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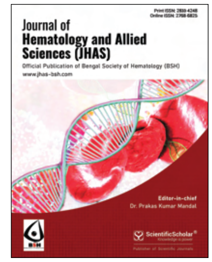

Original Article

Malaria attributable to one-third of anemia cases among febrile children in Eastern Uganda: A cross-sectional study

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ABSTRACT

Objectives: The study aims to determine the Prevalence of anemia and its association with malaria infection among febrile children under 15 years at Bududa General Hospital, Eastern Uganda.

Material and Methods: A hospital-based cross-sectional study was conducted among 347 febrile children between April and June 2023. Venous blood samples were collected for complete blood count and malaria microscopy. Stool samples were examined for intestinal helminths. A structured questionnaire was used to collect sociodemographic data. Multivariate logistic regression was used to identify factors associated with anemia. A $P \leq 0.05$ was considered statistically significant.

Results: The overall Prevalence of anemia was 225 (64.8%). The Prevalence of malaria parasitemia was 162 (46.7%), with *Plasmodium falciparum* as the dominant species (83.3%). Multivariate analysis revealed that malaria infection (adjusted odds ratio [aOR] = 8.24; 95% confidence interval [CI]: 3.63–18.70; $P < 0.001$), children aged 1–5 years (aOR = 0.24; 95% CI: 0.08–0.72; $P = 0.011$) and 6–10 years (aOR = 0.19; 95% CI: 0.05–0.66; $P = 0.009$) and a parent/guardian with secondary education (aOR = 0.40; 95% CI: 0.20–0.82; $P = 0.012$) were associated with anemia. The Prevalence of intestinal helminths was low (2.9%) and not associated with anemia.

Conclusion: This study links a high anemia rate in febrile children to malaria, particularly affecting infants and those with less-educated caregivers, necessitating combined malaria and nutrition interventions.

Keywords: Anemia, Children, Febrile illness, Malaria, *Plasmodium falciparum*

INTRODUCTION

Anemia is a global public health problem affecting over 16.4% of children under 5 years of age, with the highest burden in sub-Saharan Africa and Southeast Asia.[1] It significantly contributes to childhood morbidity and mortality, leading to impaired cognitive and motor development, reduced immune competence, and poor growth.[2,3] The etiology of childhood anemia is multifactorial, including nutritional deficiencies (iron, Vitamin B12, folate), parasitic infections (malaria, helminths), genetic disorders, and chronic diseases.[4,5]

In malaria-endemic regions, a complex bidirectional relationship exists between malaria and anemia. Malaria contributes to anemia through the hemolysis of infected and non-infected red blood cells, splenic sequestration, and dyserythropoiesis.[6,7] Conversely, anemia can exacerbate the severity of malaria infections.[8] The World Health Organization (WHO) African Region accounted for 93.6% of global malaria cases and 95.4% of deaths in 2022, with children under five being the most affected group.[9] Uganda bears a substantial part of this burden.[9]

Much of the existing Ugandan literature on malaria-anemia comorbidity comes from high-transmission lake-endemic regions or the northern parts of the country.[10] These data may not be generalizable to highland areas such as Bududa District, which are characterized by epidemic-prone, unstable transmission patterns influenced by altitude and a bimodal rainfall pattern. This ecology might influence malaria transmission and, consequently, anemia, compared to other regions in Uganda.

Despite ongoing national efforts to control malaria and micronutrient deficiencies, anemia remains a severe problem in Uganda. Previous studies have reported varying prevalence rates; however, recent data on the Prevalence and specific etiological factors of anemia remain scarce. Particularly within febrile pediatric populations presenting to health facilities in the highland/foothill regions of Eastern Uganda. Such data are crucial for tailoring local interventions.

This study was conducted to establish the Prevalence of anemia and its association with malaria infection among febrile children under 15 years of age at Bududa General Hospital. The resulting data are intended to provide a critical evidence base for informing and optimizing local and national health interventions.

MATERIAL AND METHODS

Study design and site

This research utilized a cross-sectional methodology at Bududa General Hospital, a public district hospital in Eastern Uganda. Data collection took place from April to June 2023, a period that aligns with one of the district's seasonal peaks in malaria incidence, a phenomenon influenced by its bimodal rainfall pattern.

Sample size calculation and sampling procedure

The sample size was calculated using the Kish–Leslie formula, assuming a 34.4% prevalence of anemia from a previous Ugandan study,[10] a 95% confidence interval (CI), and a 5% margin of error, yielding a minimum sample of 347 participants as below.

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where:
n = study sample size
Z = the critical value corresponding to 95% CI in a standard normal distribution curve (= 1.96)
P = Prevalence of anemia used was 34.4%.[11]
d = margin of error was 5%
Calculation:

$$n = \frac{1.96 \times 1.96 \times 0.344\ (1-0.344)}{0.05 \times 0.05}$$

n = 347

Therefore, the calculated sample size recruited in this study was 347 study participants.

Consecutive sampling was used, where every febrile child that met the inclusion criteria were recruited into the study until the calculated sample size was achieved.

Study population and selection criteria

Febrile children under 15 years presenting to the outpatient department were eligible. Inclusion criteria were: Axillary temperature ≥37.5°C or history of fever in the past 48 h, age below 15 years, and residence in the district for ≥3 months, and provision of informed consent by a parent/guardian. Exclusion criteria were: Critical illness requiring immediate intensive care, and history of antimalarial or anthelminthic treatment within 2 weeks before recruitment.

Data and sample collection

After obtaining informed consent, a structured questionnaire was administered to parents/guardians to collect sociodemographic and economic data. Approximately 4 mL of venous blood was drawn into an ethylenediaminetetraacetic acid vacutainer for complete blood count (CBC) and malaria microscopy. A single stool sample was also collected into a sterile container.

Laboratory analysis

A CBC was performed using the Huma Count 30T (Germany) hematology analyzer. Anemia was defined as hemoglobin concentration <11.0 g/dL for children aged 0–59 months, <11.5 g/dL for children aged 5–11 years and <12 g/dL for children aged 12–14 years according to the WHO hemoglobin thresholds.[12]

Thick and thin blood smears were stained with 10% Giemsa for 20 min and examined by a certified microscopist, and the detection of intestinal helminths and protozoan cysts was performed using both direct saline wet mount microscopy and the formalin-ether concentration technique, a gold standard method for enhancing parasite recovery.

Quality control

Strict quality control measures were adhered to, including daily calibration of the hematology analyzer, use of control samples, and cross-checking of a random subset of blood smears by a second senior microscopist.

Data analysis

Data were entered into Microsoft Excel and analyzed using STATA version 15.0. Descriptive statistics were computed for all variables; categorical data were summarized as frequencies and percentages, while continuous variables were expressed as means with standard deviations (±SDs). Associations between categorical variables and anemia status were assessed using the Chi-square test.

To identify factors associated with anemia, bivariate logistic regression was first performed. The following independent variables were examined: Age, sex, residence, caregiver's education level, caregiver's occupation, malaria status, helminths infection status, distance to the hospital, household income, insecticide-treated mosquito net usage, and history of malaria infection.

Variables that demonstrated an association with anemia at a significance level of $P \leq 0.1$ in the bivariate analysis were subsequently included in a multivariate logistic regression model. The results of the regression analyses are presented as crude odds ratios (CORs) and adjusted odds ratios (aORs) with their corresponding 95% CI. In the final model, a $P \leq 0.05$ was considered statistically significant.

RESULTS

Sociodemographic characteristics

A total of 347 children were enrolled. The mean age was 6.2 years with SD of ±4.95 years. Majority were aged 1–5 years (37.5%), female (53.9%), and from rural areas (89.6%). Most parents/guardians had attained secondary education (57.1%) and were engaged in subsistence farming (72.0%), as shown in Table 1.

Table 1: Sociodemographic characteristics of the study participants *n*=347.

Variables	Frequency (*n*)	Percentage (%)
Age (years)		
<1	50	14.4
1–5	130	37.5
6–10	74	21.3
11–15	93	26.8
Sex		
Male	160	46.1
Female	187	53.9
Residence		
Rural	311	89.6
Urban	36	10.4
Education level of parent/guardian		
Primary	139	40.0
Secondary	198	57.1
Tertiary	10	2.9
Occupation of parent/guardian		
Business	29	8.4
Peasant	250	72.0
Others	68	19.6
Household income		
<Ugx. 100,000/=	149	42.9
≥Ugx. 100,000/=	198	57.1
Number of children in household		
≤4	315	90.8
>4	32	9.2
Distance to hospital		
≤2 km	137	39.5
>2 km	210	60.5

Prevalence of anemia and malaria

The overall Prevalence of anemia was 225 (64.8%). Among anemic children, 32.9% had mild, 63.6% had moderate, and 3.5% had severe anemia [Figure 1]. The Prevalence of malaria parasitemia was 162 (46.7%). *Plasmodium falciparum* was the most prevalent species (83.3%), followed by *Plasmodium malariae* (15.4%) and *Plasmodium ovale* (1.3%). The Prevalence of intestinal helminths was 2.9% (10/347), primarily *Ascaris lumbricoides* and Hookworm.

Factors associated with anemia

Malaria parasitemia was strongly associated with anemia ($\chi^2 = 55.1$, $P < 0.001$). The aOR at multivariate logistic analysis for anemia in children with malaria parasitemia was 8.24 (95% CI: 3.63–18.70; $P < 0.001$) [Table 2].

Bivariate analysis revealed that age, 1–5 years (COR = 0.25; 95% CI 0.08–0.81) 6–10 years (COR = 0.21; 95% CI 0.06–0.74), parental/guardian education level (COR = 0.41; 95% CI 0.19–0.91), and malaria parasitemia (COR = 8.50; 95% CI 3.58–20.20) were significantly associated with anemia [Table 3].

This association remained strong after adjusting for potential confounders in the multivariate model. Children

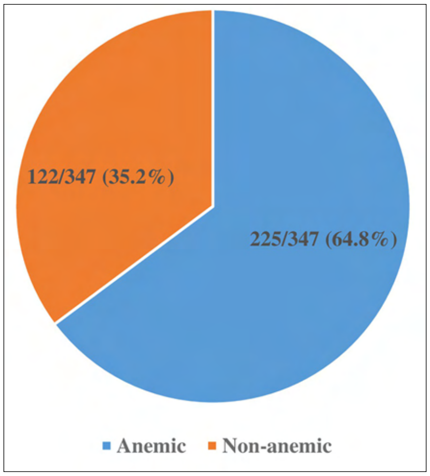

Figure 1: Prevalence of anemia among study participants.

with malaria infection had 8.24 times higher odds of being anemic compared to those without malaria parasitemia (aOR: 8.24; 95% CI: 3.63–18.70; $P < 0.001$). Children aged 1–5 (aOR = 0.24; 95% CI 0.08–0.72) and 6–10 years (aOR = 0.19; 95% CI 0.05–0.66) had lower odds/risk of anemia as compared to infants under 1 year. Furthermore, parents/guardian's secondary education level (aOR = 0.40; 95% CI: 0.20–0.82; $P = 0.012$) was associated with low risk of anemia as compared to parents/guardians with primary education only, as shown in Table 4.

DISCUSSION

This study found an alarmingly high proportion of anemia (64.8%) among febrile children in Eastern Uganda, which was overwhelmingly associated with malaria parasitemia. The finding that malaria parasitemia conferred an eightfold increase in the odds of anemia underscores it as the predominant risk factor in this population. This aligns with the established pathophysiology of malaria-induced anemia through hemolysis and suppressed erythropoiesis[6,7] and is consistent with findings from other high-transmission settings[12,13]

The observed anemia prevalence is considerably higher than the 34.4% reported in North-western Uganda[10] and rates in neighboring Ethiopia.[14,15] This disparity may be attributed to our study focusing on a febrile population, regional differences in malaria transmission intensity exacerbated by Bududa's high rainfall, and varying socioeconomic and nutritional factors. The predominance of moderate anemia suggests a chronic, unresolved public health issue rather than acute episodes.

A key finding was the significantly higher odds of anemia in infants under 1 year compared to older children. This is likely multifactorial, resulting from low iron stores at birth, inadequate iron intake from complementary foods, high physiological demands for rapid growth, passive immunity waning, and first exposure to malaria.[16] This finding is consistent with studies from other malaria-endemic regions, including Ghana and the Democratic Republic of Congo. This finding aligns with previous research demonstrating a significant association between malaria infection and childhood anemia.[13,17] This highlights a critical window for intervention, emphasizing the need for prenatal iron supplementation and postnatal nutritional counseling for mothers.

Table 2: Chi squared table for association of anemia and malaria infection.

	Malaria infection		
Anemia	**Negative**	**Positive**	**Total**
Non-anemic	98	24	122
Anemic	87	138	225
Total	185	162	347
Chi square value=55.1 and P<0.001			

The protective effect of a caregiver's secondary education against child anemia has been documented elsewhere.[18,19] Educated caregivers are more likely to have better health-seeking behaviors, improved knowledge of nutrition and malaria prevention (ITN use), timely care-seeking, dietary diversity, and higher socioeconomic status, enabling better childcare practices.

The very low Prevalence and non-significant role of intestinal helminths in this study differ from some previous reports,[4] but can be explained by the study setting (a hospital, not a community) and the focus on febrile children, who are more likely to be investigated for malaria than helminths. Furthermore, the single-stool sampling technique used in this study could also be a limiting factor, as low Prevalence, but national deworming programs may have reduced the burden of soil-transmitted helminths.

Limitations

This study is subject to several limitations. Foremost, its cross-sectional design inherently prevents the establishment of causal relationships between variables. Our findings from a febrile population at a hospital likely overestimate the prevalence of both anemia and malaria compared to the general community population, limiting the generalizability of our prevalence estimates. The absence of data on iron, folate, Vitamin B12, hemoglobinopathies (such as sickle

Table 3: Bivariate analysis of factors associated with anemia.

Variables	Crude odds ratio	95% CI	*P*-value
Age (years)			
<1	1		
1–5	0.25	0.08–0.81	0.020*
6–10	0.21	0.06–0.74	0.016*
11–15	0.37	0.10–1.30	0.121
Sex			
Male	1		
Female	0.90	0.45–1.78	0.752
Occupation			
Business	1		
Peasant	1.06	0.31–3.60	0.920
Others	1.20	0.31–4.65	0.787
Residence			
Rural	1		
Urban	1.26	0.34–4.67	0.731
Distance to hospital			
≤2 km	1		
>2 km	1.45	0.69–3.05	0.323
Education level			
Primary	1		
Secondary	0.41	0.19–0.91	0.029*
Tertiary	0.57	0.06–5.56	0.626
Household income			
<Ugx. 100,000/=	1		
≥Ugx. 100,000/=	0.87	0.40–1.89	0.717
Insecticide treated mosquito net usage			
Yes	1		
No	1.17	0.44–3.11	0.756
History of malaria infection			
No	1		
Yes	1.16	0.52–2.60	0.714
Malaria infection			
Negative	1		
Positive	8.50	3.58–20.20	<0.001*

*Significant factor, 95% Confidence interval. Statistical significance was set at $P < 0.05$. CI: Confidence interval

cell trait or thalassemia), and human immunodeficiency virus means we could not quantify the contribution of these important factors to the anemia burden.

Table 4: Multivariate analysis of factors associated with anemia.

Variables	Adjusted odds ratio	95% CI	*P*-value
Age (years)			
<1	1		
1–5	0.24	0.08–0.72	0.011*
6–10	0.19	0.05–0.66	0.009*
11–15	0.36	0.11–1.20	0.096
Education level			
Primary	1		
Secondary	0.40	0.20–0.82	0.012*
Tertiary	0.57	0.09–3.74	0.559
Malaria infection			
Negative	1		
Positive	8.24	3.63–18.70	<0.001*

*Significant factor, 95% confidence interval. Statistical significance was set at $P < 0.05$. CI: Confidence interval

CONCLUSION

This study demonstrates a high burden of anemia strongly driven by malaria infection among febrile children in Bududa General Hospital, Eastern Uganda, with infants and children of less-educated caregivers being particularly vulnerable.

Integrated public health strategies are vital to address the high burden of anemia and malaria. This includes strengthening the Integrated Management of Childhood Illness for concurrent diagnosis and treatment, combined with community-based nutritional supplementation and targeted health education for mothers and caregivers with low formal education, focusing on the importance of consistent ITN use, recognizing anemia symptoms, and providing iron-rich foods.

Future longitudinal research should integrate biomarkers of micronutrient status and genetic screening for hemoglobinopathies to clarify the distinct roles these factors play in the etiology of anemia within this population.

Author contributions: BO: Conceptualization, study design, literature review, clinical and experimental investigations, data collection; EM: Manuscript drafting, editing, and critical revision; DA: Clinical and experimental investigations, data collection; RW: Manuscript drafting, editing, and critical revision; EAJ: Manuscript drafting, editing, and critical revision; and CO: Data analysis, statistical analysis, and manuscript review.

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Ethical approval: Ethical approval was obtained from the Faculty Research Committee of Mbarara University of Science and Technology (MUST/MLS/030/2023). This study was designed and conducted in strict adherence to the ethical principles outlined in the Declaration of Helsinki of 1975, as revised in 2000.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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