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Anemia Screening and Treatment Outcomes of Children in a Low-resource Community in the Dominican Republic

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ABSTRACT

Iron is often initiated for children with low hemoglobin values in the absence of other indicators of iron deficiency in low-resource settings. Unfortunately, there are few reports describing outcomes from such an approach outside of clinical trials. This study examined outcomes of an anemia screening and treatment service in a low-resource community in the Dominican Republic. Complete blood counts (CBC) and receipt of iron supplementation were extracted from health records of young children participating in a well-baby clinic in the targeted community. Of the 265 children screened, 68.7% had hemoglobin values $<$11.0 g/dl; 61.5% of these anemic children had follow-up CBCs. While 72.3% of those with follow-up CBCs picked-up some iron supplements, only 21.4% had a follow-up hemoglobin $\geq$11.0 g/dl. Amount of iron given was not related to change in hemoglobin at follow-up. More follow-up monitoring of quality and impact of community care is required with associated evidence-informed benchmark targets.

KEYWORDS: anemia, quality of health care, iron, child, Dominican Republic.

Iron deficiency is the most common contributing factor to anemia in preschoolers [1, 2]. Extensive clinical trial evidence supports the benefits of iron supplementation to address iron-deficiency anemia (IDA) [3]; however, there is a dearth of pragmatic trials [4, 5]. In addition, there is a gap in reports on outcomes attained from existing services outside of clinical trials.

Community services may not achieve the same outcomes as clinical trials given a number of challenges, particularly in low-resource settings. These may include costs (e.g., accessing health services, laboratory costs), low priority afforded IDA in clinical encounters, poor adherence to iron supplementation for duration of treatment and nonsystematic follow-up. Such challenges may have contributed to gaps in care noted in some clinics serving low-income families in the United States. In one study, only 45% of children identified with anemia received some form of treatment [6]. In a second study, while 72% of those identified with anemia had been prescribed iron, there were low rates of follow-up [7]. A third study found that no more than 25% of children between 9 and 15 months of age identified as anemic had follow-up blood work within 6 months and no more than 12% had documented resolution [8].

This study aimed to determine the outcomes of an anemia screening and treatment service in a

low-income community in which some of the service barriers were reduced or eliminated. Indicators included (i) proportion of eligible children screened, (ii) proportion of screened children who had anemia, (iii) proportion of children with anemia who obtained iron supplementation and had follow-up blood work, (iv) amount of change in anemia status at follow-up and (v) extent to which iron supplement receipt was related to change in anemia.

METHODS

Setting

The study was based in a small low-income community (total current population estimated between 1200 and 1600 persons) located on the outskirts of Santo Domingo, Dominican Republic (DR). The community is served by a single, not-for-profit, charitable, nongovernmental organization that provides a number of clinic services in the community. The services include a free well-baby clinic (WBC) for all children in the community aged 0–6 years. The anemia screening and treatment service is embedded within the WBC. There are no similar WBCs in the immediate surrounding district; however, there are various government and private clinics and hospitals offering sick care in the larger municipality and province in which this community is located.

Sample

Based on a 2010 community census, an estimated 92% of community children (0–6 years of age) participated in the WBC at least once. Data for this study were drawn from health records of WBC attendees for whom the caregiver provided written informed consent to release health records and the child had at least one health contact between the ages of 9 months and 6 years. This age range was selected, as any blood result before 9 months would not have been a function of the screening program but related to a sick visit.

Between 6 July 2009 and 4 October 2013, a total of 335 children had at least one WBC contact. Caregivers of 313 of these children consented to health records release. Of this subgroup, 265 had a least one Complete blood counts (CBC) result in their chart. This suggests an estimated 78% of eligible community children were included in the study.

Procedures

Screening CBC is offered to all children in the WBC. A first screen has been recommended between 9 and 15 months and a second between 2.5 and 4 years of age, although screening is offered at other time points if these times are missed. The child's caregiver is given a free laboratory requisition for a CBC, although not all caregivers chose to take their child to the laboratory.

CBC results were based on analysis of venous puncture blood samples, which, as of January 2013, were obtained using a URIT-2900 Automated Hematology Analyzer (approximately 25% of the sample). Values before January 2013 were obtained using a Simex K800 (approximately 75% of the sample). All results were reviewed by a local physician who indicated iron supplementation for children with hemoglobin values <11.0 g/dl. Iron was distributed from the WBC in approximately 4 week supplies at a time and the amount distributed recorded in the health record. A repeat CBC was offered 4 weeks after the final dose of iron should have been completed.

The clinic protocol for the amount of iron recommended for anemic children changed over the study period. The most recent protocol recommended 12 weeks of 5 mg/kg (child weight)/day of elemental iron (to a maximum of 60 mg/day) [9]. The initial protocol provided less iron per day ($\sim$3 mg/kg/day) based on local recommendations for treatment of moderate-level anemia [10] and with those with milder anemia initially receiving shorter durations of treatment (8–10 weeks). Iron was prescribed in the form of liquid ferrous sulfate (40 mg ferrous sulfate/ml) and distributed free.

The WBC is free to all families, as are the CBCs, iron supplementation and physician consultation. The WBC and laboratory are located in the community and are within short walking distance of all community households. Reminders were provided to families if screening blood work was not obtained or iron not picked up. The study was approved by the Conjoint Health Research Ethics Board. All families could participate in the anemia screening and

treatment program regardless of whether they participated in the study.

Analysis

Proportion anemic: Based on those children whose hemoglobin level from their first CBC was <11.0 g/dl among all children with CBCs based on World Health Organization (WHO) recommendations for children 6–59 months of age [11]. A cut point of <10.0 g/dl was also used to allow comparison with other studies.

Proportion with anemia who received iron supplementation: Based on an indication in the chart that the caregiver had picked up at least one 120 ml bottle of ferrous sulfate following a CBC with a hemoglobin level <11.0 g/dl.

Proportion with anemia who had a follow-up CBC: Based on a follow-up CBC obtained between 4 and 32 weeks after the baseline CBC among those identified as anemic on their first CBC. If more than one CBC result was available within this period, the value closest to 16 weeks was used as this aligned with the main treatment protocol recommendation. The 32 week period was arbitrarily set as twice the recommended period to capture children for whom iron initiation may have been delayed or there may have been a lag before the child was brought back for a follow-up CBC. Values outside these time parameters were judged not to be tied to evaluating response to treatment.

Reduction in anemia: Was calculated in two ways. First, the proportion of children whose follow-up hemoglobin was ≥11.0 g/dl obtained during the same time restrictions (i.e., 4–32 weeks) after an initial hemoglobin value <11.0 g/dl was assessed using the McNemar test. Second, the amount of change in g/dl between the two hemoglobin values was assessed with a paired student *t*-test.

Relationship between change in anemia status and iron receipt: Was assessed using linear regression with (i) amount of pre-post change in hemoglobin as the dependent variable, (ii) amount of iron/child weight distributed as the independent variable and (iii) baseline hemoglobin value, baseline mean

Table 1. Summary of child characteristics related to their first CBC

Characteristic	Not anemic ($n = 83$) % (n)	All anemic ($n = 182$) % (n)	Anemic with follow-up CBC ($n = 112$) % (n)	Anemic without follow-up CBC ($n = 70$) % (n)
Child sex (male)	48.2 (40)	59.9 (109)	59.8 (67)	60.0 (42)
Mother's primary language[a]				
Spanish	58.2 (46)	57.5 (104)	63.1 (70)	48.6 (34)
French/Haitian Creole	41.8 (33)	42.5 (77)	36.9 (41)	51.4 (36)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Child age (years)[b]	3.22 (1.56)	1.80 (1.16)	1.72 (1.09)	1.92 (1.25)
Hemoglobin (g/dl)[c]	11.53 (0.46)	9.74 (0.84)	9.69 (0.90)	9.81 (0.73)
MCV (fl)[d]	87.3 (8.8)	75.8 (11.0)	73.2 (9.39)	80.0 (12.0)
Anthropometric parameters[e]				
Weight for age (Z score)	−0.34 (0.98)	−0.32 (1.04)	−0.25 (1.04)	−0.43 (1.03)
Height for age (Z score)	−0.65 (1.06)	−0.80 (1.21)	−0.73 (1.19)	−0.92 (1.24)
Body Mass Index (Z score)	0.08 (0.96)	0.21 (0.99)	0.24 (1.00)	0.17 (0.99)

[a]Five cases are missing information on primary language of mother.
[b]Nonanemic children are significantly older than anemic children ($t = 7.4$, $p < 0.001$).
[c]Nonanemic children have hemoglobin significantly higher than anemic children ($t = 22.2$, $p < 0.001$).
[d]Nonanemic children had mean MCV significantly larger than anemic children ($t = 8.4$, $p < 0.001$) [one data point each is missing for anemic and nonanemic children]; among the anemic children, those with follow-up data had lower mean baseline MCV than those without follow-up data ($t = 4.0$, $p < 0.001$).
[e]Using WHO growth parameters.

Table 2. Follow-up blood counts for anemic subgroup ($n = 112$)

Parameter	Mean (SD)
Time between 1st and 2nd CBC (weeks)	21.5 (6.0)
Hemoglobin (Hb) concentration (g/dl) at follow-up[a]	10.18 (1.04)
Change in Hb between time 1 and 2 (g/dl)	0.49 (1.00)
MCV (fl) at follow-up[b,c]	74.8 (8.4)
Change in MCV between time 1 and 2 (fl)	1.6 (6.4)
Elemental iron/child weight/day (mg/kg/day)[d]	2.2 (1.9)
	% (n)
Hb $\geq$11.0 g/dl at follow-up[e]	21.4 (24)
Picked up at least one bottle of ferrous sulfate	72.3 (81)
Receipt of at least enough ferrous sulfate to provide 3 mg/kg/day for 12 weeks[f]	34.8 (39)

[a]Paired *t*-test comparing follow-up to baseline: $t = 5.2$, $p < 0.001$.
[b]Paired *t*-test comparing follow-up to baseline: $t = 2.7$, $p < 0.01$.
[c]One value missing at baseline therefore $n = 111$.
[d]This is a conservatively low estimate, as it includes all those who received no iron and does not factor in the maximum dosing of 60 mg/day such that those with weights >12.0 kg would always receive a dose <5 mg/kg/day. If the calculation is restricted to the 81 children whose caregiver obtained at least one bottle of ferrous sulfate, the mean value would be 3.1 (SD: 1.5) mg/kg/day. If within this subgroup, a maximum child weight of 12.0 kg is used for the calculation, then the mean value would be 3.2 (SD: 1.4) mg/kg/day.
[e]McNemar test applied to pre-post categorization: $\chi^2 = 22.0$, $p < 0.001$.
[f]Using the maximum child weight of 12.0 kg as in footnote number 4 results in only a slight change in this value to 35.7% ($n = 40$).

corpuscular volume (MCV) and duration of time between two blood tests as control variables.

RESULTS

Of the 265 children with any CBC, 68.7% ($n = 182$) were anemic based on their first CBC (Table 1). Of those with anemia, 61.5% ($n = 112$) had a follow-up blood count between 4 and 32 weeks. The anemic children with and without follow-up data did not differ significantly, except the former had significantly lower MCVs.

The mean hemoglobin value at follow-up for the anemic subgroup with follow-up data was significantly higher than baseline, but only increased by a mean of 0.49 (SD: 1.00) g/dl (Table 2). The MCV value also increased significantly but only by a mean of 1.6 (SD: 6.4) fl. Furthermore, only 21.4% of this group was no longer anemic at follow-up. A substantial minority, 27.3%, did not obtain any documented iron from the program. As well, only 34.8% ($n = 39$) received what might be considered a minimally adequate quantity of iron supplement (i.e., equivalent to 3 mg/kg/day for 12 weeks). Restricting outcomes to this subsample (i.e., those who received 'adequate' iron), however, only resulted in 5.1% (2 of 39) attaining hemoglobin $\geq$11.0 g/dl.

Using a hemoglobin cutpoint <10.0 g/dl, a total of 60 children among those with follow-up data had this baseline level. At follow-up, 45% ($n = 27$) of these children had values $\geq$10.0 g/dl and experienced a mean hemoglobin change over time of 0.76 (SD: 1.06) g/dl.

Findings from the unadjusted and adjusted linear regression models are presented in Table 3. The amount of iron received was not related to pre-post change in hemoglobin in unadjusted and adjustment models. Lower baseline hemoglobin values were highly predictive of the amount of hemoglobin change.

A measure of adherence to the iron recommendations was not available for the above study sample. However, new pilot measures of adherence were added into the protocol at a later stage of the larger study. Iron supplies for the recommended 12 week course are given in three distributions each covering a 4 week period (at the start of treatment, then after 4 and 8 weeks). At the 4 and 8 week point, mothers (or alternative caregivers) are interviewed with a short structured questionnaire that asks (i) the amount of iron supply left over from the last distribution, (ii) the estimated frequency in which the

Table 3. Predictors of amount of hemoglobin change between baseline and follow-up using a linear regression model

Model	Variables	Unstandardized B (95% CI)
Unadjusted	Iron receipt[a]	−0.04 (−0.14, 0.06)
Adjusted	Iron receipt[a]	−0.11 (−0.21, 0.00)
	Baseline Hemoglobin (Hb)	−0.56 (−0.78, −0.33)*
	Baseline MCV[b]	0.00 (−0.02, 0.03)
	Time between 1st and 2nd blood count	−0.01 (−0.04, 0.03)
Adjusted with interaction term[c]	Iron receipt[a] (centered)	−0.11 (−0.22, 0.01)
	Baseline Hb (centered)	−0.53 (−0.78, −0.28)*
	Baseline MCV (centered)	−0.01 (−0.03, 0.02)
	Time (centered)	−0.02 (−0.05, 0.02)
	Iron × Baseline Hb	0.04 (−0.09, 0.17)
	Iron × Baseline MCV	−0.01 (−0.02, 0.00)
	Iron × Time	−0.01 (−0.03, 0.01)

[a]Iron receipt measured as mean mg/kg/day.
[b]While baseline Hb and baseline MCV are correlated ($r = 0.42$, $p < 0.001$), high multicollinearity was not identified using Variance Inflation Factor. Also rerunning the model without baseline Hb did not result in finding a significant relationship between baseline MCV and change in Hb.
[c]As all control variables are correlated with the independent variable (iron receipt), the model was rerun after centering the independent and control variables and adding interaction terms.
*$p < 0.001$.

iron had been given to the child and (iii) whether any problems had arisen with the treatment. The following is a summary of 186 completed questionnaires: (i) using a five-point response option, 82.3% indicated that there was no remaining iron from the previous distribution, suggesting that it had all been given, while only 2.2% indicated having a full bottle of iron remaining; (ii) also using a five-point response option, 85.5% indicating they gave iron daily, while only 1.1% reported never giving it; and (iii) only 9.7% indicated a problem with the iron, with the most common concern being that it had caused diarrhea.

DISCUSSION

Several gaps were found in this anemia service including incomplete (i) screening of the target population, (ii) delivery of iron supplementation, (iii) follow-up testing and (iv) recovery from anemia. Ideally, 100% of children eligible for screening programs would be reached. We are unaware of estimates of community coverage in other DR communities or elsewhere to compare our estimated 78% community coverage rate. This rate may be better than typical services given that some cost and accessibility barriers were mitigated.

Using the hemoglobin cut-point of <11.0 g/dl, 68.7% of the children in this sample were anemic. This is higher than the 28.1% found in children 6–59 months of age in a 2009 national study in the DR and higher than the 44.9% in their subsample aged 6–23 months [12] suggesting this is a high-risk community in the DR.

What fraction of the children in this study had anemia secondary to iron deficiency is not known given the absence of information on iron parameters. The mean MCV values were not markedly low in this sample, suggesting that at least some cases were not microcytic. In the above-cited 2009 national DR study, it was estimated that approximately one-third of anemia was secondary to iron deficiency using ferritin values after excluding those with alpha-1-acid glycoprotein values >1 g/dl [12]. While incomplete, these findings suggest a substantial proportion of the anemia found in DR children may not be secondary to iron deficiency.

The mean hemoglobin increase of 0.49 g/dl is less than the pooled estimate of 0.74 g/dl found from a systematic review of randomized control trials

of iron supplementation interventions of children [3], although a 0.76 g/dl improvement was found for those starting with Hb <10.0 g/dl. The 21.4% at follow-up with hemoglobin ≥11.0 g/dl is much less than a reported 78.0% recovery rate of anemic preschool children who received daily iron in a clinical trial in Jordan [13]. A 61% recovery rate was reported from a preschool clinic trial for those receiving daily iron treatment in Ghana using a recovery threshold of Hb ≥ 10.0 g/dl [14]. Applying this lower hemoglobin threshold to this study, the recovery rate was 45%. Perhaps greater improvements in the cited trials were secondary to delivery of a more therapeutic dose of iron, 5 and 6 mg/kg/day in the Ghanaian and Jordanian cases, respectively.

Poor adherence to iron supplementation may have contributed to lower than expected improvements in hemoglobin. However, preliminary findings from a new pilot measure of adherence within the same program suggest that the majority may have had high adherence, although this is based solely on maternal report and hence is at risk for social desirability bias. Potentially the formal monitoring structures found in clinical trials may also lead to better adherence than in typical clinical practice, although a measure of adherence was not related to outcomes in the Zlotkin et al. study [14]. In contrast, a recent report of a study in a prenatal population of women in Peru did find a positive relationship between adherence and hemoglobin improvement [15].

The lack of relationship between iron receipt and hemoglobin change was unexpected. A model based on a review of hemoglobin responsiveness to iron supplementation in children estimated that roughly one-third to two-thirds of children in non-hyperendemic malaria regions will not be responsive to iron supplements [3]. Presumably, this may be owing to some children receiving iron although they do not have anemia secondary to iron deficiency.

There are several limitations to this study. First, it is based on findings from a single community with a modest sample size and a substantial fraction of children with no follow-up data. Second, additional parameters were not available to determine extent to which the anemia was secondary to iron deficiency. The epidemiology of the main causes of childhood anemia in the DR is not reported in the literature; however, based on modeling from a global burden of anemia study, top causes of anemia in the Caribbean, in order, are iron deficiency, sickle cell and hookworm [2]. Third, counting iron receipt by caregivers as a measure of adherence may be inadequate. Fourth, an experimental design was not used.

Despite these limitations, the study provides an example of extracting indicators from a service to measures aspects of quality and outcomes. Challenges in situating the findings highlight further needs in the field. Powers and Buchanan [5] have flagged the need for pragmatic trials to tease out even basic parameters such as optimal dosing and duration of supplements for IDA. Such trials may generate benchmarks that could or should be attained in health service settings.

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