Malaria Outbreak –in Hitsats Refugee Camp, Tigray Region, Ethiopia- 2017, A Case-Control Study

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Research

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Abstract

Background: Over 80% of current refugee camps worldwide are located in malaria-endemic areas and malaria accounts for up to 50% of all deaths among refugees. In 2016, 3,152 malaria cases were reported from Hitsats Refugee Camp located in northern Ethiopia. A malaria outbreak was reported from Hitsats Refugee Camp (Population=8498) on June 19th, 2017. We investigated to describe the epidemiology, identify risk factors, and implement control measures.

Methods: We defined a malaria case as any person a resident of Hitsats Refugee camp with fever or fever with headache, rigor, back pain, chills, sweats, myalgia, nausea, and vomiting, or confirmed microscopically or by Rapid Diagnostic Test to have malaria parasites from June 6th to July 3rd, 2017. We identified cases by reviewing the refugee clinic records and conducted a 1:1 case-control study from July 3rd to 14th, 2017. Cases were selected randomly using the patient registration book and recruited neighborhood controls who have no signs and symptoms of malaria and tested negative for Plasmodium species during the outbreak period from the same camp. We collected socio-demographic, behavioral, and risk factor information using a pre-tested structured questionnaire. Data were entered and analyzed using Epi-Info version 7.2.2. Multivariable logistic regression analysis was conducted to identify independent factors associated with malaria infection.

Result: We identified 4,911 malaria cases with no death. Of those cases, 3,290 (67%) were males, and 4,322 (88%) were aged ≥ 5 years. The overall attack rate (AR) was 58% (4911/8498) and was highest among < 5 years (84%) and was 55% among people ≥ 5 years. Seventy-eight malaria cases and 78 controls were interviewed. The presence of patient/s with similar signs and symptoms at home (Adjusted Odds Ratio (AOR) =3.5, 95% Confidence Interval (CI) =1.6-7.8) was an independent risk factor associated with malaria. Owning insecticide-treated mosquito nets (ITNs) (AOR=0.17; 95%CI=0.07-0.4) and using personal protective equipment (PPE) to prevent mosquito bites when staying outdoors (AOR=0.18; 95%CI=0.08-0.4) were disease protective factors.

Conclusion: The presence of patient/s with similar signs and symptoms at home, lack of ITN ownership and not using PPE were variables associated with malaria infection. Prevention strategies that target ITN distribution and the use of PPE to prevent mosquito bites may mitigate and prevent further outbreaks of malaria in refugee camps.

Background

Malaria remains a leading cause of morbidity and mortality among refugees. Globally More than 80% of current refugee camps are found in malaria-endemic areas and malaria accounts for up to 50% of all deaths and 16% of deaths among children(1, 2).

Malaria remains a significant threat to the health of refugee populations, particularly in sub-Saharan Africa. The average annual malaria incidence rate is 95 cases per 1,000 persons among all refugees, with

the highest in camps in Tanzania. Whereas the annual malaria mortality rate is 3.6 deaths per 1,000 refugees, with the highest in Sudan and Thailand, and with the lowest in Ethiopian camps(3).

Ethiopia is hosting the largest number of refugees in Africa, with 635,956 refugees registered as of 31 August 2014. The refugees in the country are primarily South Sudanese, Somali, Eritrean, Sudanese and from several other countries, including Kenya, Djibouti, Democratic Republic of Congo, Yemen, Burundi, Rwandan, and Ugandan. Until 2016, Ethiopia is hosting 71,833 Eritrean refugees in four camps of north-western Tigray, namely, Shimelba, Mai-Aini, Adi Harush, and Hitsats with as many as 1,000 Eritrean refugees arriving each month. The government has set up a temporary and permanent medical clinic and reception facilities for arriving refugees. United Nations Higher Commission for Refugee (UNHCR) opens Hitsats Camp that can eventually house up to 20,000 Eritrean refugees in northern Ethiopia, in June 2013. Hitsats refugee camp is one of the malaria-endemic areas in the region where, malaria is the leading cause of morbidity throughout the year(4, 5).

Migration from regions of low to high malaria endemicity heightens malaria risk in susceptible refugee populations. Many factors may promote susceptibility to malaria morbidity and mortality among refugees. Pregnant women and young children are particularly at risk of severe illness and death. Malaria outbreak generally occurs when the population in an area has weak immunity to the disease because so many people in the population will be vulnerable to malaria. There could be epidemics in high transmission areas as well if there is a deterioration of the health system, interruption of anti-malarial measures, or migration of non-immune individuals, such as population movement in local conflict or war areas (6, 7).

Despite the long-term presence of refugee settlements, there is little information on malaria in the camps, patterns of transmission, or the effectiveness of malaria control(8).

Ethiopia developed national malaria elimination strategic plan, to eliminate malaria in selected low transmission areas by 2020, but there is no strategy developed on how to control and eliminate malaria in refugee settings (9).

During the WHO malaria Week 23 (June 19, 2017), a malaria outbreak was reported from the Hitsats refugee camp of Asgede Tsimbla district health office. After discussion with the district health office, a multidisciplinary team of investigators deployed on July 03, 2017, to verify the Outbreak and to determine factors associated with the outbreak, to conduct an epidemiological and entomological survey, and to implement control measures to overcome the current outbreak and prevent the occurrence of outbreaks in the future.

Methods

Study design and area

We conducted a 1:1 case-control study in the Hitsats refugee camp, found in the Asgede Tsimbla district of the Tigray region, Ethiopia from July 3rd to September 21, 2017 (Fig. 1). In July 2017, the population of the refugee camp was about 8498, and 5269(62%) of them were males. Eight percent (n = 680) of the total refugees are children under five years. There are about 1,333 households in the camp living in one-room four to twelve persons. The annual temperature of the camp ranges between 29°C and 39°C with an annual rainfall of about 500–900 mm. The altitude of the camp is 700–1900 meters above sea level with the climatic condition of lowland (*kola*) which is a malaria-endemic area. There is one health center working for outpatient and one separate inpatient clinic held by the Administration for Refugee and Returnee Affairs (ARRA) and medicine sans frontiers (MSF) respectively. There are nine non-governmental organizations (UNHCR, IRC, IOM, NRC, DRC, NRDP, and MSF), provide the most basic services including food, shelter, basic medical care, water and sanitation, and mental health. AARA takes the responsibility of monitoring and evolution for those international partners (4, 5, 10, 11)

Even though the camp is one of the malaria-endemic areas of the district, Insecticide-treated Bed Nets (ITNs) have not been distributed and Indoor Residual Spray (IRS) had also not applied one year before the occurrence of the outbreak. There was no weekly malaria surveillance report to the Public Health Emergency Management (PHEM) focal person of the district from the refugee(10, 11).

Descriptive Epidemiology

We defined a malaria case as any person a resident of Hitsats Refugee camp with fever or fever with headache, rigor, back pain, chills, sweats, myalgia, nausea, and vomiting, or confirmed microscopically or by Rapid Diagnostic Test to have malaria parasites from June 6th to July 3rd, 2017. We reviewed the previous one year's (2016) weekly report of malaria cases and doubled each week's data to set the outbreak threshold level, and then we have compared with a similar week of this year (2017) to verify the existence of the outbreak.

We identified cases from the registration book and line list records of the refugee camp clinic and conducted a house-to-house survey to search for more cases and refer to the refugee clinic for further diagnosis and treatment.

Laboratory Investigation

Blood samples were collected from malaria suspected patients and examined microscopically for the presence of blood parasites or using the malaria Rapid Diagnostic Test (RDT) for the presence of *Plasmodium* species.

Case-control study

From June 6 to July 3, 2017, we conducted a case-control study with a 1:1 ratio of cases to controls. The sample size for the case-control study was estimated using the Stat-calc function of the Epi Info software (version 7.2.1.0) by considering the following assumptions of the level of significance of 5%, power 85%,

1:1 case to control ratio, and presence of breeding site among cases of 70%, and OR to be four, from a previous study (12). The final estimated sample size was 156 (78 cases and 78 controls).

We recruited a microscopically or RDT confirmed malaria cases and controls were non-febrile patients and those who did not tested positive for malaria, during the same period living in the community where the cases were recruited. Cases were selected randomly from the laboratory registration book; we went to their room with help of a health-supporting worker. We go to the next room if either the case or control were not available or fulfill the criteria. Controls who had symptoms suggestive of malaria infection were excluded.

We have developed a structured questionnaire that comprises socio-demographic, clinical history, potential risk factors, environmental and knowledge assessment of participants on malaria to identify factors associated with the outbreak. Similarly, environmental observation of the potential mosquito breeding sites has been done. The questionnaire was developed in English and translated to the local language *Tigrigna* and translated back to English for analysis purposes. Investigator administered a face-to-face interview was conducted in the same way for all participants.

The questionnaire was pretested in 5% of participants who were not part of our study. Data collectors trained for one day on how to select cases and controls and how to administer the questionnaire and how to maintain the confidentiality of data. At the end of each day, the principal investigator checked for consistency and completeness of the filled questionnaire and if the questionnaire was incomplete we go back to fill the incomplete questionnaire.

Study Variables

Dependent variable: Malaria infection status

Independent Variables: Socio-demographic variables (Age, Sex, educational status, number of a person living in one room), staying outdoor before sleeping, presence of stagnant water, sleeping under ITNs, presence of malaria patient in the same house, using personal protective equipment, knowledge status, previous history of malaria.

Bivariate and multivariate logistic regression analysis performed using Epi info software (version 7.2.1.0) after coded, cleaned, and entered. Odds ratios (OR) adjusted using the mantel-haenszel chi-square procedure were estimated and used as a measure of association between potential risk factors and malaria. Variables from the bivariate analysis that were significant at the $p\text{-value} \leq 0.25$ have been considered in the multivariate analysis to control the effects of confounders. Two-tailed probability values less than 0.05 considered statistically significant.

Operational Definitions

Good Knowledge: When one answers correctly above or equals the mean of the questions asked, on malaria signs and symptoms, transmission, and prevention method.

Poor Knowledge: When one answers correctly below to the mean of the questions asked, on malaria sign and symptoms, transmission and prevention method

Results

Descriptive Epidemiology

Malaria outbreak that lasts for six weeks duration, verified on July 05, 2017 (Figure:2), in Hitsats refugee camp with 4911 cases and no death. Of cases, 3292 (67%) were males and 4336 (88%) were aged $\geq$ 5 years. The overall attack rate was 57.7%, with 0.36% (n = 34) admission rate and without any death. The age group under 5 years was the most affected group with an AR of 84.5%. Males are more affected than females with an AR of 62.5% and 50% respectively. ITNs were not distributed and the IRS was not applied one year before the outbreak.

Laboratory result

Of the total 4911 cases treated for malaria, 4776 (97.2%) were confirmed cases while 135(2.8%) were treated clinically. of the confirmed cases, 1965 (41%) constituted Plasmodium Vivax (PV), 1937(40%) were infected with Plasmodium Falciparum (PF) and 874(18.3%) were mixed (both PV and PF) infections.

Case-Control study

We have interviewed 78 malaria case-patients and 78 controls. Fifty-one (65.4%) of the malaria case-patients and 36(46.2%) of the controls were males. The mean age of cases was 18 (SD, 9.5), ranged 1–54 years, while the mean age of controls was 24.5(SD, 9.3), ranged 3–52 years. From the total malaria cases enrolled under the case-control study, 36(46.2%) of the cases were PV and 22 (28%) were mixed infections; all the cases were treated with Coartem. The majority of cases 36 (47.2%) arrived at the clinic 24 hours before the symptom started, and 22(28.2%) arrived 24–48 hours, while the rest arrived after 48 hours. The entire households were found within one kilometer of the intermittent rivers.

In a bivariate analysis result, the presence of a patient with similar sign symptom in the same room, stay outdoor before going to sleep, having a bed net, using a protecting method to prevent mosquito bite, the previous history of malaria in the last two months showed a significant association at p-value $\leq$ 0.25(Table 1)

Table 1
Bi-Variate analysis, factors of malaria outbreak, Hitsats refugee, Tigray, 2017.

S.No	Variables		Case	Control	Crude OR (95% CI)	P-Value
1	Presence of a patient with similar sign symptom in the same room	Yes	53	22	5.3(2.7–10.7)	0.00011
		No	25	56		
2	Stay outdoor before going to sleep	Yes	51	38	1.9 (1.0–3.7)	0.05
		No	27	40		
3	Having bed net	Yes	26	60	0.1(0.07–0.3)	0.0000001
		No	52	18		
4	Knowledge status on sign and symptoms, transmission and prevention method	Yes	53	56	0.8 (0.4–1.6)	0.727
		No	25	22		
5	Using a protecting method to prevent mosquito bite	Yes	19	48	0.2 (0.1–0.4)	0.000005
		No	59	30		
6	Previous history of malaria in the last two months	Yes	46	29	2.4 (1.27–4.6)	0.010
		No	32	49		
7	Presence of breeding site near HHs	Yes	63	64	0.98 (0.4–2)	1.0
		No	15	14		

After conducted multivariable analysis, the presence of a patient with similar signs and symptoms in the same room, having a bed net, using a personal protective method to prevent mosquito bite were variables significantly associated with contracting the disease (Table 2).

Table 2
Multi-Variate analysis result of malaria outbreak, Hitsats refugee, Tigray, Ethiopia, 2017.

Variables	Case N (%)	Control N (%)	COR(95%CI)	P-Value	AOR (95%CI)
Presence of a patient with similar sign symptom in the same room					
Yes	53(67.9%)	22(28.2%)	5.3(2.7–10.7)	0.0001	3.49(1.55–7.8)
No	25 (32.1%)	56 (71.8%)	Ref		Ref
Stay outdoor before going to sleep					
Yes	51(65.4%)	38 (48.7%)	1.9 (1.0–3.7)	0.05	
No	27 (34.6%)	40 (51.3%)	Ref		
Having bed net					
Yes	26(33.3%)	60(76.9%)	0.1(0.07–0.3)	< 0.0001	0.17(0.07–0.41)
No	52(66.7%)	18(23.1%)	Ref		Ref
Knowledge status on Malaria					
Yes	53(67.9%)	56(71.8%)	0.8 (0.4–1.6)	0.7	
No	25(32.1%)	22(28.2%)	Ref		
Using personal protecting Equipment to prevent mosquito bite					
Yes	19(24.4%)	(71.8%)	0.2 (0.1–0.4)	< 0.0001	
No	59(73.6%)	(28.2%)	Ref		
Previous history of malaria infection in the last two months					
Yes	46(59%)	29(31.2%)	2.4 (1.27–4.6)	0.01	
No	32(41%)	49 (68.8%)	Ref		

Variables	Case N (%)	Control N (%)	COR(95%CI)	P-Value	AOR (95%CI)
Presence of breeding sites near HHs					
Yes	63(80.8%)	64(82%)	0.98 (0.4-2)	1.0	
No	15(19.2%)	14(18%)	Ref		

Environmental assessment

There was no rainfall for three weeks in the refugee, following heavy rainfall on June 12, 2017. Three intermittent rivers were crossing the refugee, multiple breeding sites, and one big opened waste disposal site on the center of the Households found. Adult Mosquitos and larvae observed by the naked eye in the stagnant waters (Figure:3)

Public health interventions

Cases were managed by distributing anti-malaria treatments oral rehydrating Salt, and antipyretics. Presumptive mass fever treatments have been done for 207 refugees with Coartem for two days after the RDT shortage has been faced on these days.

We delivered an intensive health education campaign with community leaders and health professionals at the refugee camp and mobilized the community for sanitation campaigns such as drainage of stagnant waters and taught on prevention and control measures of malaria. We provided training on malaria monitoring chart to the surveillance focal person and director of the health center on how to detect future outbreaks early.

In collaboration with the Federal Ministry of Health and ARRA, ITNs was distributed and IRS has applied to households of the refugee camp using bendocarin chemical, for three consecutive days, Motor oil sprayed for about one hectare of malaria breeding sites with mosquito larvae Health professionals have mobilized and assigned to the highly affected blocks for active case search and early case management at the refugee and health facility level

Discussions

We have detected a malaria outbreak that ends with higher AR without death. Intermittent rivers crossing the refugee, presence of stagnant waters, delayed IRS application, and distribution of LLINs before the outbreak were some of the main factors that contributed to the outbreak.

The outbreak ends with an AR of 577 cases per 1000 refugees, which is so far higher compared to the outbreak investigation at Kakuma refugee camp Kenya which was 50 cases per 1000 refugees, and

Uganda refugee camp 215 cases per 1000 refugees(13, 14). Highest AR in Hitsats camp than the other refugees might due to the late identification of the outbreak and low preparedness and responses to the outbreak than the others.

Children less than five years are an at-risk age group, with an AR of 84.5%. This is similar to outbreaks investigated at Kakuma refugee camp Kenya, which showed that AR is higher in children less than five years old with AR of 30 per 1000 children(13). This might be due to the reason that in malaria-endemic areas; children are more susceptible to malaria infection than above five years old because the latest group may develop partial immunity due to repeated infections(15).

AR was higher among males than females. This is similar to the outbreak conducted in Ameya district, Ethiopia showed AR among males were 48% while among females 35%(16). This difference might be, in the refugee, females have given priority in getting the ITN especially if they are pregnant or have a child. In addition to that, males engaged more in outdoor activities, exposed them to mosquito biting.

The majority of the cases were diagnosed to have PV, this is higher to the Eritrean and Tigray region PV proportion which is 25% and 40% respectively(16, 17). The reason for the high proportion of PV in the refugee might be, because of that PV treated with Coartem rather than treated with the first drug of choice that is chloroquine (15). This might lead patients to show partial progress from PV so that comes again to the health center.

Using ITN was an independent protective factor for malaria, with lower odds of malaria. Using ITN as a way of preventing infection with malaria has shown to be effective in several studies. Malaria outbreak investigated, in Ameya district of the Oromia region and Erer district, Ethiopia Somalia region found having ITNs was associated with lower odds of malaria infection(16, 18).

Using a personal protective method when staying outdoors before dawn or after dusk was found to be independent protective factors against malaria, this is in line with Outbreak in Zimbabwe; Mutasa district showed there was eight times risk of getting malaria infection in those that were not using the protective method. Biting density peaked early in the night when people no more protected (relaxed) by the primary indoor intervention measures(19).

The presence of a patient with similar sign symptoms in the same room was an independent risk factor associated with malaria contraction, this is consistent with Malaria Outbreak Investigated in Erer Woreda, Ethiopian Somali Region, and outbreak in Asgede Tsimbla found. This might be due to that when overcrowded condition increases the bite frequency of infected mosquito.

There was no rainfall in the refugee for two weeks, following heavy rainfall on June 12, 2017. That makes it suitable for an intermittent river and many stagnant glasses of water in the refugee, which in turn creates a favorable condition for mosquito breeding so that unusually heavy rainfall followed by high temperature might consider as one of the contributed factors for the outbreaks.

A big open waste disposal site at the center of the refugee delayed IRS application and distribution of LLINs could be among the other factor contributing to the outbreak. In the refugee, there were no last five years of data, compiled weekly malaria report, malaria line list, and a malaria-monitoring chart made to monitor the progress easily.

Conclusion

The outbreak in the refugee ends without death with high AR. AR was higher among males and in children less than five years old. Heavy rainfall two weeks before the outbreak made a favorable condition for malaria breeding, no distribution of LLINS, no IRS applied, and low vector control measures were all together responsible for the outbreak. The outbreak controlled, after optimal malaria control interventions have been done, included IRS applied, LLINs distributed, and proper environmental management is done. Having a bed net, using a personal protective method, and the Presence of malaria sick patients in a Household were independent factors associated with contracting malaria Therefore we recommend regular implementation of malaria prevention and control methods like conducting Indoor Residual spray, distribution of ITNs, and Special attention may be needed for the newcomers from high lands in the prevention of malaria; health education, repellants utilization and to have early treatment. Malaria cases. outbreak early. ARRA health office with other concerned bodies should continue the distribution of ITNs and introducing mosquito repellents to those newcomer refugees. And the district health office should have to target the refugee in the regular IRS schedule. Special attention may be needed for the newcomers from high lands in the prevention of malaria; health education, repellants utilization and to have early treatment

Abbreviations

ARRA-Administration for Refugee and Returnee Affairs, AR- Attack Rate, HH- House Hold, AOR- Adjusted Odds Ratio, COR-Crude Odds Ratio, IRS- Indoor Residual Spray, ITNs- Insecticide-treated Nets, LLTNs: Long-lasting insecticide-treated nets, PPE- Personal Protective Equipment, RDT- Rapid Diagnostic Test,

Declarations

Ethical approval and consent to participant

We obtained: support letter from Tigray Regional Health Bureau and ARRA to investigate the outbreak and written consent and assent from study participants/caregivers. The activity was not considered human subjects' research since the intent was for epidemic disease control.

Consent for publication

Not applicable

Availability of data and materials

Data will be availed on request

Competing interest

The authors declared that they have no competing interests.

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There was no fund

Author contribution

The conception of the study, questionnaire preparation, data collection, analysis, interpretation of data, and preparation of the manuscript was done by MG; mentoring during the outbreak investigation, data collection, analysis, a writeup of the manuscript was conducted by SA supervision, preparation the manuscript by KT; data collection supervision and revision of the manuscript by GK, guided on the methodological preference and study design, analysis, interpretation and revision of the manuscript was done by AA. All authors read and approved the final manuscript. (MG- MekonenGebremicael(hopemerry2013@gmail.com), SA-Samuel Aregay(samuelaregai@gmail.com) KT- KissanetTsfay(tesfaykissanet@gmail.com), GK- Getahun Kebede (nunugetahun12@gmail.com), AA- Alefech Addisu(elfaddisu@gmail.com)

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Figures

Figure 1

Map of Hitsats Refugee camp found in Asgede Tsimbila District of the Tigray region, Ethiopia, 2017 Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

Figure 2

Trends of Malaria cases crossing thresholds in Hitsats refugee camp, Tigray, Ethiopia, 2017

Figure 3

Photo of mosquito breeding site in the Hitsats refugee, northern Ethiopia, 2017