Outcome of Children Identified as Anemic by Routine Screening in an Inner-city Clinic

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Background: Children found to be anemic on routine screening by HemoCue, a rapid and relatively inexpensive method of screening for hemoglobin (Hb), are often prescribed iron as a diagnostic tool and potential treatment for presumed iron deficiency anemia (IDA). We questioned this approach given the declining prevalence of IDA and the concomitant relative increase in other causes of anemia.

Objective: To evaluate the practice of Hb screening for IDA by determining the prevalence of anemia by HemoCue; the proportion of anemic patients treated with iron and followed up; the frequency of repeated Hb testing, additional iron studies, and iron prescriptions; and the 6-month outcomes of treated and untreated anemia.

Design: Retrospective cohort study.

Results: Of 1358 children aged 9 to 36 months who underwent screening, 343 (25%) had anemia, defined as a Hb level of less than 110 g/L. Outpatient medical records of 334 of the anemic children revealed that 239 (72%) were prescribed iron while 95 (28%) were not prescribed iron at the first visit for anemia. Anemia follow-up rates were low for the prescribed and not prescribed groups: 7% vs 5% returned within 1 month, while 37% vs 42% did not return within 6 months for follow-up. Of the children who were prescribed iron, 107 (71%) of 150 responded to treatment or anemia resolved within 6 months compared with 27 (68%) of 40 not prescribed iron. Children underwent repeated blood testing for measurement of Hb and complete blood cell count, but underwent few iron-specific studies.

Conclusions: Routine screening for IDA by HemoCue followed by a therapeutic trial of iron was problematic because of a high rate of anemia in this predominantly African American population, low follow-up rates, and a high spontaneous resolution rate. Prospective studies are needed to evaluate other screening methods to differentiate IDA from other forms of anemia and to improve compliance and outcome in inner-city children.


The adverse effects of iron deficiency anemia (IDA) on growth and development provide the rationale to screen all children for this nutritional deficiency.1-5 The American Academy of Pediatrics recommends that high-risk children be routinely screened for IDA by hemoglobin (Hb) level or hematocrit at the age of 9 to 12 months and again 6 months later.6 However, the Hb level and the hematocrit are measures of anemia but do not provide information about the cause of anemia. In addition to IDA, anemia may be commonly present because of thalassemia traits, chronic diseases, or recent infections.7-8

Many outpatient clinics and Women, Infants, and Children program facilities screen for anemia by HemoCue (HemoCue Inc, Mission Viejo, Calif). This rapid and relatively inexpensive method of screening for Hb is, under certain conditions, a reliable screening method when compared with the Coulter counter determination of Hb.9-13 Response to iron therapy is a valid indication of IDA. A common practice is to assume all anemia detected on routine screening represents IDA, to treat it with 1 month of iron therapy, and to measure the response. An increase of 10 g/L of Hb is considered diagnostic of IDA.6,14,15

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There are several limitations to screening for IDA followed by treatment with iron for all patients with a positive screening test result. It requires at least one timely follow-up visit to the health care provider and a second blood test. Furthermore, as the prevalence of IDA decreases,16-19 the positive predictive value of Hb level for IDA decreases and other common causes of anemia become more likely. Prior experiences in our pediatric resident continuity clinic led us to ques-
MATERIALS AND METHODS

This retrospective cohort study using medical record review was conducted in a hospital-based inner-city pediatric resident continuity clinic in Baltimore, Md. The clinic staff included pediatric residents, attending physicians, general academic pediatric fellows, and 1.5 full-time-equivalent pediatric nurse practitioners. Patients who attended the clinic were assigned to a single primary care provider who provided 85% to 90% of their health maintenance care. A yearly didactic session on anemia was attended by the residents, and suggested that screening be performed according to the American Academy of Pediatrics–recommended guidelines; that anemia be defined as a Hb level of less than 110 g/L; and that anemia be treated with iron, as recommended by the American Academy of Pediatrics and other sources.6,14,15

The hospital laboratory billing system was used to identify all children aged 9 to 36 months who underwent HemoCue tests performed in the clinic from March 1, 1995, to February 28, 1997. This age group was targeted because the clinic followed the then-current American Academy of Pediatrics–recommended guidelines for screening children for anemia, at the age of 9 to 12 months and again at the age of 2 to 5 years.20 All Hb values were obtained from the electronic patient record. Children with more than one Hb screening during the study period were counted only once. The sample population was divided into the anemic group, children with at least one Hb value of less than 110 g/L, and the nonanemic group, children with all Hb values of 110 g/L or greater. For children in the anemic group, the child’s first visit with a Hb level of less than 110 g/L was considered the “index visit,” and subsequent additional HemoCue results were considered “follow-up” data. A standard data collection form designed for this project was used to review the outpatient medical records of all children identified as anemic for 6 months from the index visit. Abstracted information included demographic data, medical history, laboratory test results, visit dates, iron therapy, and recommended follow-up. Medical history information included newborn Hb electrophoresis results if available, a previous diagnosis of hemoglobinopathy, the number of medical record–documented illnesses and hospitalizations for the 3 months before the index visit, and previous diagnosis and treatment of anemia. Because iron therapy before the index visit might represent variable degrees of treatment, the duration of and response to the iron therapy before the index visit were evaluated. The results of any anemia-related laboratory tests obtained at the discretion of the primary care provider were recorded, including HemoCue Hb level, Hb level from the complete blood count (CBC), mean corpuscular volume (MCV), red cell distribution width (RDW), reticulocyte count, lead level, serum iron level, serum ferritin level, transferrin level, total iron binding capacity, Hb electrophoresis, and sickle cell screen. Follow-up visits included all visits during which anemia was subsequently addressed, such as well-child care, acute care, follow-up, and Women, Infants, and Children program form completion; however, emergency department visits were not included. Physician-recommended time to follow-up and actual patient follow-up times were recorded.

The status of anemia during the 6 months following the index visit was determined for each child using the following definitions: resolved if the highest follow-up Hb level was 110 g/L or greater, and responded if the highest follow-up Hb increased by 10 g/L from the index visit Hb level but remained less than 110 g/L. Outcomes for children treated with iron were classified into 3 categories: “prescribed, resolved,” “prescribed, responded,” and “prescribed, did not respond or resolve.” Outcomes for children not treated with iron were classified into 3 categories: “prescribed, resolved” and “not prescribed, did not resolve.” Other outcomes were “no anemia follow-up after index visit” and “inadequate information to determine.” Once anemia resolved, subsequent follow-up data were not considered for the 6-month outcome determination. Follow-up and outcome were analyzed by Hb level (106–109 and <106 g/L) to determine if more significant anemia is addressed more vigilantly. These Hb levels were selected because the sample was largely African American and the Institute of Medicine has advocated using 4 g/L lower Hb standards for this population.14

Statistical analysis was performed using a computer program (SPSS 9.0 [Windows version]; SPSS Inc, Chicago, Ill). A t test was used to compare means, and x2 and Fisher exact tests were used to compare nominal data. Bonferroni correction was used to correct for multiple comparisons. Statistical significance was set at .05. The institutional review board approved this project.

RESULTS

During the 2-year study period, 1358 children aged 9 to 36 months were screened one or more times for anemia by HemoCue. One quarter of the children had at least one Hb value less than 110 g/L and were identified as being anemic. Nine anemic children were excluded, based on medical history, from further analysis, 6 with sickle cell anemia and 3 who were treated for lead poisoning with succimer under a study protocol in which iron therapy was contraindicated. The remaining 334 chil-
Children constitute the “anemic group” for the remainder of the analysis (Figure).

Children with a Hb value of less than 110 g/L at the index visit were categorized into 2 groups based on whether they were prescribed iron at the index visit. The groups were not significantly different for age, sex, race, and insurance status (Table 1). The rates of sickle cell trait, previous treatment with iron, serum lead levels, and number of illnesses and hospitalizations in the 3 months before the index visit were also not significantly different. Seventy-two percent of children with a Hb value of less than 110 g/L were prescribed iron at the index visit; 15 more children had iron prescribed at a follow-up visit. About half of the children had mild anemia, with Hb levels ranging from 106 to 109 g/L. Children who were prescribed iron had a lower mean Hb level, and thus more severe anemia, than those not prescribed iron (104 vs 106 g/L; P < .001); nevertheless, 33% of children who were not prescribed iron had a Hb level of less than 106 g/L at the index visit (Table 1).

Health care provider documentation of the need to return for follow-up was significantly more likely if iron was prescribed, regardless of Hb level. However, only 44% of the patients who were prescribed iron and who had a medical record–documented recommended time for a return visit were asked to return in 1 month. Patient follow-up rates for the prescribed and not prescribed groups were not significantly different. Within each group, follow-up rates did not vary significantly by level of anemia. Most notably, only 7% of patients who were prescribed iron, regardless of Hb level, and 3% with a Hb level between 106 and 109 g/L and 9% with a Hb level of less than 106 g/L who were not prescribed iron returned for follow-up within 1 month of diagnosis (Table 2).

The following outcome results include only children who received anemia follow-up care within 6 months of the index visit: 150 (64%) of 234 children from the prescribed group and 55 (58%) of 95 from the not prescribed group. Outcomes are reported by Hb level (106-109 and <106 g/L, respectively). Of the prescribed group, 77% and 67% responded or resolved the anemia and 21% and 27% did not respond or resolve the anemia, respectively. Fifteen of 55 children in the not prescribed group were subsequently prescribed iron at a follow-up visit. Of these, 44% and 83% responded or resolved the anemia, respectively. However, 84% and 40%, respectively, of children not prescribed iron also resolved the anemia without treatment (Table 3).

The 38 children in the prescribed group with a Hb level of less than 100 g/L warrant special attention because of the severity of the anemia. Only 3 (8%) returned for follow-up within 1 month, and 15 (39%) did not return for follow-up within 6 months, about the same rates as those with more mild anemia. Of the 23 who returned for follow-up within 6 months, 4 (17%) responded to iron therapy with a greater than 10-g/L increase in Hb; 10 (43%) resolved the anemia with iron therapy, 8 (35%) did not respond to iron therapy, and 1 (4%) had inadequate information to determine an outcome (percentages may not total 100 because of rounding).

In the 6-month follow-up period, children who received follow-up care were subjected to repeated testing; 19% of children who were prescribed iron and 20% who were not prescribed iron underwent 3 or more HemoCue screens, while 14% vs 9% in each group underwent at least 2 more CBCs. Despite the repeated Hb testing, iron-specific studies were infrequently performed, including only 8 children undergoing serum fer-

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Table 1. Comparison of Anemic Groups: Prescribed vs Not Prescribed Iron at the Index Visit*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Prescribed Iron (n = 239)</th>
<th>Not Prescribed Iron (n = 95)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>57</td>
<td>58</td>
<td>.92</td>
</tr>
<tr>
<td>African American</td>
<td>95</td>
<td>94</td>
<td>.64</td>
</tr>
<tr>
<td>Medicaid insurance</td>
<td>73</td>
<td>77</td>
<td>.45</td>
</tr>
<tr>
<td>Age, mo</td>
<td>19.4 (7.7)</td>
<td>19.8 (6.9)</td>
<td>.06‡</td>
</tr>
<tr>
<td>9-12</td>
<td>87</td>
<td>78</td>
<td>.001‡</td>
</tr>
<tr>
<td>13-18</td>
<td>96</td>
<td>86</td>
<td>.001‡</td>
</tr>
<tr>
<td>19-24</td>
<td>96</td>
<td>93</td>
<td>&lt;.001‡</td>
</tr>
<tr>
<td>25-36</td>
<td>89</td>
<td>83</td>
<td>.33 (0.23) 0.35 (0.23) &lt;.001‡</td>
</tr>
</tbody>
</table>

*Data are given as the percentage of each group unless otherwise indicated. †All values obtained by χ² analysis unless otherwise indicated. ‡t Test. *To convert lead from micromoles per liter to micrograms per deciliter, divide micromoles per liter by 0.0483.
ritin studies, 16 undergoing Hb electrophoresis, and 0 undergoing transferrin or total iron binding capacity studies. Similarly, 28% of children who were prescribed iron at the index visit were prescribed iron at least 3 more times (Table 4).

Because of concern that including the 63 children (48 in the prescribed and 15 in the not prescribed group) who had been treated with iron before the index visit in the analysis might skew the results, the analyses were repeated without these children. The mean age of the sample decreased by about 1 month in each group because older children are more likely to have been previously screened and treated for anemia. Otherwise, the demographics of the sample were not significantly different from those presented in Table 1. Follow-up and outcome analyses, compared by prescribed and not prescribed groups but not by Hb level, were not significantly different for this sample compared with the entire study population using \( \chi^2 \) analysis.

**COMMENT**

In summary, the prevalence of anemia, defined as a Hb level of less than 110 g/L was 25% among these inner-city, mostly African American, children screened by HemoCue in our clinic. This figure is remarkably consistent with 1997 Pediatric Nutrition Surveillance System data for African American children (24.6%), which come mostly from Women, Infants, and Children program data. The high rate of anemia could be explained by several factors. HemoCue measurement of Hb often results in slightly lower results when compared with the Coulter counter, particularly if a single drop of capillary blood is used rather than a pooled sample. We were not able to...

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**Table 2. Anemia Follow-up by Prescribed Iron Status and Hemoglobin (Hb) Level at the Index Visit**

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Prescribed Iron</th>
<th>Not Prescribed Iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb Level of 106-109 g/L</td>
<td>Hb Level of &lt;106 g/L</td>
<td>Hb Level of 106-109 g/L</td>
</tr>
<tr>
<td>(n = 110)</td>
<td>(n = 129)</td>
<td>(n = 63)</td>
</tr>
</tbody>
</table>

**Table 3. Anemia Outcome During 6 Months Following the Index Visit**

<table>
<thead>
<tr>
<th>Outcomes†</th>
<th>Prescribed Iron</th>
<th>At Index Visit</th>
<th>At Subsequent Visit</th>
<th>Not Prescribed Iron</th>
<th>During 6-mo Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb Level &gt;106 g/L</td>
<td>Hb Level &lt;106 g/L</td>
<td>Hb Level &gt;106 g/L</td>
<td>Hb Level &lt;106 g/L</td>
<td>Hb Level &gt;106 g/L</td>
<td>Hb Level &lt;106 g/L</td>
</tr>
<tr>
<td>(n = 66)</td>
<td>(n = 84)</td>
<td>(n = 9)</td>
<td>(n = 6)</td>
<td>(n = 25)</td>
<td>(n = 15)</td>
</tr>
</tbody>
</table>

* Data are given as the number (percentage) of children in each group. Percentages may not total 100 because of rounding.
† Compared by Hb level within prescribing groups (≤1 to ≥2 months): prescribed, \( P = .26; \) not prescribed, \( P = .20 \) (Fisher exact test).
‡ Compared with not prescribed: \( P < .001 \) (\( \chi^2 \) test).
§ Compared with prescribed: \( P < .52 \) (\( \chi^2 \) test).

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to identify the method of blood collection for each sample, but children who underwent concomitant lead screening should have had venous sampling performed, which is the clinic policy. Of the 40 children who underwent HemoCue and Coulter counter Hb measurements at the index visit, 75% had a HemoCue Hb result lower than the Coulter counter Hb result. Given that 52% of the sample had a Hb level of 106 to 109 g/L, even a small discrepancy between the HemoCue and Coulter counter Hb values may result in misclassification. Furthermore, African American race is associated with lower Hb values when compared with other races, and at least one study found that children with sickle cell trait have slightly lower Hb levels, controlling for race.24-26 If a Hb cutoff of less than 106 g/L is used for this group, as suggested by the 1993 Institute of Medicine recommendations, only 12% of children would be classified as anemic, which is more consistent with national data across races.17

It is not possible to determine which children have iron deficiency as the cause of the anemia based on Hb level alone. Because treatment with iron is relatively inexpensive, safe, and effective, it has been widely accepted practice to treat all children with anemia with a trial of iron.8,14,15 However, the effectiveness of a therapeutic trial of iron is uncertain for at least 3 reasons. First and most striking is that fewer than 10% of children returned for follow-up of their anemia within the recommended time of 1 month. The more time that lapses between treatment and follow-up, the more difficult it is to interpret the normalization of Hb level as a response to the iron or as spontaneous resolution due to resolved infections or dietary improvements. The anemia outcomes in this study must be interpreted with the low 1-month follow-up in mind. Second, the overall rates of anemia response or resolution within 6 months were similar for those who were prescribed iron (107 [71%] of 150) and those who were not prescribed iron (27 [68%] of 40). Children with more severe anemia were less likely to resolve the anemia whether they were prescribed iron or not, except for the children who were prescribed iron at a later visit. This may be due to the small sample of this group. Third, children were subjected to repeated blood testing and iron therapy using this approach to screening, resulting in morbidity from frequent blood testing, increased parental anxiety, possible contributions to vulnerable child syndrome, and increased medical costs.

Patients who were prescribed iron and with a medical record–documented recommended time to follow-up were not consistently asked to return in 1 month, the recommended practice. Actual anemia follow-up rates were poor. The longer the time between treatment and reevaluation of Hb level, the more difficult it is to evaluate the effect of iron therapy because of uncertainty in compliance with the medication, parental recall, and confounding factors, such as infections and dietary changes. More than a third of children did not receive follow-up for at least 6 months. Difficulty in follow-up has also been cited in the lead screening literature.23 This issue must be taken into consideration when screening practices are implemented.

These data have led us to question the practice of screening with HemoCue and prescribing iron to inner-city children identified as anemic. This practice was developed when IDA was by far the most common cause of anemia. This is no longer the case. A prospective study,24 started in the same clinic a few months after this study and using the same definition of anemia found that, despite anemia rate of 35%, the IDA rate was only 8%. The changing epidemiological features of IDA, poor follow-up rates, repeated testing and treatment, and the high rate of spontaneous resolution of those not treated have led us to consider other approaches.

Several alternatives can be considered. One alternative is to screen by ferritin level. This test can detect early iron deficiency but costs about 3 to 4 times more than a Hb or CBC screen and, because it is an acute phase reactant, can be falsely normal because of even mild recent infection. A more practical alternative would be to screen children initially with a CBC because it provides the red blood cell indices, MCV and RDW, to aid in the diagnosis of IDA as the cause of anemia. A low MCV and high RDW can help to differentiate IDA from acute infection, where the MCV and RDW should be normal, and from thalassemia trait, where the MCV should be low and the RDW normal.25-27 However, CBC results are not usually available before a child leaves the practice site and, therefore, the family must be contacted at a later time. Therefore, having the additional information must be balanced against the challenge of locating patients after discharge. Other possible screening options to consider are the zinc protoporphyrin level or the zinc protoporphyrin–heme ratio.28

Several limitations must be considered. The review of medical records carries the obvious limitations associated with documentation, such as varying levels of detail, legibility, and potential for missing (improperly filed or lost) paper encounter forms. To minimize the latter, visit dates and types and laboratory testing were verified in the electronic patient record. Patients may not have received all their health care at the clinic. Medical care is only provided to patients who choose this clinic for their medical home. Given the high penetration of managed care in the clinic, it is unlikely that anemia would

<table>
<thead>
<tr>
<th>Table 4. Proportion of Children Who Underwent Repeated Anemia Testing and Iron Treatment After the Index Visit*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Testing and Treatment</strong></td>
</tr>
<tr>
<td>HemoCue‡ screens</td>
</tr>
<tr>
<td>≥2</td>
</tr>
<tr>
<td>≥2 CBCs</td>
</tr>
<tr>
<td>≥3 HemoCue screens plus CBCs</td>
</tr>
<tr>
<td>≥3 Iron prescriptions</td>
</tr>
<tr>
<td>Any iron-specific study performed</td>
</tr>
</tbody>
</table>

* Data are given as the number (percentage) of each group. P > .05 for all comparisons unless otherwise indicated. CBC indicates complete blood cell count.
‡ Fifteen children were prescribed iron after the index visit (P = .05, Bonferroni correction).
be addressed in the emergency department or at other clinics. It is likely that recent illnesses that were not evaluated by a physician were not recorded in the medical record. However, the rates of medical record–documented recent infection were similar between the groups. Given the study design, compliance with iron treatment was not evaluated. The study was performed in a pediatric residency continuity clinic that has physicians at all levels of training, and training level was not identified during the medical record reviews. Although the mostly inner-city African American sample may limit the generalizability of the study findings to other ethnic and cultural populations, there are many community health centers and hospital-based clinics that serve similar high-risk populations.

In conclusion, HemoCue identified 25% of the children from this inner-city pediatric clinic as anemic, defined as a Hb level of less than 110 g/L. Anemia follow-up rates were low, especially at a month, the ideal time to interpret the effect of iron therapy on Hb level. Irrespective of treatment with iron, about two thirds of children resolved the anemia within 6 months. Children underwent repeated Hb screening and iron treatment, yet few iron-specific studies were obtained. Given the decline in IDA prevalence and the concomitant increase in other causes of anemia, the seriousness of missing cases of true IDA, and the limitations of the approach to screening, we suggest a CBC as a better screening test to delineate causes of anemia. Prospective studies are needed to evaluate the compliance with and outcomes from this and other methods of screening for IDA.

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