were measured in duplicate using the standard technique. The remaining portion of each sample was centrifuged, and the serum was frozen at −20°C. Serum ferritin was measured in duplicate by RAMCO commercial laboratories using an immunoradiometric assay. Infants were classified as iron deficient if their serum ferritin was less than 10 μg/L[7]; anemic if their Hct was equal to or less than 33% (standard value used by the central laboratory); and IDA if both conditions existed.

Results

From a total of 580 potential candidates 9 to 18 months of age, 161 were excluded because of current or recent infection (n=100), use of oral iron medication (n=37), previously documented anemia (n=18), or chronic illness (n=6). Lack of permission from the parent or guardian (n=67) and refusal to undergo tests at the laboratory (n=23) excluded another 90 candidates. Eight eligible candidates were not evaluated because of lost specimens, failure to test the blood specimen, or inadequate samples. There was no significant difference between the study group and the infants who were excluded with respect to mean age or sex.

Of the 321 infants included in the study, the mean age was 12.5 months (standard deviation [SD] 2.9). Approximately one half (49.8%) were Hispanic, 43% black, 2.5% white, and 4.7% mixed or other; a slight majority (50.7%) were male. The overall mean Hct and serum ferritin levels were 37% and 21.8 μg/L, respectively. No significant difference in mean Hct or serum ferritin was seen with respect to race (Table). Individual Hct and serum ferritin values for all 321 infants are summarized by group in Figure 1 and plotted individually in Figure 2. Six (1.9%) infants were anemic, 51 (15.9%) had iron deficiency, and none had IDA. There was a significant difference in mean serum ferritin levels for iron-sufficient (24.5 μg/L; SD 15.0) vs iron-deficient (7.6 μg/L; SD 1.6) groups ($P<.001$).

Table. Mean Hematocrit and Ferritin, by Race

Race	No.	Hct, % (SD)	Ferritin, μg/L (SD)
Hispanic	160	36.9 (2.1)	21.2 (15.8)
Black	138	37.3 (2.4)	23.1 (15.2)
White	8	37.1 (1.7)	22.8 (10.0)
Mixed/other	15	37.0 (2.2)	15.8 (4.2)
Total	321	37.0 (2.2)	21.8 (15.1)

SD denotes standard deviation.

Discussion

Iron deficiency has three stages: iron depletion (low ferritin); decreased iron transport (low transferrin saturation); and diminished production of hemoglobin (increased free erythrocyte protoporphyrin, anemia, and microcytosis).[8] Psychomotor deficits have been linked to the final stage of iron deficiency, ie, severe iron deficiency or IDA.[2,3] Therefore, to prevent these deficits, it is necessary to identify iron-deficient infants before they develop anemia.

This study found that 51 of the 321 infants (15.9%) were iron deficient. None of these patients had an abnormally low Hct. If not enrolled in the study, these infants would not have been identified as iron deficient by the traditional screening method. Further analysis revealed no correlation between Hct and serum ferritin levels (Figure 2). Additionally, the mean Hct of the iron-deficient group was in the normal range, which was nearly identical

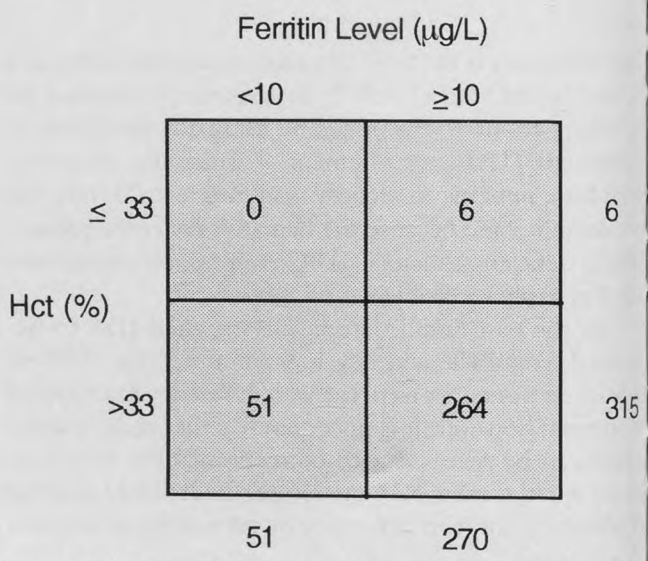

Figure 1. Hematocrit (Hct) and iron deficiency levels among 321 infants. The number in each of the four quadrants represents the number of infants with the corresponding Hct and ferritin level. The numbers to the right of and beneath the matrix are subtotals: eg, 6=all infants with Hct <33%; 51=all infants with ferritin levels <10 μg/L.

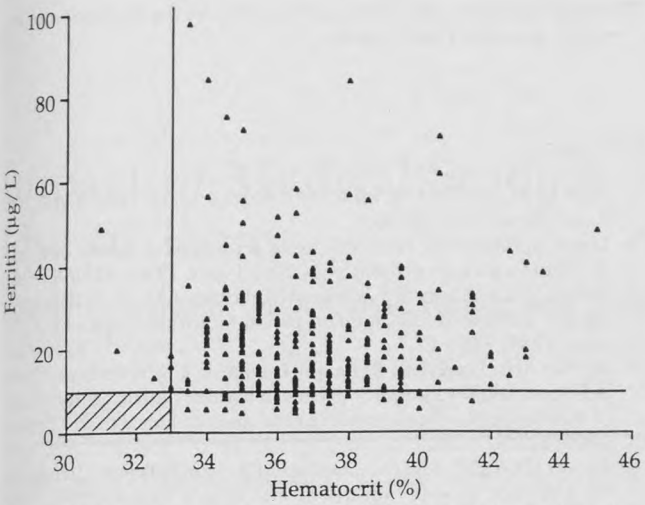

Figure 2. Ferritin vs hematocrit (Hct). Individual points (n=321) for each infant's ferritin and hematocrit are plotted. Hatched area indicates anemia (Hct ≤33%) and depleted iron stores (ferritin <10 μg/L). Note that some values are superimposed.

to that of the iron-sufficient group. Thus, in this population, Hct was an ineffective screening test for iron deficiency.

The public health burden of such an insensitive screening test becomes greater as the prevalence of IDA increases. In this study, the risk of IDA appeared to be small: only six infants (1.9%) were anemic and none were iron deficient. The study, however, was not designed to determine the prevalence of IDA. Although, there were no new cases of IDA in the tested group, 18 infants with anemia had been excluded from the study. None of these infants had their anemia evaluated further, but many were receiving iron empirically for IDA. This limitation of the study allows for only an estimate of the prevalence of IDA. If these 18 infants had not been excluded and were iron deficient, the prevalence of IDA would have been 5% (18/339). The latter is a liberal calculation since it is unlikely that all 18 infants were iron deficient, and many infants were not anemic when screened before the study but were excluded for other reasons. Additionally, the usual anemia cutoff for this age group is a Hct <33%,[7] but the laboratory used in this study includes a Hct of 33% as anemic, which further inflated the prevalence. Therefore, it is reasonable to conclude that the prevalence of IDA in this population was less than 5%. This figure is low compared with the 15.9% prevalence of anemia found by the 1987 Center for Disease Control Pediatric Nutrition Surveillance System study of 6- to 24-month-old infants from low-income families.[1(pp19-36)]

If the prevalence of IDA was low, overall iron deficiency in the group should have been mild. This appeared to be the case, as no infants had severe iron deficiency, and the mean serum ferritin (21.8 μg/L) of the sample was in the normal range. Furthermore, there was no correlation between anemia and iron deficiency, a finding typical in a population of infants with mild iron deficiency.[1(pp37-56)]

This study raises the question about the most appropriate way to screen infants for iron deficiency. The prevalence of IDA has declined across all socioeconomic groups,[1(pp37-56),9-11] leading some to recommend selective screening of individual infants at high risk for iron deficiency instead of routinely screening all infants.[12] Infants of low-income families have remained the exception and continue to be screened universally.[13] Infants of low-income families had three times the risk of iron deficiency as those above the poverty level in the 1985 Second National Health and Nutrition Examination Survey.[1(pp19-36)] The prevalence of IDA in this traditionally high-risk population of infants, however, appeared to be low. Further study of the prevalence of IDA in high-risk infant populations is needed. If IDA has declined significantly in this group, selective screening based on individual risk may be safe.

A reexamination of which iron deficiency screening test should be used for infants between 9 and 12 months of age is also necessary. This study suggests that anemia screening for iron deficiency may not be efficacious. Serum ferritin, transferrin saturation, and free erythrocyte protoporphyrin (FEP) are typically considered diagnostic tests. However, FEP has been found to be an adequate screening test for iron deficiency in infants.[14] If elevated, confirmation of the diagnosis is made with a therapeutic trial of iron.[15,16] Unfortunately, the availablility of FEP has limited its use as a screening tool. Although it is not an expensive test to perform, FEP is often not done in local laboratories, and reference laboratory prices may preclude its use as a screening test.

Primary prevention, not screening, is the ideal approach to iron deficiency in infancy.[17] The healthy iron nutritional status of the infants in this study is probably the result of dietary changes made in the last two decades: infant foods were fortified with iron,[18] the detrimental effect of cow's milk was elicited,[19] and the benefits of breast milk were espoused. The frequency of breast-feeding and the use of iron-fortified formula increased, while cow's milk consumption decreased.[1(pp37-56)] Concomitantly, the burden of iron deficiency in infants has steadily declined. Practitioners need to promote breast-feeding with iron supplementation of all breast-fed infants starting at 4 months of age,[20] recommend that no cow's milk be given during the first 12 months of life, and make sure that only formulas fortified with iron are used.

Further limitations of the study include those inherent in a cross-sectional design. Infants identified as iron deficient were not followed to see if they developed IDA.

However, abnormal test results were given to the physician so that infants could be treated to prevent IDA. Another potential problem is that Hct testing can underestimate the prevalence of anemia.[12] This may have been negated by the generous cutoff used by the clinics to define anemia. Finally, serum ferritin may identify some infants with early iron deficiency whose depleted iron stores will self-correct and not require treatment. In the age range studied, the cutoff for an abnormally low serum ferritin is 10 μg/L to 12 μg/L.[7] Therefore, 10 μg/L was chosen to account for this possibility.

Conclusions

Hct has long been the standard test used to screen for iron deficiency in infants, but in this population of infants from low-income families, it was found to be an inadequate screening test. There was no correlation between the Hct and serum ferritin. The ideal screening test for iron deficiency has not been identified. Early detection of iron deficiency prior to anemia should be the goal of screening. Further studies are needed to assess the prevalence of IDA in other high-risk populations of infants. If greater emphasis were placed on the primary prevention of iron deficiency, screening for this problem would ultimately become obsolete.

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