Prevalence and Factors Associated with Anemia among Children under 5 Years of Age—Uganda, 2009

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Abstract. Anemia in children under 5 years of age, defined by the World Health Organization as a hemoglobin concentration < 11 g/dL, is a global public health problem. According to the 2006 Demographic Health Survey, the prevalence of anemia among children under five in Uganda was 72% in 2006. The 2009 Uganda Malaria Indicator Survey was conducted in late 2009 and revealed that over 60% of children less than 5 years of age were anemic and that over half of children tested positive for malaria via a rapid diagnostic test. Children with concomitant malaria infection, and in households without any type of mosquito net were more likely to be anemic, confirming that children under 5 years, are vulnerable to both the threat of malaria and anemia and the beneficial effect of malaria prevention tools. However, prevention and treatment of other factors associated with the etiology of anemia (e.g., iron deficiency) are likely necessary to combat the toll of anemia in Uganda.

INTRODUCTION

Despite recent data that reveal a lower global prevalence of anemia in 2010 when compared with 1990, nearly one third of the world's population are estimated to be anemic.¹ Children under 5 years of age assume a disproportionate burden of anemia, defined by the World Health Organization (WHO) as a hemoglobin (Hb) level < 11 g/dL, and is an increasing prevalent global health problem.^{1–3} Although it is estimated that nearly half of all cases of anemia are due to iron deficiency, the other causes of anemia, which also disproportionately affect children and pregnant women, are multifactorial and include nutritional deficiencies and parasitic infections.^{4–8} Iron deficiency anemia (IDA) in children is particularly detrimental as it can stunt development because additional iron is necessary during growth. The role of IDA in cognitive impairment and psychomotor development is also well recognized.^{9–12} According to the 2000–2001 Demographic Health Survey (DHS), the prevalence of anemia in Uganda was 64% among children < 5 years, similar to other countries in the region.¹³ Notwithstanding global trends, a subsequent 2006 DHS noted that the prevalence of anemia had increased to 72% in Uganda.¹⁴

The causative role of malaria, particularly *Plasmodium falciparum*, in anemia is particularly important in malaria-endemic regions, including much of sub-Saharan Africa (SSA).^{15–18} The vast majority of people living in Uganda are at risk of malaria, and although malaria transmission is of varied intensity, as documented by the entomological inoculation rate, rates of malaria transmission in Uganda are among the highest in the world.¹⁹ According to the WHO, 90% of the total Ugandan population reside in areas of high malaria transmission, almost exclusively via *P. falciparum*.²⁰ Fortunately, efforts to curtail the burden of malaria are underway. Strong government support, via the Uganda National Malaria Control Program (NMCP), and external funding from donors including the Global Fund to Fight AIDS, Tuberculosis, and Malaria, the World Bank, and the U.S. President's Malaria Initiative have enabled Uganda to scale-up multiple malaria control interventions. Similarly, there have been large-scale

national efforts targeting other prevalent parasitic infections, including schistosomiasis and soil-transmitted helminths, which also have a causal relationship with anemia and are prevalent in Uganda.^{21,22}

Given the etiologic role of malaria in anemia and the recent scale-up of malaria prevention and control activities, the prevalence of anemia, if other factors responsible for anemia remained stable, would be expected to decrease.²³ Here, we characterize the prevalence of anemia among Ugandan children less than 5 years of age in 2009 and identify factors associated with the presence of anemia.

METHODS

The Malaria Indicator Survey (MIS) is a nationally representative household survey that collects data on malaria prevention and treatment, anemia, and malaria parasite prevalence. The questions, developed by Roll Back Malaria's Monitoring and Evaluation Reference Group, were adapted from the DHS and United Nations Children's Fund Multiple Indicator Cluster Survey and also include questions on demographic and socioeconomic characteristics of the household.²⁴

The 2009 Uganda Malaria Indicator Survey (UMIS) was intentionally conducted between November and December 2009 to coincide with peak malaria transmission season. The UMIS, the first nationally representative malaria survey in Uganda, used a two-stage sample design. In the first stage, 170 clusters were sampled with selection probability proportional to size based on the same sampling frame used in the 2002 National Population Census.²⁵ As the survey was intended to provide regional-level estimates, the sample was stratified into 10 regions and thus spread equally across the region. After all of the households in the selected clusters were identified, 28 households were randomly sampled from each cluster. Sample weights, using the reciprocal of the selection probability, were applied during analysis to provide unbiased estimates.

Data collection teams, which included interviewers, clinicians, and laboratory technicians, were supervised by staff from the Uganda Bureau of Statistics (UBOS) and the NMCP. The UMIS included household and individual questionnaires. The household questionnaire consisted of demographic information on the residents of the household, characteristics of the household (e.g., source of water, house construction), and ownership

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and/or utilization of malaria prevention efforts including insecticide-treated bed nets and indoor residual spraying. Data on household assets (e.g., television, radio, telephone) were collected and used to create a wealth index using principal component analysis and standardized against a normal distribution with a mean of zero and a standard deviation of one. All households in the total sample were divided into quintiles based on their asset index score as per the Demographic and Health Survey standard.^{24,26} To assess any potential interactive effects between age, wealth quintile, and mosquito net ownership, corresponding interactions terms were created. The individual questionnaire was administered to women between 15 and 49 years and asked about health-care-seeking behavior, such as the utilization of intermittent preventive treatment of malaria in pregnancy and treatment of febrile children. Data from questionnaires were processed, managed, and cleaned centrally at the UBOS. Double data entry was performed on all data and entered using CSPro (U.S. Census Bureau, Washington, DC).

In addition to the questionnaires, blood samples were collected from children under 5 years of age to measure the Hb level and detect the presence of malaria infection. Hb measurements were collected via the HemoCue® (HemoCue AB, Ängelholm, Sweden), a point-of-care test, and were adjusted for altitude as per Centers for Disease Control and Prevention recommendations ($Hb = -0.32 \times [\text{altitude in meters} \times 0.0033] + 0.22 \times [\text{altitude in meters} \times 0.0033]$).^{27,28} Children with Hb level below 8 g/dL were referred to a nearby health facility. Malaria infection was identified using peripheral blood smear to detect malaria parasites, and via the rapid diagnostic test (RDT), Paracheck-pf® (Orchid Biomedical Systems, Goa, India) that detects the presence of histidine-rich protein 2 (HRP2) antigen and is both highly sensitive (92.3%) and specific (97.2%) when compared with microscopy.^{29,30} For this analysis, we used the results of the RDT, which are characterized by high sensitivity but lower specificity as the tests detect HRP2 antigen that persists in the bloodstream after clearance of the parasite.³¹ Children with a positive RDT were offered treatment with weight-based dosing of Coartem® artemether/lumefantrine (Novartis Pharma AG, Basel, Switzerland) at the household according to guidelines from the Uganda NMCP.³²

We analyzed data on Hb levels among children under 60 months and assessed sociodemographic and clinical risk factors associated with anemia using weighted univariate and bivariate analyses. Those variable which were associated with anemia ($P < 0.20$) were included in a multivariate logistic

regression model.³³ Data analysis was performed using SPSS version 22.0 (IBM, Armonk, NY). The survey, including blood specimen collection, was approved by the Uganda National Council for Science and Technology and the U.S. Centers for Disease Control and Prevention. Informed consent was obtained for all portions of data collection by the child's parent or guardian.

RESULTS

A total of 4,421 households were randomly selected (response rate 97.5%) from the 170 clusters. Within these households there were 4,065 children under 5 years of age. Slightly more than half (51%) of the sampled children were female and over 90% were between 6 and 60 months. Of the 4,065 children in the sample, Hb measurements were obtained on 3,878 children (95%). All subsequent analyses were based on these children with Hb measures. Of these, 2,381 (61.4%) children had a Hb level less than 11 g/dL; 375 (9.6%) children had a Hb less than 8 g/dL and thus were referred to treatment as per national guidelines. Over half ($N = 2,001$; 51.6%) of children tested positive for malaria via the RDT (Table 1).

Children in the survey lived in households with a mean of 6.4 household members. The vast majority of children lived in rural areas ($N = 3,406$, 87.8%), only 472 (12.2%) children resided in urban areas. The homes had an average of two rooms which were dedicated for sleeping. Household assets included a radio ($N = 2,703$; 69.7%), bicycle ($N = 1,794$; 46.3%), and mobile telephone ($N = 1,734$; 44.8%). All other assets queried, including electricity ($N = 249$; 6.4%), television ($N = 241$; 6.2%), and motorcycle ($N = 252$; 6.5%) were less common. Nearly three fourth of the households had problems satisfying their food needs "sometimes" ($N = 1,766$; 46.1%), "often" ($N = 531$; 13.9%), or "always" ($N = 419$; 11.0%); the mean number of meals per day was 2.2 and nearly half of households ($N = 1,807$; 46.7%) did not consume meat the week before the survey. The majority of the children's mother's ($N = 2,085$; 62.5%) had a primary school education; secondary school education or higher were less common ($N = 528$; 15.8%). Although only 110 (2.8%) children lived in households with piped water to either their dwelling or property, 2,768 (71.4%) children lived in households that used an "improved" water source (i.e., piped water, public tap, tube well or borehole, protected well or

TABLE 1
Demographic characteristics by anemia severity

	Anemia ($N = 2,381$) (Hb < 11 g/dL), n (%)	Severe anemia ($N = 375$) (Hb < 8 g/dL), n (%)	All ($N = 3,878$), n (%)
Age < 12 months	460 (19.3)	106 (28.2)	684 (17.6)
Sex			
Female	1,197 (50.3)	177 (47.3)	1,970 (50.8)
Residence rural	2,124 (89.2)	360 (96.2)	3,406 (87.8)
Wealth quintile			
1 (poorest)	603 (25.3)	109 (29.2)	893 (23.0)
2	548 (23.0)	98 (26.1)	832 (21.5)
3	493 (20.7)	78 (20.7)	794 (20.5)
4	400 (16.8)	60 (16.1)	729 (18.8)
5 (richest)	338 (14.2)	29 (7.8)	629 (16.2)
Maternal education < secondary	1,777 (74.6)	307 (80.4)	2,806 (84.2)
RDT result positive	1,542 (65.0)	329 (88.0)	2,001 (51.6)

Hb = hemoglobin; RDT = rapid diagnostic test.

spring, rain water, or bottled water). On average, the nearest health facility was 3.9 km from the house. Of the children with Hb measurements, only 1,358 (35.0%) belonged to the top two wealth quintiles; 1,725 (44.5%) lived in the poorest two wealth quintiles.

Using bivariate analysis, the odds of anemia decreased with each additional month of age (odds ratio [OR] = 0.979; 95% confidence interval [CI] = 0.976, 0.983). Anemia was common among children living in rural areas (OR = 1.39; CI = 1.14, 1.69), in households in the poorest wealth quintiles (OR = 0.850; CI = 0.812, 0.891), in those households having problems in satisfying their food needs (OR = 1.11; CI = 1.05, 1.18), who lived in households that consumed fewer meals per day (OR = 0.790; CI = 0.712, 0.876), and in those households with less maternal education (OR = 0.862; CI = 0.776, 0.957). Anemia was negatively associated with ownership of any type of mosquito nets (i.e., treated or untreated) (OR = 0.747; CI = 0.650, 0.858) and strongly associated with concomitant malaria infection (OR = 4.15; CI = 3.61, 4.77). The interactions between, mosquito net ownership and age (OR = 0.979; CI = 0.974, 0.984), wealth index and age (OR = 0.994; CI = 0.993, 0.995), and wealth index and mosquito net ownership (OR = 0.886; CI = 0.855, 0.919) were each associated with anemia. Distance to the nearest health facility, household size, sex of child, and access to improved water sources ($P = 0.91$) were not associated with anemia in the bivariate analysis (Table 2). The prevalence of anemia among children who tested negative for malaria was 44.7% (831/1,859) (versus 77.0% among those who tested positive; 1,542/2,002). Similarly, 64.9% (1,542/2,373) of children who were anemic tested positive for malaria versus 31% of nonanemic children (460/1,488) ($\chi^2 = 425$; $P < 0.001$) (Table 3). Of the children with a Hb less than 7 g/dL, 87.3% (151/173) had a positive RDT. A similar percentage of children with a Hb between 7 and 8 g/dL had a positive RDT (178/201; 88.6%), however, positive test results were significantly less

TABLE 3
Relationship between anemia (hemoglobin < 11 g/dL) and RDT results

Anemia	RDT		
	Yes	Positive	Negative
	No	460	1,028
Total		2,002	1,859

RDT = rapid diagnostic test.

common among children with a Hb between 8 and 10 g/dL (783/1,174; 66.7%) and among those children with a Hb between 10 and 11 g/dL (430/825; 52.1%) ($\chi^2 = 560$; $P < 0.001$).

Using a multivariate regression model, simultaneous malaria infection (OR = 5.32; CI = 4.49, 6.31), and rural residence (OR = 0.978; CI = 0.966, 0.990) were significantly associated with anemia. The odds of anemia decreased by 2% with each additional month of the child's age (OR = 0.978; CI = 0.966, 0.990). The remaining variables included in the model, including the interaction terms, were not significantly associated with anemia (Table 2).

DISCUSSION

The prevalence of anemia among children less than 5 years has decreased in Uganda from 72% in 2006 as per the nationally representative DHS conducted that year to 61% in 2009 in this current survey.¹⁴ However, the burden of anemia clearly remains high and remains a "severe public health problem" as per the WHO.³⁴ Not surprisingly, children with concomitant malaria infection, and children living in rural households were more likely to be anemic, confirming that children under 5 years are vulnerable to both the threat of malaria and anemia.

A number of previous studies have documented the effect of malaria prevention and control efforts in decreasing

TABLE 2
Factors associated with anemia (Hb < 11 g/dL)

	Bivariate		Multivariate	
	Odds ratio	95% CI	Odds ratio	95% CI
Age				
Each additional month	0.979	(0.976, 0.983)	0.978	(0.966, 0.990)
Sex				
Female	0.947	(0.832, 1.08)	NA	
Residence				
Rural household	1.39	(1.14, 1.69)	0.768	(0.592, 0.996)
Wealth quintile				
Each increasing quintile	0.850	(0.812, 0.891)	0.910	(0.815, 1.02)
Maternal education				
< Secondary	0.862	(0.776, 0.957)	1.02	(0.898, 1.17)
Household size				
Each additional member	1.00	(0.976, 1.03)	NA	
Households with problems satisfying food needs	1.11	(1.05, 1.18)	0.970	(0.903, 1.04)
Household meal consumption per day				
Each additional meal	0.790	(0.790, 0.876)	0.932	(0.814, 1.07)
Mosquito net ownership	0.747	(0.650, 0.858)	0.709	(0.480, 1.05)
Household with access to improved water source	0.992	(0.859, 1.15)	NA	
Distance to nearest health facility				
Each additional km	1.00	(0.990, 1.03)	NA	
Malaria infection				
RDT positive	4.15	(3.61, 4.77)	5.32	(4.49, 6.30)
Interaction: age $\times$ mosquito net ownership	0.979	(0.974, 0.984)	0.994	(0.984, 1.00)
Interaction: age $\times$ wealth quintile	0.994	(0.993, 0.995)	0.998	(0.995, 1.00)
Interaction: mosquito net ownership $\times$ wealth quintile	0.886	(0.855, 0.919)	1.00	(0.886, 1.14)

CI = confidence interval; Hb = hemoglobin; km = kilometer; NA = not applicable; RDT = rapid diagnostic test.

anemia.^{35–38} Malaria prevention and effective treatment measures have dramatically expanded in the past decade. Although the UMIS was the first national survey to assess malaria prevalence in Uganda, the prevalence of malaria likely decreased during this interim given the rapid scale-up of malaria control activities.³⁹ However, we found the prevalence of malaria, as determined by Paracheck-pf RDT, among children under 5 years was still nearly 50% in this study. Although the scale-up of malaria control efforts, are likely responsible in part for the observed concomitant downward trend in anemia prevalence in Uganda, such public health endeavors are unlikely to be sufficient to reduce the burden of anemia in Uganda.

Strategies aimed at alleviating anemia are clearly paramount. However, anemia is a multifactorial process with a host of distinct and potentially interactive causes. In a recent study in Kenya, researchers found that while malaria was the leading factor associated with anemia, iron deficiency, inflammation, blood disorders, and stunting were also associated with anemia among children under 5 years.⁶ As such, interventions aimed at anemia prevention and treatment must be targeted to be optimally effective. Although the UMIS did not collect data on nutritional deficiencies, multiple previous studies have documented the high percentage of anemia attributed to iron deficiency globally.^{1,40} Given previous estimates, we estimate that roughly half of the anemia detected in our current survey was secondary to iron deficiency and as such over 30% of children under five may suffer from iron deficiency.⁴¹ However, prevention efforts for IDA are not necessarily straightforward in SSA given the interaction between malaria and iron deficiency.^{42–44}

Because of the high attributable fraction of anemia due to iron deficiency, the WHO previously recommended universal iron supplementation “in settings where the prevalence of anemia in children approximately 1 year of age is above 40% or the diet does not include foods fortified with iron, supplements of iron at a dosage of 2 mg/kg of body weight per day should be given to all children between 6 and 23 months of age.”³⁴ However, a number of studies have highlighted the relationship between iron deficiency and sequelae from malaria infection. A randomized trial in Zanzibar, Tanzania to assess the effectiveness of iron (and folic acid) supplementation on hospital admission and mortality was stopped early after results revealed an increased risk of severe morbidity and mortality among children between 1 and 35 months receiving supplementation.⁴⁵ On the basis of large part on these findings, WHO altered its recommendation to indicate that “universal iron supplementation (i.e., use of medicinal iron as pills or syrups) should not be implemented without the screening of individuals for iron deficiency, because this mode of iron administration may cause severe adverse events in iron-sufficient children.”⁴⁶ WHO now recommends for targeted iron therapy to iron-deficient children, in conjunction with malaria prevention and treatment efforts. A more recent study among HIV-infected children in Malawi found that while iron supplementation improved hematologic indices, the risk of malaria was increased, postulated to be due to the utilization of free iron by *Plasmodium* species.⁴⁷ This theory was supported by another study in Tanzania, in an area of malaria transmission intensity similar to Uganda, in which researchers concluded that the risk of parasitemia was decreased, as was all-cause and malaria-specific mortality, among children

with documented iron deficiency.⁴⁸ These studies support the role of screening for iron deficiency before supplementation and the relationship between iron metabolism and malaria. Unfortunately, given the logistic complexities involved in screening for iron deficiency, programmatic efforts to supplement iron stalled globally.⁴⁹

Screening for iron deficiency in resource-limited areas is indeed challenging, controversial, and may neither be needed nor practical.^{44,49–51} In a hyperendemic malaria region of Tanzania, over 800 infants were randomized to one of four groups—iron supplementation with anti-malarial, iron supplementation with placebo, placebo with anti-malarial, or placebo with placebo. Infants receiving iron had lower rates of severe anemia than their counterparts without an effect on acquisition of malaria, suggesting the protective efficacy of iron supplementation in preventing anemia.⁵² A separate trial in Zanzibar, Tanzania randomized children between 4 and 71 months to either receive low-dose iron supplementation (10 mg/day) or placebo, and measured prevalence of malaria; low-dose oral daily supplementation of iron did not increase prevalence of malaria infection.⁵³ A Cochrane review in 2009, which reviewed 68 trials (and over 40,000 children) concluded that iron supplementation did not increase the risk of malaria, unless malaria surveillance and treatment options were not provided to infected children.⁵⁰ Consequently, these researchers note that screening for IDA is not necessary in areas where malaria surveillance, prevention, and treatment programs are implemented. A subsequent Cochrane review in 2011 confirmed the earlier findings and found that while the risk of clinical malaria among children receiving iron supplementation was higher in regions without access to malaria surveillance and treatment, concluded that “when regular malaria surveillance and treatment services are provided” the risk of malaria is not increased.⁵¹ As such, these researchers concluded that screening for anemia was unnecessary prior to oral iron supplementation in such situations.

The interaction between anemia, iron deficiency, and infections (including malaria) is clearly complex and as noted above population trials in areas of similar malaria transmission intensity have yielded contradictory results. Given these discordant findings, updated WHO guidance on iron supplementation in areas of intense malaria transmission is forthcoming and urgently required. Additional research is also necessary to further elucidate the relationship between iron supplementation and malaria infection and the optimal methods of delivering these necessary public health interventions. In the meantime, efforts to integrate iron supplementation with malaria control programs and food-based interventions, which reduce the dose of absorbable iron, have been suggested.^{5,44,49}

A primary limitation of our study is that we did not obtain data on iron status or other nutritional indices. However, given previous estimates of the attributable fraction of iron deficiency to the global burden of anemia, the influence of iron deficiency in our population likely remains strong. Further, while the 2009 UMIS highlights the continuing association between malaria and anemia, given the cross-sectional design of our study, the direction of this relationship cannot be further elucidated from these data. This survey also did not collect data on other potential infectious causes of anemia (e.g., schistosomiasis, soil-transmitted helminths), which likely contribute to the burden of anemia in Uganda. With the continued support of national prevention campaigns against these

neglected tropical diseases, we expect the prevalence of anemia to further decrease.

The 2009 UMIS revealed an anemia prevalence of 62.2%. More recent data from the 2011 DHS, also a nationally representative household survey, noted a further decrease in anemia prevalence of 49% among children under 5 years in Uganda and corresponds to increases in malaria prevention and control activities during this interim.⁵⁴ Although not yet available, the 2014 UMIS will provide additional data regarding this relationship. Indeed a review of 29 studies in Africa revealed that malaria control activities increased Hb levels by an average of 0.76 g/dL.³⁶ However, despite increased mosquito net ownership and availability of malaria treatment options, the burden of anemia remains. Therefore, prevention of anemia via micronutrient supplementation, including iron, and antihelminthics, in conjunction with malaria prevention and treatment strategies, will likely be necessary to halt the toll of anemia in Uganda.

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