

Malaria serosurvey among acute febrile patients come for health care seeking at the high malaria-endemic setting of North West Ethiopia

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Abstract

Objectives: This study aimed to assess malaria seroprevalence among acute febrile illness cases who come for health care seeking in the high malaria-endemic setting of North West Ethiopia.

Methods: Institutional-based descriptive serosurvey of malaria infections was employed among 18,386 febrile patients from September 2020 to August 2021. Data were entered using Epi Data version 4.2 and exported to STATA (SE) R-14 version statistical software for further analysis. Bi-variable and multivariable regression analyses were conducted to identify malaria infection. Finally, variables with P-value less than 0.05 were considered significant predictors for malaria infection.

Results: The mean (\pm standard deviation) age of participants was 48.6 (\pm 18.4) years. The overall seroprevalence of malaria infection was estimated as 27.8% (95% confidence interval=27.2; 28.6, standard error=0.003). Malaria infection was significantly associated with participants being female (adjusted odds ratio=2.9; 95% confidence interval= 1.8; 3.7, P=0.01), age 5–29 years (adjusted odds ratio=2.2; 95% confidence interval= 1.7; 2.8, P=0.02), rural (adjusted odds ratio=3.9; 95% confidence interval= 1.9; 4.4, P=0.001), and Hgb \leq 11 mg/dL (adjusted odds ratio=3.4; 95% confidence interval= 1.9; 5.86, P=0.01).

Conclusion: Nearly every three to ten acute febrile cases were positive for confirmed malaria infection. The risk of malaria infection was significantly associated with respondents being female, aged 5–29 years, rural, and levels of hemoglobin were significantly associated with malaria infection.

Keywords

Malaria, prevalence, population, Ethiopia

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Introduction

Malaria is one of the life-threatening diseases caused by five species of the protozoan parasite of the genus *Plasmodium* (*Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium Ovale*, and *Plasmodium knowlesi*) that is transmitted to humans through the bites of an infected female anopheles mosquito.^{1,2} An infected female Anopheles mosquito inoculates sporozoites into a human host. The uptake of sporozoites subsequently initiates sexual reproduction, which gives rise to the formation of gametocytes to be ingested by the mosquito.³

Globally, 3.3 (40%) billion populations were at risk of being infected with malaria and developing the disease, and more than 214 million developed new cases and 438,000 deaths were reported in 2015.⁴ Of which Africa accounted for

88%, South-East Asia (10%) and the Eastern Mediterranean region (2%),⁵ children under-five years constituted 95% (292,000 deaths) were from the African Region.⁶ In Sub-Saharan Africa (SSA) where about 125 million pregnancies are at risk of malaria each year, and up to 200,000 babies die as a result.⁷ Under-five children and pregnant women are the

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most vulnerable groups affected by malaria, they account for 62% of all malaria death worldwide.^{8,9} The WHO African Region continues to shoulder the heaviest burden of malaria. Globally in 2020, the region accounted for 95% (228 million) of all malaria cases; 96% (602,000) of all malaria deaths, among this 80% of all malaria deaths in the region are children under 5 years.¹⁰ In 2018, *P. falciparum* accounted for 99.7% of estimated malaria cases in the World Health Organization (WHO)¹¹ Africa regions, 50% in the WHO Southeast Asia regions, 71% in the eastern Mediterranean, and 65% in the Western Pacific. In Ethiopia, peak malaria transmission occurs between September and December in most parts following parts, following the rainy seasons from June to August, mainly affecting young children, and *P. falciparum* and *P. vivax* are the major malaria parasites.^{8,12} About 75% of the landmass of Ethiopia are malarious, and 60% of the population are at risk of developing the disease,^{4,5} which shed 6% of malaria cases globally, and about 12% of the global mortality.¹³ The country has made a significant effort to control malaria infection since the introduction of dichlorodiphenyltrichloroethane (DDT) as an insecticide upon which the country based its indoor residual spray (IRS) in 1957.¹³ However, multi-parasitism or concomitant antigen incidence in a single host creates a great challenge, specifically falciparum with schistoma, typhoid fever, and helminthiasis in elimination programs of malaria infections.^{14,15} This study aimed to estimate malaria serosurvey among acute febrile illness patients who come for health care seeking a high endemic setting of North West Ethiopia.

Methods

Study area, design, and setting

Benishangul-Gumuz is one of the eleven national regional states in Ethiopia with three administrative zones; Metekel, Kamshi, and Asosa zones are some of the district zones. Merkel zone is topographically located within 34° 10'N and 37° 40'E and latitude 09° 17'N and 12° 06'N and constituted by seven administrative district woreda with two primary and one-referral hospitals.^{16–22} According to the 2019 National Population Projection, this region has an estimated 1.3 million inhabitants, both urban and rural. This state has diverse topographic climates including familiar traditional zones of “kola,” “dega,” and “woman dega.”^{16–24} Pawe is one of the seven district woreda in Metekel Zone and more than 75% landmass malarious and is classified as “kola,” which is below 1500 m above sea level. This serosurvey was conducted in Pawe woreda; patients come for treatment at Felege Selam Health Center.

Study design and participant populations

A facility-based descriptive cross-sectional survey was conducted on 18,386 acute febrile patients coming for health care seeking health from 1 September 2020 to 30 August 2021.

Outcome ascertainment

The dependent variables were malaria in the serum (positive/negative) after blood film was done (thin/thick). The independent variables include case socio-demographic factors and household levels of malaria exposure status. The data were collected using both interviewing and structured questions and blood sample collection. Participants were asked about socio-demographic characteristics like insecticide-treated net (ITN) conditions and availability, ITN utilization and number, IRS, presence of stagnant water, outdoor stay at night, housing condition, and previous health information about malaria in the checklist.

Sample processing and investigation

After the completion of the interview, our phlebotomist collected 5–10 mL of blood from each participant via venipuncture, and then the blood specimen was kept in an extraction tube filled with extraction buffer (300 µL) after withdrawing from each participant, at room temperature (15–30°C) by well-trained technologist. The collected blood was used for malaria thin and thick blood smear diagnosis.^{5,25,26}

Inclusion and exclusion

We only included a patient who has complained of fever $\geq 37.5^\circ\text{C}$, and excluded clients with wound care and family planning.

Operational definition

Malaria. It was defined as a positive thin or thick blood film for one of the five Plasmodium parasites species.⁵

Anemia. According to WHO, anemia was classified for both adults and children with hemoglobin concentration < 11 g/dL.^{20,27}

Bed net utilization. There was self-reported ownership and regular use of bed nets. A 15-day recall period was used to measure whether each child regularly slept under long-lasting insecticide-treated nets (LLIN) or not.¹²

Data collection procedure

A structure questionnaire was used for data collection. The tool contained socio-demographic, environmental, and malaria prevention-related questions. The tool was first prepared in the English version and translated into their local language before the final data collection data. Face-to-face interview of parents/caregivers at the pediatrics outpatient department (OPD), pregnant at the maternal and child health care room (MCH), and adults at the adult OPD was undertaken. After the interview was completed, based on the national Federal Democratic Republic of Ethiopia Ministry

of Health (FMOH)^{5,28} National Malaria Guidelines, accordingly, 5–10 mL blood was taken from each participant via a three-degree laboratory technologist for thick and thin blood film smears. The blood smear was prepared on a microscopic slide and stained using 10% Giemsa to examine under a 100× microscope for the presence of malaria parasites. The thick blood smear was used to determine whether the malaria parasite was present or absent and a thin blood smear was used to identify the types of *Plasmodium* species. A positive result was defined as the presence of one or more asexual stages of plus medium species.⁵

Data quality assurance

A three-degree laboratory technician for data collection was recruited for a full year, and two to four public health officers have interviewed study participants at under-five case management room (U5OPD), antenatal care service giving room (MCH), emergency outpatient department (EOPD), and adult outpatient department (AOPD). The data were collected first by interviewing at every four services, giving room for structured interviews about their demographic characteristics, previous malaria exposure, and preventive measures. Data collection tool was prepared after reviewing relevant previously published articles^{8,12,29,30} with 5% the total sampled survey at Pawe General and Referral Hospitals and made an amendment. Finally, the result was reported by laboratory technology, both data collectors were trained for 2 days by the principal investigators. Each filed questionnaire was checked thoroughly for completeness and consistency, while the necessary feedback was given to the data collectors. The recruitment was preceded by obtaining informed written consent from all participants before data collection. The data collection tools were tested in 52 acute febrile illness cases in the nearby Pawe General Hospital.

Statistical analysis

The collected data were entered into Epi Data Version 4.2, and exported to STATA (SE) R-14 for analysis. The descriptive statistics are presented by narration and tabulation. A variable that had a P-value < 0.2 in the bivariable analysis was selected for candidate transfer for multivariable logistic regression analysis. A P-value < 0.05 was considered to determine significant variables for the risk of acquiring malaria infection.

Result

In this study, a total of 18,386 clients' blood was tested for malaria infection testing since September 2020 to August 2021. The mean (\pm standard deviation (SD)) age of the respondents was 41 (\pm 21.45) years with a minimum and maximum of 3 and 90 years, respectively. The largest proportion of participant cases were farmers 7465 (40.6%), and

of them, 6555 (35.65%) lived in rural dwellers. More than two in five of the 7634 (41.52%) respondents were in the age group 41–60 years following 573 (3.12%) of age >60 years. The majority of 9919 (53.95%) of the respondents' economic class was found at 21–99.9US\$ per month (Table 1).

Respondent clinical presentation

The majority of 14,305 (77.8%) of the respondents had impregnated bed net in their houses. Nearly half 8762 (47.66%) of the participants had a one-bed net in their house, followed by the smallest proportion of 2997 (16.30%) who had more than three. The largest proportion 14,024 (76.28%) were acute febrile illness treatment-seeking while 13.64% (N=2506) were from chronic follow-up, 6.69% (N=1230) antenatal care (ANC), and 3.4% (N=636) were from anti-retroviral therapy (ART) OPD, sexually transmitted disease (STI), and tuberculosis (TB) treatment sections. Of the total participants presenting for health care, 9894 (53.81%) had joint pain, 14,873 (80.89%) had a history of high-grade fever, and 11,363 (61.80%) had body fatigue.

Prevalence of malaria infection

In our serosurvey study, the prevalence of malaria infection was found at 27.8% (95% confidence interval (CI)=27.2; 28.6, standard error (SE)=0.003). Of the total cased respondents, about 2313 (12.58%) were infected by *P. falciparum*, with the following to 7.9% (N=145/18,386) were *P. vivax*. Whereas, the majority of 3356 (65%) and 2909 (56.8%) cases were female in gender and were from rural inhabitants. Ninety-five (N=17,517) percent of participants had LLINs. Whereas, only 2.06% (N=376) had three and above LLIN for \geq 5 family members in their house. In the same way, 39.5% (N=2219/5121) of confirmed malaria infection was predominantly distributed within \geq 5 family members. About 31.5% of confirmed malaria infections were covered by age \leq 20 years, while the smallest 89 (1.8%) proportions were \geq 61 age group (Table 2).

Factors associated with malaria infection

In this study, both bivariable and multivariable binary logistic regression analyses were done to identify factors associated with the risk of acquiring malaria infection. In a bivariable analysis, categorical variables with $P \leq 0.2$ and a total of (N=10) candidate variables (age, sex, residence, marital status, headache, not having LLIN, comorbidity, temperature $\geq 37.5^\circ\text{C}$, hemoglobin ≤ 11 mg/dL and number of LLIN households) had $P < 0.2$ and entered into multivariable logistic regression models. In the final model of multivariable logistic regression, five variables were retained their statistical significance at end of the adequate and final model. In the final adjusted model, respondents being female in gender had adjusted odds ratio (AOR)=2.9 (95% CI=1.8; 3.7, $P=0.01$)

Table 1. Socio-demographic characteristics of respondents of acute febrile patients during health care seeking at Felege Selam Health Center.

Variables	Categories	Numbers	Frequency
Sex	Male	8601	46.78
	Female	9785	53.22
Age	5–29 years	3997	21.74
	31–40 years	5937	32.29
	41–60 years	7875	42.83
	≥61 years	577	3.14
Marital status	Married	11,474	62.41
	Unmarried	6912	37.59
Number of families in a household	≤2	4795	26.08
	3–4	5501	29.92
	≥5	8090	44.00
Resident	Urban	5414	29.45
	Semi-urban	6417	34.90
	Rural	6555	35.65
Educational status	Illiterate	6649	6649
	Complete junior	6920	37.64
	Complete preparatory	2391	13.00
	Diploma and above	2426	13.19
Economic class per month	<20US\$	5150	28.01
	21–99.9US\$	9919	53.95
	>100US\$	3317	18.5
Occupational status	Farmer	7465	40.60
	Merchant	2073	11.27
	Student	5303	28.84
	Employed	3545	19.28
Long-lasting impregnated bed net	Yes	14,879	80.93
	No	3507	19.07
History of body fever	Yes	16,966	16,966
	No	1420	7.72
Headache	Yes	11,391	61.95
	No	6995	6995
Abdominal cramp	Yes	12,302	66.91
	No	6084	33.09
Joint pain	Yes	9770	53.14
	No	8616	46.86
Vomiting	Yes	6147	61.47
	No	7085	38.53
Presenting body temperature	≥38°C	14,873	80.89
	<38°C	3513	19.11
Generalized body fatigue	Yes	11,363	61.80
	No	7023	38.20
Hemoglobin	≤11 mg/dL	6145	33.45
	>11 mg/dL	12,228	66.55
Diarrhea during presenting	Yes	9716	52.84
	No	8670	47.16
Baseline comorbidity	Yes	576	576
	No	17,810	96.8

as compared with their counter groups, and had age 5–29 years (AOR=2.2; 95% CI=1.7; 2.8, P=0.02) as compared with age ≥61 years. Moreover, respondents from rural residents had 3.9 times more likely to acquire malaria infection

(AOR=3.9; 95% CI=1.9; 4.4, P=0.001) as compared with their respondents being from urban inhabitants. Whereas, respondents having Hgb ≤11 mg/dL during the serosurvey study had 3.4 more likely to develop malaria infections

Table 2. Malaria seroprevalence among selected socio-demographic variables for acute febrile illness cases during health care seeking Felege Selam Health Center, 2022.

Malaria test result		PF		PF + I		PF + 2		PF + 3		PF + 4		PF + PV		PV		Total
No. %	Category	2313	12.58	314	1.17	235	1.3	178	0.97	465	2.53	53	0.29	1453	7.9	5121
Sex	Male	808		114		104		77		143		32		436		1714
	Female	1505		200		131		101		322		21		1017		3297
Age	5–29	714		105		74		36		150		9		523		1611
	21–40	710		73		71		61		128		17		389		1449
	41–60	840		126		84		76		169		24		494		1813
	≥61	49		10		6		5		18		3		47		89
Resident	Urbane	1018		143		122		94		188		35		546		2146
	Rural	1295		171		113		84		277		18		907		2865
		Tested and positive for <i>P. falciparum</i> = 3505 (68.5%)														
		Tested and positive for both or mixed (PF + PV) = 53 (1.05%)														
		Tested and positive for <i>P. vivax</i> = 1453 (28.4%)														
Total		Tested and microscopically confirmed = 5121/18,386 (27.8%)														
		Tested and microscopically negative = 13,265/18,386 (72.2%)														

PF: *Plasmodium falciparum*; PV: *Plasmodium vivax*.

Table 3. Factors associated with malaria infection for acute febrile illness cases during health care seeking Felege Selam Health Center, September 2020 to August 2021.

Variables	Categories	Suspected and DX	Confirmed	COR	AOR	P-value
Sex	Male	8601	1765	1	1	
	Female	9785	3356	3.4 (2.9; 4.2)	2.9 (1.8; 3.7)	0.01*
Age	5–29	3997	1644	2.6 (1.8; 3.6)	2.2 (1.7; 2.8)	0.02*
	21–40	5937	1484	1.3 (1.34; 1.5)	1.14 (0.93; 1.4)	0.38
	41–60	7875	1852	1.97 (1.88; 2.5)	1.1 (0.86; 1.7)	0.39
	>61	577	141	1	1	
Marital status	Married	11,474	3500	1.4 (1.3; 1.5)	1.43 (0.94; 1.5)	0.12
	Unmarried	6912	1621	1	1	
Resident	Urbane	10,777	2212	1	1	
	Rural	7609	2909	3.7 (2.2; 4.6)	3.9 (1.9; 4.4)	0.01*
Body Temperature	≥37.5°C	14,873	4341	1.6 (1.32; 2.5)	1.4 (0.9; 3.9)	0.21
	<37.5°C	3513	780	1	1	
Hemoglobin	≤11 mg/dL	6145	1985	1.7 (1.49; 2.8)	3.4 (1.9; 5.8)	0.01*
	>11 mg/dL	12,228	3133	1	1	
Comorbidity	No	17,810	4849	1	1	
	Yes	576	272	1.7 (1.4; 3.9)	1.3 (0.94; 2.9)	0.39

COR: crude odds ratio; AOR: adjusted odds ratio.

*Chronic comorbidity = TB, HIV, asthmatics, diabetes, and renal disease.

(AOR=3.4; 95% CI=1.9; 5.86, P=0.01) as compared with their counter group who had >11 mg/dL (Table 3).

Discussion

The overall estimated seroprevalence of malaria infections among acute febrile illness was found to be 27.8% (95% CI=27.2; 28.6, SE=0.003). This result is lower than the finding reported at 36.5% in Demabia North West Ethiopia,²⁵ 36.8% in Southern Ethiopia,³¹ 46.5% in Halaba districts, Southern Ethiopia,⁴ Manukush district, North West Ethiopia 51.04%,³² and 37.6% Nigeria.²⁶ The variations in the report

might be due to the climatic change, and the laboratory capacity to detect the parasite load contributed to the differences. Conversely, our study result is higher than the findings in 11.79% in the Gedeo zone, southern Ethiopia.³³ The possible reason might be due to the differences in the study population, distribution of LLIN, and microclimatic/altitudinal differences. In addition, the relative higher malaria frequency reported might be associated with on-demand-concerted efforts toward the deployment of effective malaria prevention and control strategies in the study area. On the contrary, the positive rate of malaria infection with *P. falciparum* is higher than 3505 (68.5%), *P. vivax* 1453 (28.4%).

However, according to the federal ministry of health report of 2017, the relative frequency of *P. falciparum* and *P. vivax* was 60% and 40%, respectively.⁵ The observed variation is attributed to the difference in altitude expansion of development projects like Great Ethiopian Renaissance, damp community awareness about malaria transmission, prevention, and control measure employed in the study, and prevention practices have a higher impact on *P. falciparum* than *P. vivax*. In cases of *P. vivax*, the dormant stage of the parasite in the liver can be relapsed at any time and relatively maintain its prevalence in the community. However, dominance of malaria species is to be expected, *P. falciparum* is associated with higher parasite density and more serious clinical outcomes than *P. vivax*, and as such leads to the poor correlation of *P. vivax* prevalence in patients. In Ethiopia, *P. falciparum* and *P. vivax* account for 60% and 40% of malaria infections.^{9,25,34,35} Regarding the predictors for risk of malaria infection, unlike finding in Myanmar,³⁶ in this study, the proportions of malaria were higher in female gender 3356 than in male 1765 and had a statistically significant association ($\chi^2(1)=432.3290$; $P=0.001$). This is in line with our report being female in gender had 2.9 (AOR=2.9; 95% CI=1.8; 3.7, $P=0.01$) times more likely to develop malaria as compared with their counter group. This is also consistent with the findings in the Mankush Health Center in Northwest Ethiopia,³² and a higher proportion of females were treated as compared with males in the Gedeo zone, southern Ethiopia.^{4,9,25} Consistent with a previous finding in northwest Ethiopia in shekrole, wager a district^{25,37,38}. Ahmed et al.⁸ and Tsegaye et al.¹² and Democratic Republic of Congo.³⁹ In our study, there was a significant association between age and the risk of developing malaria infection with strong correlations ($\chi^2(3)=451.8$; $P=0.0001$). Equivalent to this, being aged 5–29 years were nearly two times the increased the likelihood hood to develop malaria infections (AOR=2.2; 95% CI=1.7; 2.8, $P=0.02$) as compared with age ≥ 61 years. This might be due to the low immune response against malaria infection and inappropriate use of bed nets and antimalarial drugs in the case of adolescents and under-five children. Furthermore, despite to intensify implementation of the malaria control and prevention program in Ethiopia,⁵ malaria accounted for 38% morbidity and 36% of overall mortality in 2018 for under-five children.^{11,13}

The odds of malaria infection were higher for respondents from rural residents and 3.9 times increased likelihood for hood to develop it compared to their counter group (AOR=3.9; 95% CI=1.9; 4.4, $P=0.001$). This narration is parallel to our report. The largest proportion of malaria infection rate was high in our study compared to urban dwellers, that is, 2909 (56.8%) versus 2212 (43.4%), respectively. This might be because people living in urban dwellers might have good knowledge and prevention practices of malaria, especially the utilization of LLIN as compared to rural dwellers.^{9,40} In line with previous findings,³

the proportion of malaria gametocyte positive rate for all malaria species had significant disruption with the level of hemoglobin. However, *P. falciparum* gametocytes were more common in patients presenting black water fever, rupture of red blood cells, and linked with severe anemia.^{13,25,41} Consistent with this report, respondents present in cing with Hgb ≤ 11 mg/dL during the serosurvey had a 3.4 times increased likely hood of developing malaria infection (AOR=3.4; 95% CI=1.9; 5.86, $P=0.01$) as compared with their peers who do have Hgb >11 mg/dL. This is enhanced by reported on a systematic review.⁴² In some instants, the overlap/co-infection rate of typhoid fever with malaria parasites is recognized to be responsible for a significant decrement in blood hemoglobin levels in a given population including children.³

Limitations of this research

There are several limitations to this research, first, we did not use a power approach for sample size estimation, coupled with the performance of the test depending on a one-time test for each acute febrile case, since malaria, life cycles have three-stage (i.e. febrile stage, cold stage, sweating stage) to confirm diagnosis and the study was only on febrile patients.

Conclusion

Nearly every three to ten acute febrile cases were positive for confirmed malaria infection. The risk of malaria infection was significantly associated with respondents being female, aged 5–29 years, rural, and levels of hemoglobin were significantly associated with malaria infection.

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Author contributions

F.K. and T.K. conceived the study, supervised the data collection, and did the analysis, and wrote the manuscript. The authors commented, edited the draft, and approved the final version of this manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

All methods were performed following the relevant guidelines and regulations. The study was conducted following the principles of the Helsinki declaration. The Ethical Review Board of Pawe Woreda Health Bureau ethically cleared this research to conduct

with protocol number (reference no. PHB-119/2014). In addition, an official letter was submitted to Felege Selam Health Center requesting permission for the data extractions with meeting no. 012/2014.

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Informed consent

Written informed consent was taken from the participants and legally authorized representatives of minor participants before the study initiation.

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Supplemental material

Supplemental material for this article is available online.

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