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Comparison of Iron Supplementation and Albendazole  
on Anemia in Ghanaian Children

Megan M. Zitting

A thesis submitted to the faculty of  
Brigham Young University  
in partial fulfillment of the requirements for the degree of  
Master of Science

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## ABSTRACT

### Comparison of Iron Supplementation and Albendazole on Anemia in Ghanaian Children

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Half a billion school aged children suffer from anemia, with the majority of anemia caused by iron deficiency. Researchers have shown a strong correlation between low hemoglobin levels and presence of intestinal parasites in children with anemia. Childhood anemia has profound negative effects on physical growth, maturation, and cognitive development leading to poorer educational achievement.

Using hemoglobin as a measure of anemia, this quasi-experimental study investigated impact of either iron supplementation or an antiparasitic medication on hemoglobin levels in two groups of children in a rural region of Eastern Ghana. Surprisingly, after a 6-month intervention period, hemoglobin levels in both groups significantly decreased. Further research is needed to investigate other factors impacting nutrition and incidence of anemia in pediatric populations in developing countries.

Keywords: anemia, albendazole, iron supplementation, iron deficiency, Ghana

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## Comparison of Iron Supplementation and Albendazole on Anemia in Ghanaian Children

Anemia is defined as a lack of hemoglobin (Hgb) or red blood cells in the body and is a common symptom of iron deficiency due to malnutrition. Iron-deficiency anemia (IDA) is considered a national health threat when anemia rates reach 40% or more of the population (World Health Organization/Unicef/United Nations University, 2001). Anemia is a worldwide concern in children due to adverse health effects, especially in rural Africa. World Health Organization (WHO) data indicate half a billion children in the world and more than 67% of all children in Ghana have anemia (WHO Global Database on Anemia, 2008).

Children with anemia experience adverse effects including weakness, fatigue, poor concentration, and shortness of breath. Additionally, infants and young children suffer impairment of motor, behavior, and cognitive development limiting the probability of success in school and workforce (De-Regil, Jefferds, Sylvetsky, & Dowswell, 2011). Behavior-cognition impairment during fetal and early postnatal ages appears irreversible, but school-aged children (5-12 years) have responded positively to increased iron intake (WHO Global Database on Anaemia, 2008).

### **Literature Review**

An electronic search between 2013 and 2015 was completed to identify studies from the following databases: CINAHL, Medline, and the Cochrane library. Search terms included anemia, iron deficiency, antiparastic, and helminth infestation. The search was limited to English, peer-review studies. Utilizing these criteria, 180 articles were initially identified. Search terms were narrowed, focusing on pediatric anemia and high-risk populations. Studies were further limited to clinical trials, meta-analyses, and epidemiological studies. Animal studies were



excluded. Additional relevant sources were identified from articles' references, bringing the total number of significant articles to 19. Reviewed articles were placed into three general categories including iron intake, iron supplementation, and parasite infection and treatment.

### **Iron Deficient Diet**

Inadequate iron intake is a primary factor in Hgb production with at least half of anemia cases resulting from diets deficient in iron. Nutritional anemia occurs when lowered dietary iron results in decreased mature red blood cells leading to lowered Hgb levels (Stephenson, Latham, & Ottesen, 2000). Iron is derived from meat and plant sources, but iron obtained from meat has the greatest bioavailability for producing Hgb (Koury & Ponka, 2004). Iron deficient diets, with low availability of meats, are primarily the cause for anemia prevalence among school-aged children in developing nations, including rural Ghanaian populations (WHO Global Database on Anemia, 2008).

### **Iron Supplementation**

Because iron deficient diets cause anemia, researchers have studied effects of iron supplementation on Hgb levels. Specifically, studies have compared low dose intermittent (LDI) iron supplementation (non-consecutive iron supplement doses one to three days a week) versus daily iron supplementation. In a meta-analysis of 33 studies, researchers found LDI iron supplementation was as effective as daily iron supplementation in improving ferritin (an iron binding protein) and Hgb levels in children age 12 and under (De-Regil et al., 2014).

Some side effects of iron supplementation include abdominal pain, constipation, foul taste, and teeth staining. However, LDI may have fewer side effects than daily dosing (De-Regil et al., 2014).

### **Parasite Infection and Treatment**

Even if children receive enough iron nutritionally, malabsorption may also contribute to anemia. Intestinal parasites, acquired through contaminated water and food, cause malabsorption of nutrients leading to symptoms such as diarrhea, stomachache, and decreased appetite (Stephenson, et al., 2000). Ghana Eastern Region health reports from the Atiwa District indicated greater than 90% of children had intestinal parasites during 2012 (T. Djangmah personal communication, May 29, 2013).

Treating children for intestinal parasites every 3 months in the Ghanaian healthcare system with 400 mg albendazole, an antiparasitic medication, is standard; however, it is not widely used as healthcare is difficult to obtain. Pediatric dosing is not used with albendazole in this population since only the 400 mg vial is available. Since 2008, various health clinics in the Atiwa region have given albendazole to the population to treat intestinal parasites (T. Djangmah personal communication, May 29, 2013). While albendazole eliminates many parasites, it may not kill all. Most common albendazole side effects are constipation, nausea, headache, and diarrhea (Samuel, Degarege, & Erko, 2014).

Conflicting research exists regarding efficacy of antiparasitic medications on anemia. Researchers sponsored by Benson Institute (The Ezra Taft Benson Agriculture and Food Institute, Provo, UT) found the majority of children with intestinal parasites had anemia in an Ecuador province (The Otovalo Project, 2005). Likewise, Huong, Brouwer, Verhoef, Khan, and Kok (2007), discovered intestinal parasitic infections doubled anemia risk in Asian children. Conversely, Bechir, Schelling, Hamit, Tanner, and Zinsstag (2012) concluded intestinal parasites did not cause anemia even though 54% of Chadian children who had intestinal parasites were anemic.

### **Further Research**

Prior research on Ghanaian schoolchildren indicated additional study is needed to identify potentially effective interventions to improve anemia in rural African pediatric populations (WHO Global Database on Anemia, 2008). While studies regarding iron supplementation and correlation between intestinal parasites and anemia exist (De-Regil et al., 2011), no studies comparing efficacy of LDI iron supplementation with antiparasitic medications to treat pediatric anemia were found. Treatment of iron deficiency and/or intestinal parasitic infections could potentially provide groundwork for further study to determine if using both treatment modalities will result in improved cumulative Hgb levels.

### **Statement of Problem**

Children in developing nations are especially at high risk for anemia due to multiple environmental stressors influenced by nutrition, acute and chronic disease, financial, and educational factors. Therefore, this study compares efficacy of two treatment modalities that may decrease incidence of pediatric anemia in children from the Atiwa District of Ghana.

### **Research Questions**

1. Does dietary supplementation with 50 mg liquid iron preparation administered non-consecutively three times a week for 6 months to kindergarten children in the Atiwa District of Ghana increase Hgb levels?
2. Does prophylactic administration of a 400 mg/10 mL dose of liquid albendazole, used to eradicate intestinal parasites, administered every 3 months for 6 months (two doses) to kindergarten children in the Atiwa District of Ghana increase Hgb levels?
3. Are gender, intervention group, anemia status at pretest, change in height, and change in weight predictors of anemia after treatment?

## Methods

### Setting

This study took place in the Atiwa District of Eastern Ghana, West Africa. The Atiwa District was chosen because it has a predominantly agricultural based economy with a higher rate of poverty and dietary deficiencies than urban areas of Ghana (T. Djangmah personal communication, May 29, 2013). The district health commissioner decided which schools would participate in this study, while the village Headman approved research and participant schools.

### Subjects

Subjects of this study were a convenience sample of kindergarten children enrolled in two primary schools. All children were of native Ghanaian/African descent, ranging in age from 4-10 years old. In the Ghanaian school system, children advance to the next grade based on standardized test results rather than by age, explaining the wide age variation.

Screening children for renal, hepatic, and neurological diseases, including neurocysticercosis and hydatid disease, was completed due to potential adverse effects of albendazole, the antiparasitic medication. After screening all children, none were excluded based on this criteria.

Apriori power analyses were conducted to assess sample size needed to detect differences for the between subjects factor and the within subjects factor for a repeated measures ANOVA. A medium effect size ( $f=0.25$ ) and a desired power ( $power=0.8$ ) and standard type 1 error rate ( $alpha=0.05$ ) indicated a sample size of 82 individuals was needed to detect a difference for the between subjects factor and a sample size of 24 was needed to detected difference for the within subjects factor and the interaction. Research began with 324 enrolled subjects (iron supplementation group  $n = 141$  and antiparastic group  $n = 183$ ), but attrition was great.

However, the needed number of paired subjects for each group was still surpassed (iron supplementation group  $n = 88$  and antiparasitic group  $n = 90$ ). Because it was culturally unacceptable to offer treatment to only a few students, all enrolled school children received medication. Only data of students present at both pre and post interventions were included in Table 2.

### **Design**

Since no randomization was possible, a quasi-experimental design was used. The primary investigator randomly assigned schools to one of two intervention groups either iron supplementation group (ISG) or antiparasitic group (APG). ISG children received 50 mg liquid iron supplement on each Monday, Wednesday, and Friday while attending school over a 6-month period. Liquid medication is standard for pediatrics in this population, and teeth staining was an accepted side effect. APG children were given 400 mg/10 mL liquid albendazole, an antiparasitic medication, at the beginning of the intervention period and again at 3 months. Children in both groups acted as their own control. The village Headman and the local village healthcare provider supervised administration of iron supplementation and antiparasitics to children. Missed doses were not made up, but children still remained in the study though absences were common.

### **Procedures and Data Collection**

Institutional IRB approval was obtained for this study. A graduate nurse practitioner student and nursing research assistant documented gender, age, and measured pretest and posttest weights, heights, and Hgb levels to evaluate growth and iron status. Children's weights were obtained in kilograms using a single Taylor medical grade electronic scale placed on a firm flat cement surface. Children were measured standing with feet within drawn footprints on scale

surface. Heights were obtained using a stadiometer, attached to a flat cement wall. Each day of use, the scale was checked for accuracy by zeroing then weighing a known measure. Using a single point of care monitor STATSite M<sup>Hgb</sup> from Stanbio Laboratory, Hgb levels were measured. Through assigning participants study ID numbers used during data collection, the primary investigator, with the school headmasters' help was able to correctly identify each participant at pretest and posttest.

### Data Analysis

Research assistants recorded measurement data onto data collection instruments. A research assistant entered this data into an Excel spreadsheet, and the primary investigator, along with a second research assistant, independently verified data entry. Data were imported from the Excel spreadsheet into SPSS® version 21 for statistical analysis. Using descriptive statistics, research assistants reviewed data for pretest and posttest missing values and outliers. The relationship between predictors of gender, age, intervention group, change in height, change in weight, anemia status at pretest, and anemia status at posttest were examined using logistic regression.

### Results

Descriptive statistics for study variables, such as height and weight, for all subjects are reported in table 1. Table 2 displays data of paired subjects only. From pretest and posttest dates, paired ISG children grew an average of 2.2 cm, whereas paired APG children grew an average 2.6 cm. During the interval between pretest and posttest measurements, weight increased by an average of 0.45 kg for ISG and by 0.40 kg for APG. Of the 324 participants, children were ages 4-10 years ( $M = 5.71$ ,  $SD = 1.508$ ), 138 (42.6%) were female, and 186 (57.4%) were male. One child in APG was eliminated due to incorrectly entered measurements at pretest. Of the 178

paired subjects, children were aged 4-10 years ( $M = 5.98$ ,  $SD = 1.392$ ). Of these, 72 (40.4%) were female, and 106 (59.6%) were male.

Pretest comparisons for height, weight, and Hgb levels indicated no significant differences between paired subjects in intervention groups. Significant proportions of study participants in both groups were anemic (Hgb levels  $< 11$  g/dl) at pretest with a prevalence of 40.4% in the ISG and 30.1% in APG.

Using Hgb as a measure of anemia, Hgb levels in both intervention groups decreased after the 6-month intervention period. Simple effects comparing changes over time for each group separately were conducted:  $F(1, 176) = 9.86$ ,  $p = .002$ , Partial Eta Squared = 0.053 for the ISG and  $F(1,176) = 27.07$ ,  $p < .001$ , Partial Eta Squared = 0.133 for APG. Mean Hgb for the ISG dropped from 11.2 g/dL to 10.5 g/dL and the mean Hgb for the APG dropped from 11.2 g/dL to 10.0 g/dL.

A repeated measures ANOVA was conducted to assess changes in Hgb levels from pretest to posttest for the two study groups. The within-subjects variable was time with two levels (pretest, posttest). The between-subjects variable was the study group with two levels (iron supplementation, antiparasitic). The intervention was insignificant, indicating both groups displayed similar changes in Hgb levels over time. The main effect of group was insignificant, indicating both intervention groups showed similar Hgb levels at pretest and posttest. The within-subject effect of time was significant,  $F(1, 176) = 34.7$ ,  $p < .001$ , partial eta squared = .165. Follow-up pairwise comparisons between pretest and posttest indicated a significant drop in Hgb level for both groups. The mean difference from pretest and posttest dropped by .949 mg/dL (pretest,  $M = 11.19$  and posttest,  $M = 10.24$ ).

A logistic regression was conducted to assess the relationships between changes in height, changes in weight, by gender, by intervention group, pretest anemia status and posttest anemia status. The beginning block classification table indicates 62.1% correct when classifying everyone into the largest category of being anemic at posttest. The omnibus test of model coefficients was significant, Chi-square ( $df = 5$ ) = 12.40,  $p = .03$ , indicating the model with predictors was significantly better than the model without predictors. The Cox & Snell R Square = .068 and the Nagelkerke R Square = .092, indicating the model explains between 6.8% and 9.2% of the variance in anemia status at posttest. The Hosmer and Lemeshow test was insignificant, indicating the predictors may be somewhat useful in predicting anemia at posttest. The final classification table reports 66.7% correct classification. Regression coefficients and odds ratios are reported in Table 2. None of the predictors were significant predictors of anemia status at posttest except anemia status at pretest. Neither intervention was found to improve anemia status.

### **Discussion**

ISG and APG both showed similar expected increases in height and weight. According to charts provided by WHO, increases in height and weight were considered appropriate for this age group (World Health Organization, 2015). Hgb levels at pretest in both schools indicated a comparable degree of anemia; however, the major findings of this study were unexpected. Mean Hgb levels actually significantly decreased from baseline in both ISG and APG after 6 months of intervention. While no studies were found looking at the outcomes of albendazole on pediatric anemia, decreases of Hgb levels in ISG is inconsistent with previous LDI iron supplementation studies (De-Regil et al., 2011).

Drop in Hgb levels, especially in ISG, is confounding. To the best of our knowledge after interviewing children, teachers, the local village healthcare provider, the district health



commissioner, and village Headman, children did, indeed, receive the medications as scheduled. Without a researcher present at each administration, noncompliance with medication delivery cannot be excluded as an explanation of low Hgb levels after intervention.

Children may have received much less medication than hoped. School absences were common, but it is unknown how many doses children missed. All APG students did at least receive the first of the two doses. Administration of all medication took place during lunchtime, when children were most likely to be at school. However, iron absorption might have been decreased at this time since iron absorption is decreased by calcium, eggs, tannis (from tea), and fiber (Zijn, Korver, & Tijburg, 2000).

Seasonal growing pattern may have had a marked effect on Hgb levels. Initial pretest measurements were taken at the end of the wet growing season, while posttest measurements were collected at the end of the dry season, when presumably availability of iron-rich food could have been significantly decreased. Unfortunately in Eastern Ghana, plants are the main source of iron (Baynes & Bothwell, 1990). The inconsistency of diets through seasons is a possible reason for drop in Hgb for both groups.

### **Limitations**

A noted weakness of this study is attrition of enrolled participants. A significant number of children were absent from school in both groups at pretest and posttest. The ISG started with 141 subjects; 22 absent on pretest measurement and 48 absent at posttest measurement. In APG 184 children were enrolled; 56 were absent on pretest, and 64 were absent at posttest. Although attrition is expected in any longitudinal study, numbers may have been higher than expected due to frequency of school absences in the Atiwa District, meaning they would miss scheduled dose

administrations. Children commonly tend younger siblings and work alongside parents in agricultural and sales activities and miss school.

Furthermore, it is unknown how many doses were missed, as monitoring medication administration was another limitation. The local village healthcare provider and village Headman were present and oversaw teachers administering medications to children, but researchers were not on site other than the first day of administration. On randomly chosen days the district health commissioner made visits to schools during administration. As the study was in Ghana over a period of several months, it was not feasible for researchers to personally oversee every administration. Without researchers present, validity is threatened.

Despite accuracy of tools used to measure height and weight, obtaining accurate measurements, even while using appropriate measurement tools, was difficult. However, finding an appropriate surface on which to place the scale was a challenge as floors rarely are flat in Ghana.

Cultural practices related to hair grooming also had potential to affect height measurements. Children in public schooling are required to have short hair; boys may have a maximum measurement length of 1 cm, while girls may have a maximum length of 2 cm. Variance in hair length risks height accuracy.

### **Recommendations**

Closer medication administration is priority in future studies. Having a researcher present during administration is ideal, however potentially difficult. Additionally, a system to document medication administration will provide great insight to actual medication received since children are likely to be often absent.

Iron intake may be varied due to food availability from season to season, so Hgb levels need to be measured through another wet and dry season cycle with treatment, ideally in 4 month increments. Performing a similar study for at least a year might show fluctuation of Hgb levels correlating with children's dietary intake through growing seasons. Ideally, this study would be conducted with a researcher on site supervising administration of treatment medications.

Because nutritional intake significantly varies with growing seasons and because this study did not have a control group, a study investigating change in iron levels in a non-interventional control group would be helpful. Unfortunately, such a study is not culturally appropriate in this population; however, a similar study may be culturally appropriate in a group with similar socioeconomic status and agricultural lifestyle.

WHO Global Database on Anemia (2008) states "approaches that combine iron interventions with other measures are needed" (p.1) where there is more than one identified cause of anemia. Two major anemia contributors exist: intestinal parasites and nutritional iron deficiency. Further research is needed to explore the potential benefits of antiparasitics and iron supplementation as well as the combination of two to tackle anemia with a multi-pronged approach to improve growth, cognitive development, behavior, and growth in children worldwide.

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Table 1  
Demographic Characteristics for  
Entire Sample

Characteristic	ISG		APG	
	Pretest	Posttest	Pretest	Posttest
Age	M(5.56)	M(6.06)	M(5.83)	M(6.23)
Gender				
Female	65 (46.1%)		69 (37.7%)	
Male	76 (53.9%)		99 (54.1%)	
Height (cm)	105.0 (8.5)	109.4 (7.80)	108.1 (9.69)	110.6 (9.28)
Weight (kg)	17.0 (2.67)	17.8 (2.74)	17.5 (2.97)	18.0 (3.01)
Hgb (g/dl)	11.1 (1.68)	10.5 (1.71)	11.08 (1.83)	9.98 (1.73)
Anemic				
Yes	57 (40.4%)	55 (39.0%)	55 (30.1%)	81 (44.3%)
No	62 (44.0%)	41 (29.1%)	72 (39.3%)	38 (20.8%)
Missing	22 (15.6%)	45 (31.9%)	56 (30.6%)	64 (35.0%)
Height Change (cm)		2.2 (.90)		2.6 (.74)
Weight Change (kg)		.45 (.50)		.40 (.64)
Hgb Change		-.72 (1.98)		-1.18 (2.30)

*Note.* Capillary Hgb measurements were used. A correlation between venous blood Hgb levels and capillary blood Hgb levels using STATSite M<sup>Hgb</sup> from Stanbio Laboratory has been established at appropriate levels ( $r^2 = .646$ ). Gómez-Simón et al. (2007) found no significant differences using venous blood levels and capillary levels ( $p = 0.372$ ). Because the accuracy of STATSite M<sup>Hgb</sup> from Stanbio Laboratory was determined to be adequate, capillary Hgb measures were used.

Table 2  
*Demographic Characteristics for  
 Paired Pre/Post Test Subjects*

Characteristic	ISG		APG	
	Pretest	Posttest	Pretest	Posttest
Age	M(5.68)	M(6.18)	M(6.25)	M(6.75)
Gender				
Female	38 (43.2%)		34 (37.8%)	
Male	50 (56.8%)		56 (62.2%)	
Height (cm)	107.2 (8.14)	109.4 (7.90)	110.1 (8.31)	112.7 (8.01)
Weight (kg)	17.7 (2.67)	17.9 (2.78)	18.1 (2.67)	18.5 (2.68)
Hgb (g/dl)	11.2 (1.64)	10.5 (1.74)	11.2 (1.88)	10.0 (1.73)
Anemic				
Yes	43 (48.9%)	51 (58.0%)	40 (44.4%)	63 (70.0%)
No	45 (51.5%)	37 (42.0%)	50 (55.6%)	27 (30.0%)
Height Change (cm)		2.2 (.90)		2.6 (.74)
Weight Change (kg)		.45 (.50)		.40 (.64)
Hgb Change		-.72 (1.98)		-1.18 (2.30)

*Note.* Capillary Hgb measurements were used. A correlation between venous blood Hgb levels and capillary blood Hgb levels using STATSite M<sup>Hgb</sup> from Stanbio Laboratory has been established at appropriate levels ( $r^2 = .646$ ). Gómez-Simón et al. (2007) found no significant differences using venous blood levels and capillary levels ( $p = 0.372$ ). Because the accuracy of STATSite M<sup>Hgb</sup> from Stanbio Laboratory was determined to be adequate, capillary Hgb measures were used.

Table 3 *Regression Coefficients*

Variable	b	SE	Wald	p	exp (b)	95% CI	
						Lower	Upper
Anemic at pretest	-.782	.332	5.547	.019	.457	.239	.877
Height Change	.191	.214	.799	.371	1.211	.796	1.842
Weight Change	-.404	.286	1.996	.158	.668	.381	1.169
Gender	-.447	.343	1.705	.192	.639	.327	1.251
Study Group	-.404	.331	1.490	.222	.668	.349	1.277
Constant	1.068	.575	3.458	.063	2.911		

*Note.* The Taylor medical grade electronic scale and the Seca 216 wall stadiometer were deemed acceptable in measuring height and weight in this study. According The Taylor USA Medical Company, the Taylor medical grade electronic scale is typically accurate plus or minus two lbs for weights under 200 lbs (Taylor Precision Products, 2015). The Seca 216 wall stadiometer was mounted, improving accuracy (Seca, 2015).