Malaria Elimination in Unguja Island Zanzibar: Individual Risk Factors for Continued Transmission.

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Abstract

Introduction: To achieve malaria elimination, understanding of the individual risk factors for malaria infection is critical to inform strategic planning and implementation. To address this, a community-based individual risk-factor study was conducted in Unguja Island Zanzibar.

Methods: A matched case control study with a sample size of 103 cases and 309 controls was conducted in Unguja Island. Malaria cases from health facilities were reported via Unstructured Supplementary Service Data (USSD) mobile phones to a central database, after which an SMS alert was sent to the District Malaria Surveillance Officer's (DMSO) mobile phone. DMSO followed up index cases up to household level and performed malaria test on all household members using rapid diagnostic tests (mRDT). Family members tested negative were considered as controls. Both cases and controls were interviewed with the same questionnaire. Data were analyzed using Epi-info version 3.5.1 using conditional logistic regression model.

Results: The findings revealed that chance of malaria infection was higher among individuals who travelled outside Zanzibar [AOR = 60.47, 95% CI 15.73 - 232.44], who spend their time in outdoor activities during the night [AOR = 8.53, 95% CI 1.96 - 37.11], whose rooms were not sprayed with indoor residual spray (IRS) [AOR= 29.60, 95% CI 2.68 - 326.49] and those who did not have a bed net [AOR=16.25, 95% CI 3.32 - 79.50].

Conclusion: Travel outside Zanzibar, outdoors activities during the night, lack of access to malaria interventions (IRS or bed nets) were the risk factors for malaria infection in Unguja. Ministry of Health should set a mechanism of encouraging people who travel to malaria endemic areas to attend the nearby health facility for malaria screening. Sensitizing people on using protective gear during the night and ensuring good coverage of malaria interventions would reduce the risk of malaria in Unguja Zanzibar.

1.0 Background

Globally, malaria remains to be among major public health problems. In 2015, there were the number of 214 million estimated malaria cases to be and 438,000 deaths worldwide (WHO Malaria report 2016). About 3.2 billion people almost — half of the world's population — are at risk of malaria (1). In Tanzania mainland malaria prevalence varies by region from <1% in the highlands of Arusha to 26% along the Lake Victoria shores (2). In Zanzibar, the malaria level in the population has declined from greater than 10% in 2005 to less than 2% in 2010, whereas the incidence of new malaria episodes has reduced from 16/1000 to 2/1000 in children under five years and from 4/1000 to 2/1000 in above five years of age (3).

Despite reduction of malaria cases following effective intervention measures, like indoor residual spray, long lasting insecticide treated net, using malaria rapid diagnostic test and using Artemisinin based combination therapy as first drug for malaria treatment in Zanzibar, malaria cases are still found sporadically with few focal transmissions. Surveillance records show that infections arising from the identified index cases affect only few individuals among contact family members. From 2012 to 2016 approximately 5% of contact family members tested positive each year (reference needed). However, risk factors for malaria infections remain largely unexplored.

Previous research has identified various known individual risk factors for malaria transmission such as age, sex, travel to malaria endemic areas, visitors from malaria endemic areas, bed net use, outdoor/indoor activities, late

hour's activities, low malaria knowledge, sleeping on the floor, cattle settlement nearby sleeping quarters, and rooms with incomplete walls(4). Residential structures not sprayed with indoor residual spray (IRS) have also shown to increase risk for malaria infection. Understanding the malaria risk factors in the local context is crucial to compliment the efforts to formulate a successful nationwide malaria-elimination strategy to further reduce and ultimately eliminate malaria in Zanzibar.

This study aimed to identify the individual risk factors that will assist in developing evidence-based nationwide malaria elimination strategy by Zanzibar Malaria Elimination Program (ZAMEP).

2.0 Methods

2.1 Study area

Zanzibar is a semi-autonomous territory of Tanzania and has its own president and parliament. It has its own government ministries, including the Ministry of Health under which Zanzibar's malaria elimination efforts are based. Zanzibar is primarily comprised of the islands of Unguja and Pemba. Unguja lies 35 km off the coast of mainland Tanzania and is 85 km long by 30 km wide with an area of 1,666 km^2. Unguja island has a population of 896,721.

Zanzibar has an equatorial climate, characterized by year-round high temperatures and humidity. There are two rainy seasons: the long rains last from March to June and the short rains fall from October to December. Malaria rates peak at the end of each rainy season, with the highest number of cases identified between May and July(5). There were 154 public and 42 private facilities where malaria cases are diagnosed and reported to the system.

2.2 Study design

A matched case-control study with a ratio of 1:3 was conducted in Unguja from February through May 2017. Cases and controls were matched on household.

A case: Any individual currently living in the study area who tested positive by mRDT or microscopy with or without signs and symptoms of malaria, and with no history of malaria within the last two months.

A control: Any household member currently living with index case who tested negative by mRDT.

2.3 Study population and sample size

Study population included all people living in the study area from February to May 2017. Only households with minimum number of controls (three negatives) who are >15 years of age and able to consent and respond to questions (physically and mentally) were included in the study.

Sample size was calculated based statsDirect 3 software for matched case control. Correlation = 0.2, probability of exposure in controls = 0.48 hence net utilization for those who are malaria negative were approximately to

48% according to Zanzibar surveillance data, odds ratio = 2, controls per case subject = 3, alpha = 0.05 and power = 0.8. Estimated minimum cases required were 103 and minimum sample size was 412. All districts in Unguja Island were considered for this study. At household level simple random sampling was applied when there were more than three controls. Probability proportion for each district was calculated based on previous year data (February – May, 2016) to estimate number of cases to be included from each district. The data collection tool was pretested in cases reported in previous month (January). Thereafter the tools were revised to improve clarity before execution of the study.

2.4 Data collection process

Structured questionnaire and observation checklist were used to collect information. Research assistants were surveillance officers who are experienced with routine malaria surveillance system. They were oriented for a single day on how to use the questionnaires and observation checklist.

The questionnaires were developed in English first and then translated to Swahili language which is a National language spoken by the study population. The study participants were informed about the importance of the study before being interviewed.

The study relied on routine surveillance system in Zanzibar. Malaria case-based surveillance system is also known as malaria case notification. When a malaria case was reported at a health facility and notified through mobile phone, District Malaria surveillance officers (DMSOs) /research assistants got a message informing them that there was a case reported from a certain health facility. After receiving a message, the research assistant first went to the health facility that reported the case. He/ she obtained the necessary information including patient's phone number, street/ village and the name of ten cell leaders which facilitated the tracking of the case's house.

At household level, all family members were tested for malaria by using mRDT test and given antimalarial as per Zanzibar malaria guideline for positive family members. Then the interview was conducted to those households meet inclusion criteria. Research assistants interviewed both cases and controls using the same questionnaire. Observations checklists were used to document the presence and utilization of net, quality of the net, conditions of the room, sleeping place and whether the sleeping room was in close proximity with domestic animals settlement.

Malaria rapid diagnostic test used in the study was SD Bioline Malaria Ag Pf/Pv, manufactured by Standard Diagnostic, INC 156-68 Borahagal – dong, Korea**.** The test was carried out according to the instructions from the manufacturer.

2.5 Data management and analysis.

During data collection, daily questionnaires were counted, checked for completeness and compared with the number of participants interviewed. Data were entered, cleaned and analyzed using EPI info version 3.5.1. Cases and control were matched in household identity number. The association between dependent variable and independent variable was quantified using odds ratio.

Social demographic characteristic were presented in simple frequency tables. Social demographic variables, behavioral risk factors, environmental factors and malaria knowledge with P value < 0.05 in univariate analysis were included in bivariate analysis. Then all individual risk factors from social demographic, behavioral factors, environmental factors and malaria knowledge with P value of <0.2 at bivariate level were entered together in a conditional logistic regression model using stepwise elimination method to determine the independent risk factor and control for confounders. A p-value of <0.05 was set as a level of significance at 95% confidence interval.

3.0 Results

3.1 Distribution of cases in Unguja

A total of 106 eligible cases interviewed out of 414 cases reported for the period of February – May from all six districts in Unguja. Majority 64% of cases occurred in west and central districts as shown in **figure 1.**

3.2 Social Demographic Characteristics of the respondents

Overall, the study participants were between age 15 and 79 years, with the most between 15 and 24 years (47.6%). Cases were younger (p=0.0137), and less likely to be married (p=0.0021) than controls **(Table 1).** No differences in sex or education were observed.

3.3 Association of risk for Malaria and behavioral factors

Behavioral factors observed to be risk factors for malaria include an individual who traveled to malaria endemic areas for the last one month, had outdoors activities during night and had no bed net, while net utilization had no association with malaria infection **(Table 2).**

3.4 Association of Risk for Malaria and Environmental Factors.

People who slept in rooms that were never sprayed or sprayed more than 9 months ago were likely to get malaria compared with those whose rooms were sprayed within 9 months (Table 3).

3.5 Association of Risk for malaria and Malaria knowledge

There was no association between malaria knowledge and malaria infection (Table 4)

4.0 Discussion

This study showed travel outside Zanzibar presented a greater risk for malaria infection. This could be due to areas surrounding Zanzibar (including Tanzania mainland) having high level of malaria transmission compared to Zanzibar. Zanzibar has strong transport network to mainland Tanzania where malaria transmission levels are higher (6). Ferry travel from Dar es Salaam and informal movement on small fishing and trading vessels are

likely to present the highest risk pathways for imported infections. These findings are corroborated by a study done in China which showed that increasing travel to malaria-endemic countries results in imported cases of malaria remaining common in non-endemic countries (7).

Importation of malaria parasites from endemic to non-endemic areas has been demonstrated in different areas. An earlier study showed that imported malaria to Bioko Island by travellers from mainland Equatorial Guinea where transmission is substantially higher is a major impediment to reducing the malaria burden on the island. The prevalence of malaria in boat passengers leaving the mainland was higher than that of passengers leaving Bioko (8). Therefore, in order to eliminate malaria, importation of cases should be addressed by tracing and encouraging those who travelled to endemic area to have present to the nearby health facility for malaria screening.

Engagement in outdoor activities during the night presented a greater risk for malaria infection in this study. This is possible due to shifting of mosquito bites from indoors to outdoors. Shifting of mosquito habit was also observed in Bioko Island, Equatorial Guinea where *Anopheles gambiae* species were historically documented to feed almost entirely indoors but following introduction of mass coverage campaigns with indoor-insecticide based interventions, the vector species behavior has switched to an almost 50:50 split between indoor and outdoor biting (9).

These findings are at variance with another study done in Bioko which found no evidence that spending time outdoors at night is a risk factor for malaria even though human catchers outdoors caught more mosquitoes than those stationed inside (10). There is therefore a need for further research in this area to come up with clear explanation on association between outdoors/indoors activities and malaria infection.

Sleeping in a room which was not sprayed with insecticides or sprayed more than 9 months was significantly associated with malaria infection. IRS is used as an intervention measure to prevent malaria in many countries. Indoor residual spray, in addition to ITNs, is a mainstay of malaria control to many countries. IRS is based on the notion that mosquitoes feed and rest indoors, thereby coming in contact with the sprayed surfaces.

This findings do not differ with the study done in Amhara, Ethiopia, where malaria prevalence was lower if the house had been sprayed within the previous 12 months than if it had not, but this was not statistically significant ($P = 0.072$)(11). This observation could be due to shifting of IRS implementation in Zanzibar from blanket spray to focal spray due to reduction of malaria cases. To address these findings, Zanzibar Malaria Elimination Program should assess the best IRS practice on Unguja Island.

The study found that, individuals who did not have a bed net were more likely to get malaria, but that net utilization was not significant associated with malaria. This differs from other studies where net ownership and net utilization are associated with malaria reduction. Study done in Ghana revealed that having a bed net influences use which may lead to reduced transmission, if all other factors are controlled (12). Bed nets act as a physical barrier, repel and kill mosquitoes when they contact a treated net(13) (14)..

The study revealed that, there was no association between malaria infection and having low knowledge on malaria. This differed with a study done in Mexico which showed that low and medium knowledge levels of malaria were associated with an increased risk of malaria (4).

The study indicated that there is no association between sleeping on the floor and contracting malaria. This finding do not agreed with the study done in Kenya carried out in children under five years of age which showed that sleeping on the floor was associated with malaria infection compared with those slept on bed. The possible explanation was that children were not able to hang it properly. Also it is difficult to spread the LLIN properly without a bed frame and make body parts to be attached to the net or outside the net during the sleep and hence contact with mosquito bite, which can apply to adult also(15).

Strength and limitation of the study

The study involved all districts of Unguja Island which provided a wide geographical coverage .

Furthermore, cases were diagnostically-confirmed by mRDT at a health facility, reducing misclassification bias.

Among limitations of this study include recruiting controls from the same household. Although this study was aimed to identify individual risk factors for malaria infection, some environmental factors such as net use, room condition, use of IRS and the number of people per room might be shared with the selected controls. To overcome this effect, the numbers of controls were increased to lower the chances of overmatching.

Large AOR observed could be due to controlled confounders which had a strong positive effect because of matching by household. Taking a case and a control from the same house automatically other variables (various behavioral factors related to malaria exposure) were matched. Another explanation for large confidence interval could be due to small cell numbers during stratification in regression.

Conclusions And Recommendations

The study conclude that travel outside Zanzibar, outdoors activities during the night, not sprayed or sprayed more than nine months with indoor residual spray and not having a bed net were observed to be a risk factors for malaria infection in Zanzibar.

Based on the findings it is recommend that; Ministry of Health through the Zanzibar Malaria Elimination Program should put a mechanism of tracing people from Unguja who traveled outside Zanzibar to have self-referral to the nearby health facility for malaria infection screening. Also the Ministry of Health should sensitize people on using protective gears during the night (body covering clothing and application of topical mosquito repellants), discouraging unnecessary outdoor activities and promoting bed net ownership would effectively facilitate malaria elimination in Unguja Zanzibar.

Declarations

Ethical approval:

The ethical clearance was obtained from MUHAS IRB and permission to conduct the study was obtained from Ministry of health – Zanzibar. Informed consent was obtained from all respondents before recruiting to participate in the study.

Concert for publication:

The details will be freely available on the internet and may be seen by the general public

Competing interests:

The authors declare that they have no competing interests

Abbreviations:

USSD, Unstructured Supplementary Service Data; DMSO, District Malaria Surveillance Officer's; mRDT, Malaria Rapid Diagnostic Test; ZAMEP, Zanzibar Malaria Elimination Program; IRS, Indoor Residual Spray; ITN, Insecticide Treated Net; CDC, Centre for Disease Control

Authors' contributions:

.AA, AW, WHS, MA and HM managed the Malaria case notification surveillance system. IAG, DBG and RK designed study. DBG, RK supervised data collection process. IAG undertook data collection, analyzed the data and drafted the manuscript, which all authors reviewed and approved

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Tables

Table 1: Socio-demographic characteristics of the study participants in Unguja Island in Zanzibar, February – May 2017

Characteristic	Cases (106) n (%)	Controls (318)	n(%)	Total (424)	pValue
Age Group (Years)					
15-24	65(61.3)	137(43.1)		202(47.6)	0.0137
25-34	17(16.0)	79(24.8)		96(22.6)	
35-44	13(12.3)	56(17.6)		69(16.4)	
45+years	11(10.4)	46(14.5)		57(13.4)	
Sex					
Female	54(50.9)	158(49.7)		212(50)	0.91
Male	52(49.1)	160(50.3)		212(50)	
Education					
Not went to school	21 (19.8)	58 (18.2)		79 (18.6)	0.0923
Primary and above	85 (80.2)	260 (81.8)		260(81.4)	
Marital status					
Single	67(63.2)	149(46.9)		216(50.9)	0.0021
Married	39(36.8)	169(53.1)		208(49.1)	

Table 2: Behavioral factors associated with malaria infection in Unguja Island in Zanzibar, February – May 2017

Variables	Cases(106)	Control(318)	Total(424)	OR (95% CI)	AOR (95% CI)
Travel history					
Travelled (1)	84(79.2)	32(10.1)	116(27.4)	37.6(15.9-88.94)	**60.47(15.73-232.44)**
Not travelled (2)	22(20.8)	286(89.9)	308(72.6)	Ref	Ref
Activities during the night					
Outdoors (1)	53(51.5)	228(74.1)	281(66.6)	4.84 (2.56 - 9.15)	**8.53(1.96- 37.11)**
Indoors (2)	53(48.5)	80(25.9)	133(31.4)	Ref	Ref
Having Bed Net					
No Bed Net(1)	67(63.2)	82(25.8)	149(35.1)	6.4(3.48- 11.8)	**16.25(3.32-79.50)**
Having Bed Net (2)	39(36.8)	236(74.2)	275(64.9)	Ref	Ref
Net Utilization					
Not using(1)	79(74.5)	178(56.0)	257(60.6)	2.9(1.63-5.39)	4.3(0.08- 2.20)
Using (2)	27(25.5)	140(44.0)	167(39.4)	Ref	Ref

Table 3: Environmental factors associated with malaria infection in Unguja Island in Zanzibar, February – May 2017.

Variable	Cases	Control	Total	OR (CI 95%)	AOR (95% CI)
Sleeping location					
On Floor (1)	43(40.6)	66(20.8)	109(25.7)	4.0(2.16 -7.42)	3.13 (0.72 - 13.68)
On Bed (2)	63(59.4)	252(79.2)	315(74.3)	Ref	Ref
IRS					
Not sprayed/sprayed > 9 Months(1)	78(75.5)	184(61.1)	262(61.8)	10.5(2.78-40.19)	**29.60(2.68-326.49)**
Sprayed within 9 months(2)	28(24.5)	134(38.9)	162(38.2)	Ref	Ref

Table 4: Association of malaria knowledge with malaria infection in Unguja Island in Zanzibar

Variable	Cases	Control	Total	OR (CI 95%)	AOR (CI 95%)
Malaria Knowledge					
	69(65.1)	132(41.5)			
	37(34.9)	186(58.5)			
Lower level of knowledge			201(47.4)	3.7(2.1 - 6.3)	1.77(0.61-5.12)
Higher level of knowledgeable			223(52.6)	Ref	Ref

Figures

Figure 1

Distribution of malaria cases in Unguja island Zanzibar, February – May 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.