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Impact of a Collaborative Childhood Anemia Intervention Program in Peru

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Abstract

Objectives: To evaluate the impact of a 12-month multi-modal public health intervention program for treating and preventing anemia among children aged 6 months to 4 years in an underserved community in Peru.

Methods: The intervention included nutritional education, use of a Lucky Iron Fish® cooking tool, and dietary supplementation. The primary outcome measure was anemia resolution. Secondary outcomes included absolute changes in hemoglobin, change in knowledge survey scores, and adherence to interventions. Chi-square and Mann-Whitney-U tests were employed to identify associations between anemia and intervention-related measures. Variables found to be significantly associated in bivariate analysis or of clinical importance were included in a logistic regression model.

Results: Of the 406 children enrolled, 256 (63.1%) completed the program. Of those, 34.0% had anemia at baseline; this decreased to 13.0% over 12 months. The mean hemoglobin for all ages at baseline was 11.3 g/dL (SD 0.9). At 12 months, the mean was 11.9 g/dL (SD 0.8), with a mean increase of 0.5 g/dL (95% CI 0.4-0.6). Children with anemia at baseline saw an increase of 1.19 g/dL at the 12-month follow-up (95% CI 1.12-1.37). Parents correctly answered 79.0% of knowledge assessment questions at baseline, which increased to 86.6% at 12 months.

Conclusions: We observed a reduction in the prevalence of mild to moderate anemia among study participants in this vulnerable population and conclude that multi-modal intervention programs providing nutrition education in conjunction with low-cost iron supplementation and easy-to-use Lucky Iron Fish® cooking tools may reduce and prevent anemia in children.

Keywords: childhood anemia, anemia prevention, Lucky Iron Fish®, Peru

Sustainable Development Goals (SDGs): Good health and well-being, Reduced inequalities.

Introduction

Anemia is a condition of low blood hemoglobin concentration. It may be acute as with traumatic blood loss, or chronic as with nutritional deficiency or other acquired diseases. Iron deficiency anemia (IDA) is the most common

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cause of chronic anemia worldwide and has been shown to affect all ages and all socioeconomic groups with devastating health, social, and economic outcomes if left untreated.(1) (2)

Children are at increased risk for IDA due to their rapid growth rates and potentially inadequate iron intake. In 2011, WHO estimated that 273 million children (42.6% of those aged six months to five years) suffered from IDA. It is well-documented that anemia in childhood causes significant long-term health effects, including cognitive impairment, growth and developmental delay, heart failure, and increased risk for infection.(3-5) Risk factors such as poverty and inadequate access to medical care and sufficient nutrition increase both the risk of IDA and overall childhood mortality from anemia.(6)

Several programs have studied the success of a multifaceted approach to improving anemia in vulnerable populations. These include direct nutritional education, general education in school, supplemental cash and food provisions, and multivitamin use.(7-9) Data suggest that iron supplementation alone could increase mean blood hemoglobin concentration by 0.8 mg/L (95% CI: 0.5-1.1). This translates to an opportunity for resolution of anemia in as many as 42% of cases in children.(1) Researchers have also been evaluating the use of cooking tools to increase iron in the diet for the last 50 years. Use of either an iron pot or an iron ingot while cooking has been shown to increase hemoglobin in children and reproductive-age women with minimal side effects and high rates of compliance.(10-12)

Nonetheless, according to 2019 estimates published by the Peru Ministry of Health (MINSA), the national incidence of anemia in children under three years of age was 31.2% and as high as 43.7% in the city of Arequipa, the second-most populous city in Peru. Chronic malnutrition rates in children under five years of age are estimated to be between 15.0-27.2% nationwide and 8.0% in Arequipa.(13, 14)

Addressing iron deficiency anemia should focus on prevention and treatment and consider cultural and social constraints that influence treatment adherence. To this end, a coalition comprised of MINSA, a local Catholic Diocese, and the non-governmental organization Health Bridges International, developed and implemented a multi-modal program to address anemia among vulnerable populations living in the Cayma district of Arequipa. The aim of this study is to evaluate the impact of this collaborative program for treating and preventing iron deficiency anemia in an underserved community.

Materials and Methods

This is a retrospective observational study evaluating the outcomes of a multi-modal public health program to reduce the prevalence of anemia in children between 6 months and 4 years over the course of 12 months in the Cayma district of Arequipa, Peru. Interventions included use of an iron cooking tool, an educational program, and dietary supplementation with ferrous sulfate and micronutrients.

This study was carried out in areas under the jurisdiction of the Francisco Bolognesi Health Micro Network of MINSA and the Parish of Santa Helena in the District of Cayma, Arequipa, Peru. Only families living in this jurisdiction were recruited for participation. Participants included children between 6 months and 4 years of age. Recruitment occurred in two periods separated by a timespan of 6 months. Group 1 was enrolled from July 2017-July 2018, and

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group 2 from January 2018 to January 2019. Only participants with baseline and 12-month hemoglobin values were included in the final analysis. Retrospective analysis of the deidentified dataset was deemed exempt by the Icahn School of Medicine at Mount Sinai Institutional Review Board.

Interventions

Lucky Iron Fish®: The Lucky Iron Fish® is a cast iron fish-shaped ingot used to provide dietary iron supplementation to people with or at risk of developing iron deficiency anemia. Developed and patented by the Canadian Lucky Iron Fish Enterprise (LIFE; B-Corporation), the ingots were purchased for use in the study by Health Bridges International. The effectiveness of this intervention has been demonstrated in studies conducted in rural populations in Cambodia.(10) Families received the LIF tool and participated in demonstration sessions on use with various forms of food preparation according to research data provided by LIFE. Participants were instructed to use LIF a minimum of three times per week, either placed directly in a pot or pan while cooking or in 4 cups of water boiled for 10 minutes and consumed with 3 drops of lemon juice. Either method is reported to provide 6-8 mg of absorbable iron with each use.(15)

Nutritional Educational Intervention Plan: The educational sessions were developed by the person responsible for the Sanitary Strategy of Healthy Food and Nutrition (ESANS) of the Francisco Bolognesi Micro Health Network of MINSA (Micro Red de Salud de Francisco Bolognesi del MINSA), Health Bridges International (HBI), the College of Nutritionists of Arequipa, the Professional School of Nutritional Sciences of the National University of San Agustin and the local health promoters of the Catholic Parish of Santa Elena. Training included a group workshop session as well as longitudinal reinforcement via home monitoring visits at 3, 6, and 12 months. These visits were used to retest hemoglobin as well as observe the correct use of LIF and to reinforce proper dietary training and multi-micronutrient use.

The team developed a series of posters to help participants consider the various ways in which food and LIF can be used to prevent and control anemia. The posters outlined how to identify foods with high iron content and foods that facilitate or decrease iron absorption, as well as key facts about anemia and its effect on brain development.

Iron Supplementation: The following treatment guidelines were used for participants enrolled in the project; a licensed physician was available for review and criteria determination. There were three categories of intervention. If the patient had no anemia at the baseline testing, family members attended the group educational workshop, were provided with and instructed on the use of LIF, and given supplemental micronutrients according to MINSA protocol. If the patient had mild or moderate anemia, treatment for IDA with ferrous sulfate was added to this regimen. Any child with severe anemia was triaged to a local health clinic and cleared for participation before receiving the same regimen as the mild and moderate group. The MINSA standards for treatment of pediatric IDA recommend daily supplementation with ferrous sulfate oral solution dosed at 3 mg/kg of elemental iron.(16)

Outcome measures

Capillary blood samples for hemoglobin were taken at the beginning of the study as a baseline measure and at 12

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months. Hemoglobin measurements were collected through the use of the novel point of care Aptus Hemoglobinometer (Entia Corporation, London, UK), enabling immediate results for the research team and the patients enrolled in the study. This device was approved for use by the MINSA Directorate General of Medicines, Supplies and Drugs (DIGEMID).

Hemoglobin values were adjusted for altitude to capture the impact of the reduced partial pressure of oxygen found at higher elevations. This has been studied and accepted as a standard method for evaluating anemia in a population by The United Nations Children's Fund (UNICEF), United Nations University (UNU), and WHO. The hemoglobin values were reported after using an individual correction factor of -1.3 g/dL for elevation according to the standard technical protocol for altitude of ≥2250 m to <2750 m.(17) The elevation of our study population in the District of Cayma is 2,510 m above sea level. Using the WHO parameters for anemia in children younger than 5 years of age, anemia was defined as hemoglobin concentration less than 11 mg/dL, and severe anemia as a hemoglobin concentration less than 7 mg/dL.(18)

A non-validated pre- and post-test survey was employed to assess caregiver knowledge and understanding of the diagnosis of anemia, current dietary practices, and treatment mechanisms and prevention measures. The survey, which was developed by MINSA and the Colegio De Nutricionistas Del Peru-Arequipa and was in use by the group prior to this study, included nine multiple-choice questions. Caregivers were also asked to report the frequency of use of LIF and adherence to treatment with iron and micronutrient supplements. The survey and adherence questions were deployed at the beginning as a baseline measure, with interval questionnaires at 6 and 12 months. They were completed in real time with the interviewer.

The primary outcome measure was the number of participants with resolution of anemia at 12 months. Secondary outcomes included absolute changes in hemoglobin value, differences in scores on the pre- and post-intervention knowledge survey, and adherence to treatments. As these interventions may also be beneficial for those at risk of IDA, we also evaluated how many children may have been prevented from developing anemia, defined as maintaining a hemoglobin value of 11 g/dL or greater throughout the 12-month intervention. Using the annual targeted goals as stated by the Peruvian government of reducing the prevalence of anemia, and the reported baseline prevalence of anemia in Arequipa as 43.7%, we determined that 147 patients were required to identify a 10% difference in the prevalence of anemia with 80% power and an alpha level of 0.5.

Statistical Design

Data was entered and stored using Research Electronic Database Capture (REDCap). REDCap is a secure, web-based software platform designed to support data capture for research studies.(19, 20) Demographics were evaluated descriptively. Hemoglobin values were reported in g/dL. Frequencies and descriptions of central tendency were calculated for the variables using SAS v9.4 (Cary, NC). Chi square and Mann-Whitney-U tests were employed to identify associations between the presence of anemia and patient and intervention-related measures. Variables found to be significantly associated in bivariate analysis or of clinical importance were included in a logistic regression model to identify factors that were independently associated with the resolution or prevention of

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anemia.

Results

A total of 406 children were enrolled. Of these, 256 completed the 12-month program and were included in the final analysis and 150 were lost to follow up. Table 1 lists participant characteristics.

Table 1. Participant Characteristics (n=256)

	Completed Program	Lost to Follow Up
Mean Age	1.7 years (SD 0.1)	1.7 (SD 0.8)
6 months-1 year	24 (9%)	15 (10%)
1 year-2 years	85 (33%)	44 (29%)
2 years-3 years	89 (35%)	65 (43%)
3 years-4 years	58 (23%)	26 (17%)
Female	136 (53%)	80 (53%)
Baseline hemoglobin (SD)	11.3 (0.9)	11.3 (0.9)
>11 g/dL (no anemia)	169 (66%)	98 (65%)
7-11 g/dL (mild-moderate anemia)	87 (34%)	52 (35%)
<7 g/dL (severe anemia)	0 (0%)	0 (0%)

Of the 256 children analyzed, 87 (34.0%) had anemia at baseline; this rate decreased to 13.0% by the conclusion of the study. Of those with anemia at baseline, 69 (79.3%) saw resolution of anemia. Among the 169 (66.0%) without anemia at baseline, 16 (9.4%) demonstrated anemia at the 12-month visit and 153 (90.5%) maintained or increased their hemoglobin at the conclusion of the study (Figure 1). There was an observed increase in hemoglobin for the majority of participants who completed the program. The mean hemoglobin value for all ages at baseline was 11.3 g/dL (SD 0.9). For the group completing the program, the mean hemoglobin was 11.9 g/dL (SD 0.8), with a mean increase of 0.5 g/dL (95% CI 0.4-0.6). Children with anemia at baseline saw an increase of 1.19 g/dL in Hgb at the 12-month follow up (95% CI 1.12-1.37). Of the 150 children lost to follow up, 52 (34.6%) had anemia at baseline. The mean baseline hemoglobin for this group was 11.3 g/dL. There were no children with a hemoglobin level of less than 7 g/dL at any time during the intervention.

Figure 1. Flow diagram of the study

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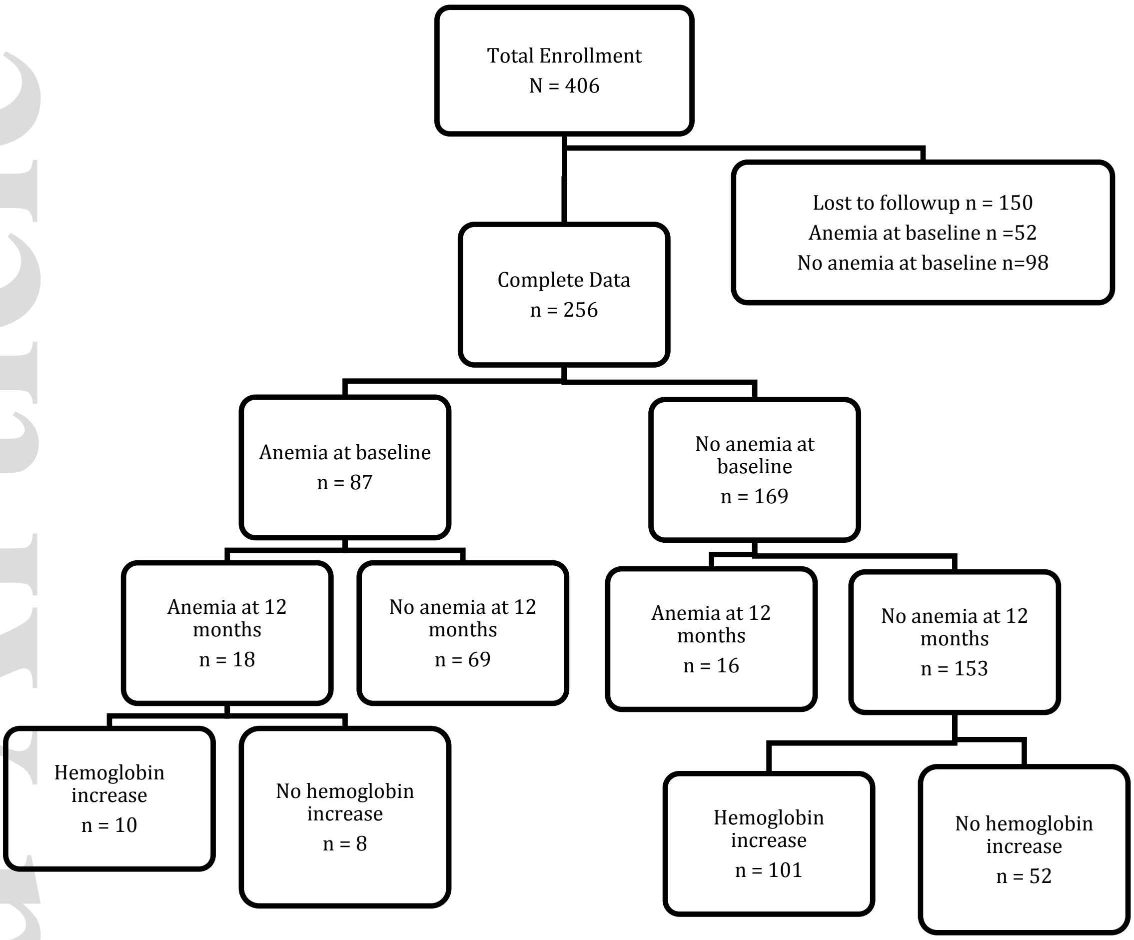

Participants correctly answered 79.0% of knowledge assessment questions at baseline, which increased to 86.6% at the 12-month assessment. Reported adherence to program elements is listed in Table 2. The initial protocol called for children with a hemoglobin less than 11 g/dL to be given ferrous sulfate. However, a proportion of children with hemoglobin levels higher than 11 g/dL reported use with ferrous sulfate. It is unclear if this was a deviation from protocol, if the family was otherwise instructed to take ferrous sulfate from an outside source such as a physician not associated with the program, or there was a misunderstanding of the question. Therefore, we included all 256 children in the analysis of ferrous sulfate use.

Table 2. Adherence measures for those completing program

Ferrous Sulfate Use	
At least once a week	96 (37.5%)
At least three times a week	29 (11.3%)
LIF use	
At least three times a week	224 (87.5%)

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Micronutrient use	
At least once a week	93 (36.3%)

On bivariate analysis, only ferrous sulfate use once a week was found to be positively associated with resolution of anemia (Supplemental Table 1). Author: Suppl Table 1 shows **uni**variate analysis. A logistic regression model with ferrous sulfate use, LIF use, age, and sex was used to analyze their association with resolution of anemia. Children who reported using iron sulfate at least once a week any time during the program time course were 1.9 (95% CI 1.1-3.4) times more likely to have resolution of anemia, and 3.1 (95% CI 1.8-5.3) times more likely to have prevention of anemia. Age, sex, and LIF use were not found to be independently associated with resolution or prevention of anemia in the final model (Table 3).

Table 3. Logistic regression model for resolution of anemia

Variable	*B*	*SE B*	*Wald* χ^2	*p*	*OR*	95% *CI*
Female vs. Male	-0.67	0.29	0.26	0.61	0.8	0.4-1.5
Age	0.02	0.15	0.02	0.89	1.0	0.7-1.4
Ferrous Sulfate use at least once a week	0.66	0.30	4.89	0.03	1.9	1.1-3.4
LIF use	-0.16	0.43	0.14	0.70	0.9	0.4-2.0

Discussion

We describe a successful multi-modal anemia intervention program for children 6 months to 4 years old in a low-resource community at high altitude. Combining family nutrition education, ferrous sulfate, micronutrients, and LIF, we observed a reduction in prevalence of anemia among study participants in this vulnerable population.

The Peruvian government has aggressively targeted anemia reduction in vulnerable and underserved areas. Annual targets for anemia in children younger than 36 months for the Arequipa Region include a reduction of rates to 29.1% for 2019, 24.3% for 2020, and 19.4% for 2021.(21) Our study group found a reduction in prevalence of anemia from 34% to 13% after participation in our 12-month intervention program. We also report an overall increase in hemoglobin concentration of 0.5 g/dL and a more marked increase of 1.19 g/dL over the study period among children with anemia at baseline, which is consistent with available data on iron supplementation.(1)

Our analysis focused specifically on resolution of anemia: a change in hemoglobin from less than 11 g/dL to that value or greater. However, we also found that 90.5% of enrolled children did not progress to anemia during the 12-month time period. While this may have occurred despite our intervention, when compared to the general population data, it suggests that participation in the program may have had a protective effect against anemia.

Ferrous sulfate was shown to be independently associated with resolution of anemia in our study, despite

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relatively low compliance with use. Anecdotal and empiric evidence supports the belief that adherence to the MINSA prescribed 12-month ferrous sulfate treatment regimen is low, with many patients discontinuing care after only one week of treatment due to adverse effects and intermittent availability of supplements at clinics.(22) As such, it is difficult to fully quantify the impact of community-based iron supplementation programs due to poor treatment adherence and regimen completion. However, our findings suggest that ferrous sulfate supplementation may be contributory and should remain in the national treatment protocol despite reported low compliance, raising the possibility that even intermittent supplementation can offset IDA.

Reported compliance with LIF was high at 87.5% in our cohort, and prior studies have found similar adherence rates.(23-25) This could suggest that cultural and cognitive barriers to use are minimal in this population and long-term, continued use is a feasible goal. Regional diet may be undermining the potential impact of LIF. Corn flour, a staple of the Peruvian diet, contains phytic acid, a powerful inhibitor of iron absorption.(9) As elemental iron generally has poor absorption, concomitant citrus intake can improve bioavailability. However, citrus is not necessarily prevalent in the regional diet. Although analysis of the number of families using LIF at least three times per week in accordance with manufacturer's instructions was conducted, we did not examine citrus and corn flour use. These factors could have negatively affected the efficacy of LIF despite such high compliance. As LIF has been shown to be effective in other similar settings, more study is needed to evaluate the true efficacy of LIF in this specific patient population.

This program was implemented with the goal of reducing anemia in the population as broadly and effectively as possible, though some salient findings bear discussion as limitations. As a retrospective review of evaluation data from a public health intervention, the study is underpowered to assess the impact of individual components. This initial investigation suggests the need for a prospective, controlled trial to more clearly evaluate the efficacy of individual and bundled components, including education, micronutrients, LIF, ferrous sulfate and hemoglobin levels.

The use of a survey to report frequency of use for ferrous sulfate, micronutrients, and LIF does allow for both recall and self-reporting bias, which may have affected the outcome data.

There were also a significant number of children lost to attrition. There was documented difficulty in contacting families due to telecommunication failures, geographical barriers for house visits, and the high rate of migrancy amongst families seeking work. However, based on the analysis of this group, the baseline rates of children with and without anemia were nearly identical to the study group, but patterns of attrition could not be specifically identified thus may have impacted the results. The prevalence of IDA peaks between 9-18 months. Despite not being significantly associated with resolution of anemia in our multivariable logistic regression model, the natural improvement of hemoglobin without intervention may have contributed to the findings in this study.

There is also controversy surrounding hemoglobin adjustment for altitude. While this is the accepted practice by consensus statement of the WHO and adopted by the Peruvian government, some have voiced concern that this practice may overestimate the prevalence of anemia for those living at altitude.(26, 27) There is ample and recent evidence to support adjusting hemoglobin levels as evidenced by a physiologic rise in hemoglobin levels with altitude, independent of malnutrition, poverty, or unsafe drinking water. And while age and sex do affect

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hemoglobin levels in infants and preschool age children, at higher altitudes this effect becomes insignificant, leaving hypobaric hypoxia associated with increasing altitude to be the dominant influence on hemoglobin levels. However, the current calculation for an adjustment likely overestimates the coefficient.(14)

In conclusion, our findings suggest that a multimodal approach may potentially reduce the prevalence of mild to moderate iron deficiency anemia among children in this resource-limited setting in Peru. Anemia reduction is a current national health priority, and resources need to be tailored toward efficacy within a given region. Therefore, more holistic and community-based intervention programs that address nutrition and diet diversity education in conjunction with low-cost supplementation and easy-to-use tools such as LIF may reduce and prevent anemia in children. More rigorous study is needed for definitive conclusion on the success of independent interventions to help resolve and prevent anemia. Programs that include longitudinal nutritional education and iron supplementation with a focus on reducing chronic malnutrition should be at the center of this effort.

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