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Malaria Prevalence and Associated Factors in Children Under Five Years in Dokolo District, Northern Uganda: A Community-Based Cross-Sectional Study

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Abbreviations: ABO: Blood Group Systems; ACTs: Artemisinin Combined Therapies; INT: Indoor Residual Net; IPD: In-patient department; IRS: Indoor Residual Spray; LLINs: Long Lasting Insecticide Treated Mosquito Nets; MIS: Malaria Indicator Survey; MOH: Ministry of Health; OPD: Outpatient department; UMRSP: Uganda Malaria Reduction Strategic Plan; UNICEF: United Nation International Children Emergency fund; WHO: World Health Organization.

Abstract

Introduction: Malaria remains a major public health problem affecting children <5 years because of the weak immune system. Uganda set targets to control and eliminate malaria with interventions of most at-risk groups; however, infection rates remain high in Northern Uganda, especially Lango region. This study determined the prevalence and risk factors of malaria and identified among children <5 years in Agwata Sub-county, Dokolo District, Northern Uganda.

Methods: We conducted a cross-sectional study among children aged six months to <5 years in Agwata Subcounty in Dokolo District from 25 April to 10 May, 2021. A three-stage sampling method was used to select participants. Blood samples were examined by smear microscopy for malaria parasites, and ABO blood grouping system was used to establish blood groups of the study participants. Data on demographics and malaria exposure were captured using an interviewer-administered semi-structured questionnaire. Multivariable logistic regression was used to identify factors associated with malaria.

Results: We enrolled 405 children with a mean age of 2.5 (±SD, 1.4-3.6) years; 53% were male. Of these, 118 tested positive for malaria with a prevalence of 29% (95%CI: 24.7-33.8%). Having blood group A (aOR= 1.7, 95% CI:1.1-2.7), households with >3 children (aOR= 2.6, 95% CI: 1.5-4.5), rural residence (aOR=5.7,95% CI: 3.5-8.6), absence of long lasting insecticidal mosquito nets (LLINs) over the children' beds (aOR=5.1, 95% CI: 2.8-7.4), presence of holes in the LLINs (aOR=2.2, 95% CI: 1.5-4.1) and children staying in tra-

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ditional households (aOR=4.2, 95% CI: 2.4-8.6) were significantly associated with malaria.

Conclusion: Approximately one-third of the children <5 years in this survey had malaria, highlighting a high malaria burden in Dokolo District. Children with blood group A, those staying in households of >3 children, those from poor or rural households, and those from households with poor use of LLINs were more likely to be diagnosed with malaria compared to their counterparts. There is a need for routine screening and chemoprophylaxis in children for malaria, given the high malaria burden. The community should be availed with LLINs and sensitized on their proper use.

Introduction

Despite reductions in malaria morbidity and mortality across Sub-Saharan Africa (SSA) over the last two decades [1], there are sub-regional and country-specific disparities in its distribution [2]. For Instance, Uganda has the 3rd highest global burden of malaria cases and the 8th highest level of deaths globally [3]. It also has the highest proportion of malaria cases in East and Southern Africa 23.7% [3]. Moreover, Uganda has a stable, perennial malaria transmission, with Anopheles gambiae and Anopheles funestus being the most common malaria vectors [4].

The highest burden of malaria is registered in rural areas in Uganda [5,6]; Lango sub-region found in Northern Uganda, registered the prevalence of 23% in 2019 [5]. Nevertheless, efforts are underway to reduce malaria-related morbidity and mortality in Uganda. For instance, the new Uganda Malaria Reduction and Elimination Strategic Plan 2021-2025 aims to reduce malaria infection by 50 percent, morbidity by half, and mortality by two-thirds, by 2025 [7].

In malaria-endemic areas, the development of naturally acquired immunity to malaria takes about 10 to 40 days after repeated exposure to malaria parasites [8]. The clinical outcomes of malaria are associated with erythrocyte polymorphisms including the ABO blood groups [9]. However, some studies have reported conflicting findings on the significant association between ABO blood group system and malaria infection [10,11]. Studies have shown a high frequency of malaria among blood group 'A' individuals as compared with other blood group individuals [12]. Other studies have also revealed an association of ABO blood group with susceptibility, resistance, and severity of malaria infection [13]. Blood group "O" may be a protective factor against severe malaria by virtue of reduced rosetting of infected RBCs [14].

Understanding the effect of the ABO blood group on the risk of malaria infection may contribute to the understanding of the pathogenesis and clinical morbidity of malaria and the anticipation of malaria management interventions in highly endemic areas [15,16]. There is limited information about the association between ABO blood group systems and malaria infection in low-income settings.

The Ministry of Health distributed 27.5 million LLINs (long-lasting insecticidal mosquito nets) from March, 2020 to March, 2021 to all households in Uganda [17]. Dokolo District in particular, received LLINs in June 2020. However, by the end of December, 2020, the district had reported a total of 90,165 malaria cases. These data were facility-based and may not give a proper representation of the magnitude of malaria burden in the rural setting , due to misdiagnosis [18]. We therefore conducted a community-based study to establish the prevalence of malaria risk factors and its association with different ABO blood groups among children <5 years in Agwata Subcounty, Dokolo District, Northern Uganda.

Methods and materials

Study area, Design, and study population

This was a community-based cross-sectional study utilizing quantitative method of data collection. We conducted the study in Agwata Sub-county, Dokolo district, from 25 April to 10 May, 2021. Dokolo District is located in Mid Northern Uganda. It is bordered by Lira in the North, Amolatar in the south, Kaberamaido in the East, and Apac district in the West. Agwata subcounty has an estimated population of 25,200 with a population density of 141.0/ km2. Lake Kwania passes through Agwata Subcounty. The district is also bordered by Lake Kyoga in the south with a lot of swampy areas, thus creating breeding sites for mosquitoes **(Figure 1)**. The district receives about 268.94 millimeters (10.59 inches) of precipitation and has 266.54 rainy days (73.02% of the time) annually.

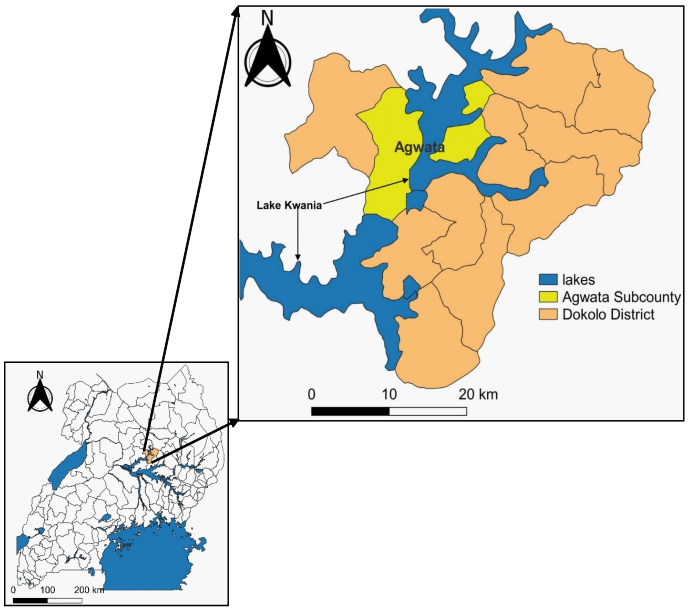

Figure 1: Location of Agwata Subcounty in Dokolo District, Northern Uganda.

We recruited children between 6 months and 5 years of age. The respondents were their respective mothers/care takers who had lived in Agwata Subcounty for at least one year at the time of this study.

Sampling size determination

We determined the sample size using Kish Leslie (1965) formula [19] with a 95% level of significance, the estimated proportion of children below 5 years with malaria at 23% in Northern Uganda [20] and maximum error of 5%. With the design effect of 1.5, we obtained a minimum sample size of 408 of children (between 6 months and 5 years) and their mothers/care takers.

Sampling procedure

We used a three-stage sampling method. We randomly selected 5 parishes out of 8 using a table of random numbers from Agwata sub county. In the second stage, 3 villages were randomly selected using a table of random values from each of the 5 parishes. In the third stage, village mapping was done

with the help of the village health teams and the village Local Council chairpersons to identify households with children 6 months and below 5 years of age.

Data Collection procedure

We adapted a household survey questionnaire from prior malaria surveys conducted in Uganda including the National Malaria Indicator Survey (MIS) [21]. The questionnaire was administered to mothers/care takers of children to obtain information on age of the child, gender, ABO blood group system, number of children in a household, area of residence, presence of LLINs over the beds of children, condition of the LLINs, presence of stagnant water and wealth of households.

A household wealth index was generated using principal component analysis of data based on ownership of assets, household characteristics, and type of household construction materials; a single wealth index was calculated, categorized into terciles [22]. Houses were defined as 'modern' if they had cement or wood or metal walls, a tiled or metal roof, and closed eaves [23], while traditional were characterized by thatched roofs, mud walls and open eaves [24].

Laboratory analysis

We collected 4 mls of venous blood from each child using Ethylene Diamine Tetracetic Acid (EDTA) vacutainer. We picked 2mls of whole blood for microscopy and rapid malaria diagnostic test (RDT), while the rest was used to determine ABO group and the Rhesus factor (RhD). Slides were dried and kept in the field for not more than two days to avoid auto fixation and were periodically transported to Agwata HCIV laboratory in Dokolo District for processing and reading.

We prepared thick blood smears by spreading a drop of blood in a circular pattern until we obtained the size of a dime (diameter 1-2 cm). We stained the slides with 2% Giemsa for 30 minutes and read by experienced laboratory technologists. Parasites and densities were calculated from thick blood smears by counting the number of asexual parasites per 200 leukocytes, assuming a leukocyte count of 8000/µL. A thick blood smear was considered negative when the examination of 100 high power fields did not reveal asexual parasites. For quality control, all slides were read by a second experienced laboratory technologist and a third technologist settled discrepant readings with the parasite density differing by ≥25%.

We performed ABO grouping using monoclonal anti- serum using the tile method. A drop of antisera A, B, and Rhesus D was applied onto the differently divided columns of a clean white blood grouping tile and an equal amount (of approximately 20ul) of 20% washed red cell suspension was added using a micropipette, mixed well using clean applicator sticks. We rocked the tile for about 3 minutes at room temperature. Hemagglutination was observed to determine the blood group.

Data management and analysis

We entered the data into the EPI DATA version 3.02 (Epi-Data, Odense, Denmark) and exported it to STATA version 15.0 (StataCorp, College Station, Texas, USA) for analysis. The outcome variable was the prevalence of malaria among children between 6 months and 5 years which was dichotomised as "Positive or negative". Socio demographic characteristics were presented in the form of proportions. The association between malaria prevalence and risk factors was determined using normal logistic regression. Variables from bivariate analysis with p values ≤0.2 were considered for multivariable regression analysis. We built the model using a backward stepwise method until we remained with significant variables at p values of <0.05.

Results

Socio-demographic characteristics of children between 6months and 5 years and their mother/caretakers in Agwata subcounty, Dokolo district.

We recruited 408 children, 6 months and below 5 years; the majority 75% (306/408) were >1- 5 years. Almost half 53.4% (218/408) of the children were males.

More than a third of children (40% (155/408) were blood group A **(Table 1)**.

Table 1: Shows the sociodemographic characteristics of children between 6 months and 5 years in Agwata Subcounty, Dokolo district.

Variable	Frequency (408)	Percentages (%)
Age of the child		
<1	102	15
1-5	306	75
Gender of the child		
Male	218	53.4
Female	190	46.6
Blood group of the child		
O	119	29.2
B	102	25
AB	32	7.8
A	155	40
Number of children in household		
1-3	200	49
>3	208	51
Area of Residence		
Urban	199	48.8
Rural	209	51.2
Received LLIN in 2020		
Yes	217	53.2
No	191	46.8
Net hanged over child's bed		
Yes	231	56.6
No	177	43.4
Conditions of LLINs		
No holes	197	48.3
Had holes	211	51.7
Presence of stagnant water in compounds		
Yes	183	48.1
No	198	51.9
Household type		
Modern	249	61
Traditional	159	39

Prevalence of malaria

Out of the 408 children sampled, 120 tested positive for malaria infection giving a prevalence of 29.4% (95%CI: 24.7-33.8).

Malaria positivity rate in individual blood groups

Blood group A had the highest number of positivity rate of47.5%, followed by blood group O (25.4), blood group B (18.6), and lastly blood group AB (8.5) (Table 2).

Factors associated with malaria

In a multivariable analysis (Table 2), children with blood group A were 1.7 times more likely to suffer from malaria compared to those with blood group O (aOR= 1.7, 95% C.I: 1.1-2.7). Households with more than three children were 2.3 times more likely to be diagnosed with malaria compared to those with 1- 3 children (aOR= 2.6, 95% C.I: 1.8 -4.1). Children who were staying in rural areas were 5.7 times more likely to be diagnosed with malaria compared to children who were staying in urban (aOR=5.7, 95%CI: 3.5-8.6). Children whose nets were not hanged from their beds were 5.1 times more likely to be diagnosed with malaria compared to children whose nets were hanged over their beds (aOR=5.1, 95%CI:2.8-7.4); children who slept under LLINs with holes were 2.2 times more likely to be diagnosed with malaria compared to children sleeping under LLINs without holes (aOR=2.2, 95%CI: 1.5-4.1) and children from poor households were 4.2 times more likely to be diagnosed with malaria compared to children from modern households (aOR=4.2, 95% CI:3.4-8.6).

Table 1: Multivariable analysis showing the association between malaria and risk factors among children <5 years in Agwata subcounty, Dokolo District.

Risk factors	Malaria status		Crude OR (95%CI)	aOR (95%CI)
	Positive, n =120(%ge)	Negative, n=288 (%ge)		
Age of the child (years)				
<1	21(17.5)	81(28)	REF	
≥1-5	99(85.2)	207(72)	1.7(0.9-2.5)	
Gender of the Child				
Male	55(46.6)	163(56.1)	REF	
Female	65(53.4)	125(43.9)	1.5(1.0-2.3)	
Blood group of the Child				
O	30(25.4)	89(31)	REF	
B	22(18.6)	80(27.9)	0.8(0.4-1.5)	0.8(0.4-1.5)
AB	11(8.5)	21(7.3)	1.4(0.6-3.3)	1.6(0.7-3.9)
A	57(47.5)	99(33.8)	1.7(1.0-2.9)	1.7(1.1-2.7)
Number of children in household				
1-3	30(25)	170(55.5)	REF	REF
>3	90(75)	118(40.9)	2.1(1.6-4.5)	2.3(1.8 – 4.1)
Area of Residence				
Urban	19(15.1)	180(62.5)	REF	REF
Rural	101(84.9)	108(37.5)	78(6.1-9.6)	5.7(3.5-8.6)
Received LLIN in 2020				
Yes	58(47.9)	159(52.2)	REF	
No	62(52.1)	129(47.8)	1.3(0.9-1.8)	
Net hanged over the child's bed				
Yes	42(35)	189(66)	REF	REF
No	78(65)	99(34)	3.6(2.1-6.7)	5.1(2.8-7.4)
Condition of the LLIN				
No holes	46(38.3)	151(52.3)	REF	REF
Had holes	74(61.6)	137(47.7)	2.1(1.9-3.6)	2.2(1.5-4.1)
Presence of stagnant water in compound				
Yes	36(55.3)	147(51.1)	REF	
No	57(44.7)	141(48.8)	0.9(0.6-1.3)	
Household type				
Modern	41(34.2)	208(72.2)	REF	REF
Traditional	79(65.8)	80(27.8)	5.2(3.1-7.9)	4.2(3.4-8.6)

aOR: Adjusted odds ratio; CI: Confidence interval; LLIN: long-lasting insecticide-treated net.

Discussion

This community-based cross-sectional study determined the prevalence of malaria and associated factors among children below 5 years in Dokolo District. The study findings found that about one-third (29%) of the children in the community had malaria. Being of blood group A, being from households with >3 children, residing in rural areas of the district, having LLINs not hanged over children's beds, poor condition of the LLINs, and poor wealth index of the households were significantly associated with increased risk of malaria.

The study findings established a higher malaria prevalence compared to the two previous national malaria surveys conducted in the Uganda with 22% and 19% respectively [25,26]. The difference may be due to the coverage of these national survey studies that considered the whole country.

Malaria prevalence has remained high in Uganda for the last two decades, despite the various malaria intervention strategies put forth to control the disease. These interventions include integrated vector management approaches such Indoor Residual Spraying (IRS) in hyper endemic areas such as northern Uganda [27,28], mass distribution of LLINs [29], provision of Artemisinin-based combination therapy (ACT) for treating uncomplicated malaria and intermittent preventive treatment in pregnancy (IPTp) during pregnancy among others [30].

Further studies are needed to establish the uptake of intermittent preventive treatment of malaria in pregnancy (IPTp) through the use of evidence-based approaches. Secondary, to investigate the factors that influence providers in private public health facilities and their clients in the community to adhere to the recommended national malaria prevention and treatment guidelines that will guide the development of efficient engagement strategies and modalities for malaria patients in the public and private sector, and a robust evaluation of the impact, operational feasibility and cost effectiveness of intermittent preventive treatment of malaria in infants (IPTi) with sulphadoxine pyrimethamine (IPTi-SP) that will accelerate the adoption and scale-up of IPTi in infants.

The study findings also established that children with blood A were more likely to be diagnosed with malaria. Our findings are in agreement with studies conducted in Ethiopia, India [13,32] suggesting that individuals with blood group A are more susceptible to malaria infection than those with O group. Blood group 'AB' has also been reported to be associated with severity of malaria in Sri Lanka [33], Mali [34] and Ethiopian populations [35]. There are no reports implicating blood group 'B' with malaria infection [32]. Blood group 'A' in Uganda and Gambia [36], and 'B' group in Thailand and 'AB' group in Kenya [37] have been associated with increased rosetting phenomenon. Antigens of blood groups A and B play important roles in cytoadherence [38]. Due to the absence of A and B antigens on the surface of blood group O erythrocytes, cytoadherence, and hence rosetting and sequestration, it is reduced in individuals with blood group O [39]. It has been observed that blood group O individuals are less likely to suffer from malaria [35].

In agreement with other studies, households with more than three children were more likely to be diagnosed with malaria [35,40]. In contrast, a previous study done in Mozambique that showed no association between malaria infection and number of children per household [41]. By the end of 2020, Uganda had a total fertility rate of 4.8 births per woman with the dependence ratio of 92.3 [42]. In 2020/ 2021, the government of Uganda conducted a mass distribution of LLINS to all households where each household received a maximum of four LLINs. Households with more than three children were most likely to receive inadequate mosquito nets to cater for all family members. LLINs implementers should always consider the number of members in each household in the subsequent national LLINs distribution.

The study findings further revealed that children from traditional houses had a 4.2-fold increase of testing positive for malaria. This is in agreement with cross sectional studies conducted in Uganda [43], Tanzania [44] and a longitudinal study conducted in India [45].

Malaria is considered to be a disease of the poor [46]. Poor living conditions are often characterized by inadequate housing and overcrowding, which can increase the risk of malaria [43]. Dwellings that are poorly constructed, or made of readily available materials, might allow mosquitoes to enter more easily than well-constructed housing with screened windows, thus increasing vector contact [47]. Evidence also suggests that overcrowding might increase the risk of malaria, because mosquitoes are attracted by the higher concentration of carbon dioxide and other chemicals in crowded house [48]. Improving income levels and supporting the poorer rural community would be a great achievement in reducing malaria in Uganda. Further interdisciplinary research is needed to understand fully the complex pathways between poverty and malaria and to develop strategies for sustainable malaria control.

The findings from this study demonstrate that malaria infection among children <5 years is an important public health problem in the rural area of Agwata Subcounty, Dokolo district. LLIN use should therefore be optimal and surveillance of malaria at health facilities should be stepped up to closely monitor and safeguard the gains made in malaria control. Furthermore, the Ministry of Health and implementing partners should also consider developing malaria control programmes that target improvement of household livelihoods and behavioural change communication. For example, using community-based, peer-to-peer malaria education model.

Study limitation

This study had limitations. First, we did not establish Plasmodium species during laboratory diagnosis. Secondary, this study was limited to Agwata subcounty, Dokolo district, thus it may not be generalizable to other geographical settings in Uganda. However, due to the nature of this study being community-based, it was able to establish the scope and magnitude of malaria cases in the whole Agwata Subcounty.

Conclusion

Malaria was a major health challenge in children under the age of five in Agwata Sub-county, with nearly one-third of the children surveyed being infected. Blood group A, crowded households, poor housing conditions, and nonuse of LLINs were all associated with an increased risk of malaria. There is a need for routine screening of children for malaria infections and for enhancement of current malaria control interventions like the use of insecticide mosquito-treated nets. Given the high prevalence of malaria in this setting, seasonal malaria chemoprevention may be considered in these children under the age of five.

Declarations

Ethical consideration

Approval was sought from the Ethics review committee of Mbarara University of Science and Technology. Permission to carry out the research was also sought from District Health Officer, Dokolo district, In-charge health sub district, and In-charge Agwata health Centre III. We obtained written informed consent from the participants before participation in the study.

Mothers/ care takers consented on behalf of their children to withdraw blood from them. Participants were told that their participation was voluntary and that there would be no negative consequences if they refused to participate. During data collection, respondents were assigned unique identifiers instead of names to protect their confidentiality. Information was stored in password protected computers and was not shared with anyone outside the study team. We followed the guidelines of Helsinki and CIOMS-2002 (Council for International Organizations of Medical Sciences) regarding research on humans, avoiding any type of physical or moral harm. Children who tested positive for malaria were referred to nearby health facilities for treatment.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

EA, HD, MN, PMO, MT, EM, RK, EJN, RM and AB, contributed to study design, data collection, drafting of the Manuscript, data analysis, and interpretation of the findings. EA, HD, MN, PMO, AB, contributed to proposal writing, dissertation writing, and review of the manuscript. RK, EM, EJN, and RM contributed to review of the manuscript. All authors contributed to the write-up, and all read and approved the final manuscript.

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