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ORIGINAL RESEARCH

Evaluation of Iron Deficiency Anemia in a Pediatric Clinic in the Dominican Republic

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Abstract

BACKGROUND Iron deficiency and iron deficiency anemia affect billions of people worldwide. Infants and young children are the most vulnerable. The Niños Primeros en Salud pediatric clinic aims to follow the American Academy of Pediatrics (AAP) recommendation to screen all children at 12 months of age, a vital period for development and the time of greatest risk.

OBJECTIVES To evaluate the clinic's performance screening for, diagnosing, and treating iron deficiency anemia; and to describe the prevalence and severity of anemia in infants and children attending a perirural clinic in the Dominican Republic.

METHODS A total of 293 charts were reviewed for hemoglobin tests performed between 9 and 15 months of age. If a hemoglobin screening was performed, then sociodemographic characteristics, medical history, and laboratory data were collected. If blood tests revealed anemia, then the presence or absence of documented anemia diagnosis as well as the presence or absence of documented provision of iron therapy were recorded.

FINDINGS Less than one-third (87, 29.7%) of patients had a documented hemoglobin test performed in this age range. Of these, 89.6% indicated anemia and nearly half (48.6%) revealed moderate anemia. One-third (34%) of hemoglobin results revealing anemia were not accompanied by a documented diagnosis. The vast majority (86.5%) of results indicated microcytosis, yet just more than half (50.8%) of anemic patients received iron therapy.

CONCLUSIONS Many children at the clinic were not screened for iron deficiency anemia during the period of highest risk. In the participants screened, iron deficiency anemia was underdiagnosed and often untreated. Anemia is a significant burden in this community—one demanding reliable screening and universal supplementation.

KEY WORDS Caribbean, iron supplementation, pediatric, quality improvement, resource limited setting.

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INTRODUCTION

Iron deficiency is the most common nutritional disorder worldwide, and iron deficiency anemia is among the most important contributors to global disease.[1] Anemia is estimated to affect at least 30% of the global population, or more than 2 billion people, and 50%-80% of this is attributable to iron deficiency anemia.[2,3] The disorders of iron deficiency and iron deficiency anemia exist on a broad spectrum and have profound consequences, including increased rates of prematurity, maternal and fetal mortality, neurodevelopmental deficits, increased infectious risks, and decreased productivity.[1,4] Although the impact of anemia and iron deficiency anemia is geographically variable, resource-limited settings are the most affected. Despite iron deficiency anemia's global influence, several institutions (eg, World Health Organization [WHO], the United Nations Children's Fund [UNICEF]) acknowledge that little improvement has occurred in decades.[5]

Infants and young children are among the most vulnerable to iron deficiency and iron deficiency anemia. Newborns accrete 80% of their iron stores during the third trimester, making preterm infants and those born to iron-deficient mothers particularly susceptible. Rapid growth and neurologic development in the first 12 months demand the highest daily iron requirement of any period in life.[6] This period is also marked by a transition to solid foods, which if insufficient in quantity or quality can exacerbate iron deficiency. Infants and young children in resource-limited settings often have increased iron needs because they are born iron deficient, have increased losses from parasitic infections, or both. All these factors increase the risk and prevalence of iron deficiency and iron deficiency anemia and the subsequent negative health consequences.[3]

Of particular importance are neurodevelopmental deficits accrued in children with iron deficiency and iron deficiency anemia—psychomotor delay, impaired cognitive performance, and decreased energy. Research by Lozoff et al of children 12-23 months of age found that children with moderate iron deficiency anemia (hemoglobin [Hb] < 10 g/dL) had lower mental and motor functioning both before and after iron supplementation despite a robust hematologic response (Hb increased on average 3.7 g/dL).[7] In a follow-up study of the same population, the authors found that nearly all children had comparable iron stores at 5 years. Yet the children who had either moderate iron deficiency or refractory iron deficiency in infancy had lower neurodevelopmental scores that persisted at 5 years.[8] Other studies found similar results while adjusting for socioeconomic and infectious factors, validating the concern that iron deficiency in infancy impairs motor and cognitive performance and is associated with potentially irreversible deficits.[9-11]

Unfortunately, conflicting results abound on the impact of iron supplementation on neurodevelopmental outcomes.[12,13] These discrepancies are possibly attributable to variability in timing of diagnosis, treatment, and follow-up, yet without unifying evidence to support intervention, global iron deficiency and iron deficiency anemia have remained a low priority. Anemia prevention programs may be warranted for preschool-aged children in areas with high iron deficiency anemia prevalence.

The Ministry of Health of the Dominican Republic does not have a recommendation on screening for anemia but recommends iron supplementation to all children from ages 6 months through completion of primary school. However, this occurs infrequently. American-trained pediatricians often work at the clinic where this study was performed and the American Academy of Pediatrics recommendation to ensure that all children are screened for anemia at approximately 1 year of age, starting as early as 9 months, has been accepted as a practice guideline. The objectives of this assessment were to review the clinic's performance screening for, diagnosing, and treating iron deficiency anemia. Further, the authors aimed to describe the prevalence and severity of anemia in infants and children attending Niños Primeros en Salud, a perirural clinic in the Dominican Republic.

METHODS

Setting. Data collection occurred at a pediatric clinic, Niños Primeros en Salud (NPS), located in Consuelo, Dominican Republic (perirural, population ~36,000) that cares for children younger than 5 years of age. NPS cares for children who live in 6 barrios (neighborhoods) that were chosen for proximity to the clinic and severity of poverty. These barrios are a good representation of many communities in the Dominican Republic. The pediatric clinic is staffed with a Dominican pediatrician, a Global Health Fellow from the United States, 1-2 rotating Dominican pediatric residents, and a Dominican registered nurse. The nurse is present 5 days a week, conducts home visits, and provides continuity for patients. NPS conducts deworming every 6 months, during which clinic providers travel door to door to dispense albendazole to

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adults and children. Within the barrios, poverty is widespread and access to all but emergency health care is nonexistent. Most adults have only a primary school education, and many residents are undocumented Haitian immigrants. The World Bank classifies the Dominican Republic as an "upper-middle income" country.[14] However, the per capita income in Consuelo is US$2,000 per year—70% less than the national average.[15] In 2015, UNICEF reported that the child mortality rate (younger than 5 years of age) in the Dominican Republic was 28 per 1000 (rank 78th) and that 40% of the population lived in poverty.[16] Though nationally the country is "middle income," the patients treated at NPS, and accordingly, the data obtained from the clinic, are more generalizable to a resource-poor setting.

Data Collection. Data collection took place between February and March 2015. The charts for all patients attending NPS between February 2010 and March 2015 were reviewed for eligibility, and if eligible, the following information was collected: sociodemographic characteristics (age at enrollment, age at data collection, gender, and barrio), chronic diseases (HIV, sickle cell disease), and nutritional status (obesity or malnutrition). If a complete blood cell count (CBC) or Hb laboratory report was included, or if a provider transcribed one, the following information was extracted: Hb and indexes (eg, red blood cell distribution width, mean corpuscular volume [MCV]), microcytosis if noted by the provider, age when Hb was collected, and reason Hb was drawn (eg, routine screening, concern for infection, follow-up). Also extracted was the presence or absence of anemia diagnosis and the presence or absence of documented provision of iron therapy if a hemoglobin result was <11 mg/dL.

Exclusion and Inclusion Criteria. For the purposes of assessing the prevalence of anemia, all documented hemoglobin values within eligible charts at the time of collection were included. For assessing the age-related targeted screening practices, participants younger than 9 months at the time of data collection or older than 15 months at enrollment into care were excluded. Before 9 months of age, it is not recommended that children receive a screening CBC, and after 15 months, the patients are well beyond the age range for the recommended first screening CBC (1 year). A range up to 15 months was used to maximize capture of screening events.

Definitions. WHO definitions were used for identification of anemia and stratification into severity subgroups.[17] For preschool-aged children (age younger than 5 years), anemia was defined as a Hb concentration <11.0 g/dL. Severity of anemia was divided into the 3 WHO subgroups: mild anemia (Hb 10.0-10.9 g/dL), moderate anemia (Hb 7.0-9.9 g/dL), and severe anemia (Hb <7.0 g/dL). Microcytosis was defined as an MCV >2 standard deviations (SD) below the mean for age or documentation by a provider of the presence of microcytosis when indexes were not available.[18]

This protocol was submitted to the Children's Hospital of Philadelphia Institutional Review Board and exempted from review because the protocol was not deemed human participant research and represented an evolving standard of care in the spirit of quality improvement.

RESULTS

Patient Population. A total of 371 unique patients visited NPS between February 2010 and March 2015; 51.4% were female. On enrollment into care, the majority (288, 77.7%) were younger than 6 months of age, and 335 children (90.3%) were enrolled by 15 months.

Assessment of Targeted Screening Practices. At the time of chart review, 43 children were younger than 9 months of age, and on enrollment at NPS, 35 children were older than 15 months. Together, these 78 children (21.0%) were excluded, leaving 293 charts (79.0%) available to assess screening performance for anemia of infancy (Figure 1). Of these 293 children, 99 (33.8%) had no documented Hb at any age, 107 (36.5%) had an Hb value on file but outside the 9-15 month age range, and 87 children (29.7%) had at least 1 Hb test documented between 9-15 months. These 87 children were represented by 105 Hb samples on file during the screening period. The vast

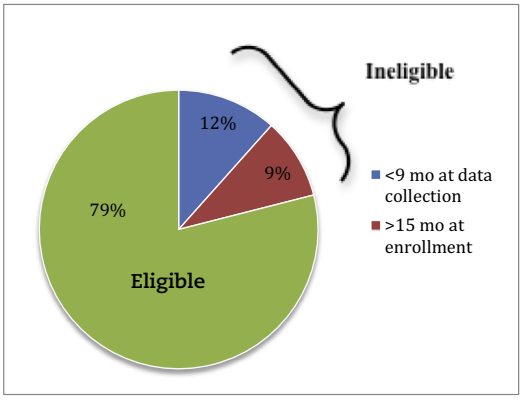

Figure 1. Children eligible for assessment of Niños Primeros en Salud screening practices.

Table 1. Distribution of Hemoglobin (Hb) Values Among the 105 Visits for the 87 Children with Documentation of Hb Between 9 and 15 Months of Age

Classification	Hb Range	Number of Visits	Percent of Visits
Nonanemic	Hb ≥11.0	11	10.5%
Mild anemia	Hb 10.0-10.9	42	40.0%
Moderate anemia	Hb 7.0-9.9	51	48.6%
Severe anemia	Hb <7.0	1	1.0%
Total		105	100%

Table 2. Correlation Between Documented Diagnosis of Anemia and Treatment Among All Encounters (317) with Anemia (Hb <11.0 g/dL)

	Treatment Provided	No Treatment Provided	Totals
(+) Anemia diagnosis	152	43	195
(–) Documented anemia diagnosis	9	113	122
Totals	161	156	317

HB, hemoglobin.

majority of these Hb results (94, 89.6%) were indicative of anemia (Hb <11.0 g/dL), with moderate anemia (Hb <10.0 g/dL) being the most common severity subgroup (51, 48.6%; Table 1).

Of these 94 laboratory values indicating anemia, 62 (66.0%) were accompanied by a documented diagnosis of anemia by the provider, yet 32 (34.0%) had no such diagnosis listed or relevant treatment offered. Among the 32 visits with undiagnosed anemia, the median Hb was 10.2 g/dL (SD 0.71). Undiagnosed anemia was mild in most (22, 68.8%) of the undiagnosed cases. See Figure 2 for details of the Hb values.

Prevalence of Anemia and Iron Deficiency Anemia. Among the 220 children with 1 or more Hb test at any age on file at NPS, 184 (83.6%) children had at least 1 sample revealing anemia; 125 (56.8%) had at least 1 Hb that met criteria for moderate anemia. The 220 children with available Hb data were represented by 409 visits that resulted in Hb testing. There were more than 3 times as many Hb test results indicative of anemia compared with Hbs within normal limits, 317 (77.5%) versus 92 (22.5%), respectively. Moderate anemia remained the most common subgroup (163, 39.9%).

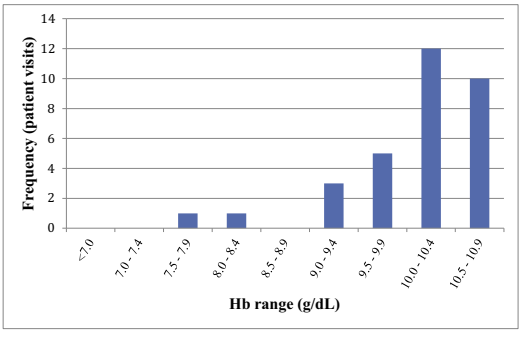

Figure 2. Distribution of hemoglobin (Hb) values among 32 visits of undiagnosed anemia in patients aged 9-15 months.

Of the 409 Hb test results, 215 (52.6%) were accompanied by provider documentation of red blood cell morphology. These 215 visits corresponded to 156 unique children. Of the 156 children, 135 (86.5%) had at least 1 laboratory value revealing microcytosis—101 with a laboratory MCV <80, and 34 with documented diagnosis of microcytosis without mention of MCV.

Diagnosing and Treating Anemia and Iron Deficiency Anemia. Of the 317 patient visits with a documented Hb test result indicative of anemia, only 195 (61.5%) were with patients who had a documented diagnosis of anemia. An even lower proportion of patients with anemia were prescribed iron therapy (161, 50.8%; Table 2).

DISCUSSION

The WHO recommends universal iron supplementation in regions where the anemia prevalence is higher than 40%.[19] This recommendation stems from the fact that only 30%-40% of children and women with iron deficiency have anemia.[20,21] The inverse of this proportional relationship is used to project the prevalence of iron deficiency in a population by measuring the prevalence of anemia alone. This holds true even when other contributions to anemia are present (eg, vitamin A deficiency, hookworm infection, malaria) because iron deficiency remains a primary contributor in the majority of circumstances.[1,19] Therefore, in resource-limited settings, Hb serves as a proxy for the prevalence of iron deficiency anemia. Further, WHO guidance suggests that when the prevalence of anemia exceeds 30% for a subgroup or community, it can be assumed that the remainder of that group is iron deficient.[1]

In our setting, fewer than one-third of children (87, 29.7%) had a documented Hb test between 9 and 15 months of age—a generous age range for screening derived from the American Academy of Pediatrics recommendation, which is also accepted at

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the local screening standard.[22] The overwhelming majority of these 87 Hb values were indicative of anemia, and nearly half (48.6%) were moderate in severity. If one assumed that all 151 children with no Hb data were *not* anemic—certainly yielding an underestimate—the prevalence of anemia at NPS would still be an impressive 49.6% (184 of 371). Our values dovetail well with a 2009 national survey that revealed that 51.5% of rural-dwelling Dominican children aged 6-23 months were anemic.[23] This constitutes a "severe public health problem" by WHO guidelines.[23]

Accordingly, the Ministry of Health of the Dominican Republic has acknowledged anemia as a significant problem and recommends universal iron supplementation for children. The decreed annual supplementation for children are as follows: for normal-weight children from 6-12 months, 2 separate cycles of 8 weeks of 12.5 mg/day iron; from 12-24 months, 4 cycles of 6 weeks of 25 mg/day iron; and from 24 months until completion of primary school, 60 mg of iron weekly for 36 weeks.[23]

Unfortunately, universal supplementation is not the reality in many communities and it does not happen in Consuelo. The 2009 national micronutrients survey revealed that only 20.5% of rural children had received any iron supplements in the preceding 12 months.[24] A more recent study found that fewer than one-third of children in a suburb of the capital received regular supplementation.[25] Prevalence studies of iron supplementation practices are needed in other communities throughout the country, both rural and urban, to describe the actual nationwide response to iron deficiency and microcytic anemia.

Though iron deficiency anemia is well understood within and is a priority for pediatric clinics, this clinic too struggles with inadequate screening, underdiagnosis, and undertreatment. Of patients cared for at NPS, 33.8% had no documented Hb testing at any age and only 29.7% had an Hb test documented between 9-15 months. Among visits with patients with Hb levels indicative of anemia at NPS, 61.5% had documentation of anemia by the provider and only 50.8% were prescribed iron therapy. Using a combined endpoint of documentation of anemia or treatment with iron therapy as a proxy for diagnosis of anemia, the diagnostic accuracy for anemia at NPS is 69.1%, thus indicating that nearly a third of cases go unrecognized. It is possible that this merely reflects poor documentation, but the data suggest that a meaningful proportion of children are undiagnosed and untreated.

This is in contrast to the 78% of patients who had an Hb test result on file and the 83% of anemic children who received iron supplementation at a periurban clinic near Santo Domingo.[25] The screening and treatment at NPS may fall short of this because patients must pay a small fee for both visits and laboratory tests—a constraint applicable to most care settings—but notably not required at the aforementioned periurban clinic. Consistent with national trends, 68.7% of periurban children had an Hb <11, whereas at NPS, in a rural area, 83.6% of patients had an Hb level indicative of anemia at any age.[25] If this is true nationally, then it is likely that solutions, strategies, and funding to prevent iron deficiency anemia in rural areas need to be considered separately from those in urban locales.

This study was a retrospective review of a moderate number of charts in 1 pediatric clinic, in 1 part of 1 small town, and as such has several limitations. First is choosing as an outcome the documented hemoglobin values because it is possible that hemoglobin values were obtained and reviewed but not documented in the chart. A log of hemoglobin values obtained at the laboratory would have been a purer source of data; however, such a log does not exist. Another limitation is that the protocol relied on MCV as a surrogate marker of iron deficiency. More informative would be ferritin, transferrin, and transferrin saturation values, and in addition, ideally the results would be shared alongside the prevalence of sickle cell disease and other microcytic anemias. However, these values are not often available in resource-limited primary care settings.[25] Lastly, it is unclear how closely this population's hemoglobin and MCV values relate to values in other impoverished communities in the Dominican Republic and abroad.

Iron deficiency and iron deficiency anemia have a multitude of effects on individual and community health: increased maternal and fetal mortality, increased risk of infection, impaired cognitive development, and decreased productivity. There is evidence that infants with iron deficiency and iron deficiency anemia in infancy have neurodevelopment deficits compared with their peers that persist at 5, 10, and 19 years of age of age despite iron repletion and normalization of Hb.[7-11,26] The prevalence and severity of anemia and the lack of routine screening make children in resource-limited settings particularly vulnerable.

Unfortunately, a focus on improved screening, treatment, and follow-up alone will fall short because there are many challenges for both the providers and patients. For clinics, increasing the volume of blood

draws would stress operating budgets, and many patients are lost to follow-up or cannot afford the time or cost of attending appointments. These realities are acknowledged in the WHO's recommendation to provide universal supplementation for prevention when prevalence is >40%.[19]

CONCLUSIONS

The findings presented here confirm that universal communitywide iron supplementation (in addition to screening) is indicated in Consuelo. Though the Ministry of Health has designated anemia and iron supplementation an area of focus, the results presented here add to prior data in revealing that much work remains to be done. There are a multitude of challenges to iron supplementation in the developing world, such as the required supply chain, provision of refills, and the creation of significant waste. These difficulties and the reported results call for investigation of clinic processes for screening, population-specific factors contributing to iron deficiency, education of community and clinic personnel, and a review of currently employed methods for diagnosing, treating, and preventing iron deficiency anemia. Further research is needed to document the burden of pediatric anemia in resource-poor communities across the Dominican Republic and the mechanisms and magnitude of the public health response. In the interim, the prevalence and severity of disease as well as the current hurdles beg for novel, sustainable means of supplementation to stop the continually occurring and insidiously devastating population-wide effects of iron deficiency.

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