Recent Change of Locality as Risk Factor for Malaria Fever Among New Residents of Ahoada East Local Government Area in Southern Nigeria

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ABSTRACT

Background: Relocation which is a well known determinant of malaria in non-immune travelers to malarious areas, has also been found to be a risk factor for malaria among semi-immune persons who change locality within endemic regions. Further research evidence suggests that the higher transmission intensity at the travel location is an underlying factor which may indicate exposure to new variants of P. falciparum for which specific immunity is lacking. This study was conducted to determine if recent change of locality increased the risk of malaria fever among semi-immune National Youth Service Corps members serving in a district in southern Nigeria.

Method: Ninety six corps members who had just been posted to Ahoada-East LGA in southern Nigeria and 83 others that had been in service for six months, were followed up for malaria fever in a prospective cohort design over a 3 month period from September 2010 to December 2010. Active surveillance was used to obtain reports of fever among the cohort, followed by medical examination at designated local health facilities.

Results: No significant differences in age and use of protection against malaria were found between the study groups. The incidence proportion of malaria for the recently relocated group (34%) was significantly higher than that of the resident group (15.7%). Recent change of locality was more associated with malaria fever (RR 2.19, 95% CI 1.243.88, AR 54.4%).

Conclusion: The recent change of locality within an endemic region, which serves as an indicator of exposure to new variants of P. falciparum; for which specific immunity is lacking, is a significant risk factor for malaria fever. Protection against malaria is recommended for semi-immune individuals moving to new locations with significant risk of malaria transmission.

Key Words: Change of Locality; Malaria

INTRODUCTION

Half of the world's population is at risk of Malaria, and an estimated 247 million cases led to nearly 881,000 deaths in 2006 [1]. Beyond the human toll, malaria wreaks significant economic havoc in high-rate areas, decreasing Gross Domestic Product (GDP) by as much as 1.3% in countries with high levels of transmission [2]. In some heavy-burden countries, the disease accounts for up to 40% of public health expenditures, 30% to 50% of inpatient hospital admissions, and up to 60% of outpatient health clinic visits [2]. Nigeria ranks first amongst heavy burden countries, with 57,506,000 cases of malaria occurring annually [3]. The level of malaria parasite transmission is high in the entire country, with transmission occurring all-year round in the south but more seasonally in the north [4]. Almost all cases of malaria are caused by Plasmodium falciparum [4].

Since the launch of the Roll Back Malaria (RBM) Partnership, global control efforts have only resulted in reduction in the estimated number of malaria deaths from nearly 1 million in 2000 to 781,000 in 2009 [5]. This indicates that the morbidity and overall burden of malaria still

remains high. One factor that is generally known to be associated with malaria in non-immune individuals is travel to areas where malaria is endemic. Less known is the finding from a few studies that travel within an endemic region also puts semi-immune persons at increased risk of malaria [6-8].

The few studies that showed that travel was associated with malaria had identified the movement from areas of low transmission to areas of high transmission as the underlying factor for the association [6-8]. However, other studies have demonstrated the existence of a diversity of genetically distinct forms of P. falciparum (variants) [9] as well as the fact that immunity to the parasite is variant-specific [19-22]. This might explain the incomplete immunity observed in semi-immune individuals in spite of repeated exposure to malaria parasites [9]. It would appear that individuals build up substantial immunity by experiencing a repertoire of strains over time and still remain susceptible to new strains whenever encountered.

Malaria is an acute febrile illness caused by infection with the protozoa of the genus Plasmodium, family Plasmodiidae, suborder Haemosporidiidae, and order Coccidia [23]. Four of the about 120 identified species of Plasmodium are known to cause malaria in humans, namely: P. vivax, P. malariae, P. falciparum, and P. ovale [23]. The shortest known prepatent period following a mosquito bite is five days, and the shortest incubation period is seven days [24]. With most studies and textbooks focusing on groups at risk of serious or complicated malaria, there is paucity of information on the natural history of malaria in semi-immune adults living in endemic or stable transmission areas [25].

The frequency of transmission or endemicity of malaria depends on the density and infectivity of anopheline vectors and also on the fluctuations of the sources of infection, namely gametocyte carriers. Other factors include temperature, rainfall, and personal protection against bites, vector control measures and immunity [26].

A descriptive cross-sectional study in 2004 in Kenya reported an increased risk of malaria parasitaemia with travel, mainly in children aged < 5 years, on the tea estates of western Kenya [6].

In this study, travel is assumed to indicate an increased chance of exposure to new strains of parasites for which immunity is lacking, but travel in itself may be associated with stress that is capable of causing a breakdown of immunity [27]. However, the level of stress required to suppress immunity is believed to far exceed what is encountered in most journeys, judging from findings in a meta-analysis study on the immune effects of stress [27].

Thus, the study aimed to determine if recent change of locality, which is a proxy indicator of exposure to new variants of P. falciparum, is associated with malaria fever in semi-immune National Youth Service Corps members that served in Ahoada-East Local Government Area (LGA) in southern Nigeria.

MATERIALS AND METHODS

Study design and population:

This prospective cohort study, which was done between September 2010 and December 2010 compared the risk of malaria fever among recently posted (i.e. exposed, at least one week old batch B) and old (i.e. non-exposed, at least 6 months old batch A) youth corps members at Ahoada-East, Local government area (AELGA) of Rivers state. AELGA is one of the 23 Local Government Areas of Rivers State, south-south of Nigeria.

Malaria is holoendemic in Rivers State [28], with seasonal fluctuations in malaria incidence with two peaks in the months of August and November [29**]**.

The minimum duration of stay of one (1) week used to guide the selection of subjects in the exposure group. This was in line with the known shortest incubation period for P. falciparum seven (7) days [30], beyond which the outcome of interest resulting from new exposure could have been missed.

The minimum duration of stay of six months was used as the criterion for selecting non-exposed subjects. This is based on the assumption that strain-specific immunity would have been acquired to most new variants of the parasite within this period; as it has been shown that most patients (65-95%) with imported malaria have been found to develop symptoms within 1 month of arriving back from endemic areas they had traveled to [30]. Also, subjects were through study instrument asked what form of protection (i.e. insecticide treated nets, insecticide spray or prophylactic treatment) the subjects used. Question like: 'How will you describe your use of any of insecticide spray, bed net or prevention drug for malaria protection in the last 3 months; regularly, occasionally, rarely?'

Furthermore the average 10 month short service period for NYSC members implies that any duration of stay beyond six months would make them unavailable and invalid for the follow-up/surveillance period of three months for the study.

Inclusion criteria: All consecutive consenting newly posted corps members with duration of stay less than one week (exposed) and corps members who had been resident for at least six (6) months with an expected further duration of stay of 4 months (non exposed) in Ahoada-East local government area of river state, south south Nigeria, were recruited.

A sample size of 85 was calculated for each group based on the formula for comparison of two proportions [31]. All of the available corps members in two batches were approached to participate in the study, comprising 112 and 97 members in the new and six-month old batches, respectively. Eventually, 96 and 83 subjects, who were found eligible and accepted to participate, were enrolled as the exposure and comparison groups, respectively. The decision to approach all individuals in the study population, rather than sample, was based on the need to adjust for non-responses and possible losses to follow-up [32].

Data collection and analysis: Four (4) trained research assistants viz two medical officers, a laboratory scientist, and a logistics officer distributed and retrieved self administered questionnaires which explored sociodemographic and history of malaria data. Wet and dry giemsa blood film staining were done and the subjects followed up by text messages and home visits in some cases. Data for subjects who reported ill and their subsequent treatment were also kept. Data were then analysed using percentages, frequencies and Chi Square.

Ethical consideration: Ethical clearance for this study was sort, and approval gotten, from the Ethics Committee of the University of Port Harcourt Teaching Hospital. Detailed information about the study and request to participate were made as prelude to the questionnaire for baseline information. Consent was indicated by response to the questionnaires. Confidentiality and privacy was assured.

RESULTS

A total of 179 eligible corps members consisting of 96 newly posted (recently relocated) corps members and 83 (resident) corps members who had served at least 6 months were enrolled

Table 1: Socio-demographic Characteristics of the study cohorts

Characteristics		Recently Changed Locality (Exposure)		Statistics
		Exposed Freq (%)	Non-exposed Freq (%)	
Age				
	20-24	14 (14.6)	11 (13.3)	$X^2 = 0.262$,
	25-29	76 (79.2)	68 (81.9)	df = 2,
	≥30	6 (6.2)	4 (4.8)	P = 0.877
Sex				
	Female	36 (37.5)	33 (39.8)	$X^2 = 0.096$, df = 1,
	Male	60 (62.5)	50 (60.2)	P = 0.757
Religion				
	Christian	75 (78.1)	63 (75.9)	$X^2 = 0.116$, df = 1,
	Muslim	21 (21.9)	20 (24.1)	P = 0.733
Total		96 (1000)	83 (1000)	

There was a statistically significant difference in the proportion of recently relocated (35.4%) and resident (15.7%) corps members that reported

Table 2: Fever and malaria fever outcomes among the study cohorts during the three months follow-up period

Parameter		Recently Changed Locality (Exposure)			Statistics
		Exposed Freq (%)	Non-exposed Freq (%)	Total Freq (%)	X^2 = 4.873, df = 1, P = 0.0273
Fever	**Yes**	34 (354)	17 (15.7)	51 (20.5)	
	No	62 (64.6)	66 (84.3)	128 (79.5)	
					Relative Risk (RR)=2.19 (95%CI 1.24 -3.88)
	Total	96 (100.0)	83 (100.0)	179 (100.0)	
Malaria Fever	**Yes**	33(34.4)	13(15.7)	46(25.7)	Attributable Risk(AR)=54.4%
	No	63(65.6)	70(84.3)	133(74.3)	
	Total	96(100.0)	83(100.0)	179(100.0)	

The mean (geometric) parasite densities of the relocated and resident subjects who came down with fever was 1544±621 parasites/uL and 965±326 parasites/uL, respectively. The difference between these means was statistically significant (t = 3.19, df = 44, P = 0.005) (Table

Table 3: Parasite Densities of the Cohorts Who Had Fever and P. falciparum Parasitaemia during the Three Months of Follow-up

Parasite Density (Parasites/uL)	Cohorts With Fever and P. falciparum Parasitaemia			Statistics
	Exposed Freq (%)	Non-exposed Freq (%)	Total Freq (%)	
20*-500	1 (3.0)	4 (30.8)	5 (10.9)	X^2 = 8.176
501-2,500	29 (87.9)	9 (69.2)	38 (82.6)	df = 2
>2,500	3 (9.1)	0 (0.0)	3 (6.5)	P** = 0.017
Total	33 (100)	13 (100)	46 (100.0)	

*The upper limit of threshold at which malaria parasite can be detected in a thick blood film by an experienced technician [56]

** **An expected value is < 5. Chi-square not valid**

The proportion of subjects who used protection (i.e. insecticide treated nets, insecticide spray or prophylaxis) regularly in the 3 month period of the study was not significantly different in both

Table 4: Use of Malaria Protection among Corps Members Who Recently Changed Locality and Their 6-Month Old Counterparts

Used Malaria Protection	Exposure Status			Statistics
	Exposed Freq (%)	Unexposed Freq (%)	Total (%)	
Rarely	51 (55.4)	34 (41.5)	85 (48.9)	X^2 = 0.952,,
Occasionally	39 (42.4)	44 (53.6)	83 (47.7)	df = 2
Regularly	2 (2.2)	4 (4.9)	6 (3.4)	P = 0.329
Total	92 (100)	82 (100)	174 (100.0)	

DISCUSSION

The key finding of this study is that recent change of locality by semi-immune young adults within Nigeria is associated with increasing risk or incidence malaria fever. This is not surprising since geographical differences in P. falciparum isolates have been demonstrated [10-18] and immunity to P. falciparum has been shown to be strain-specific [19-22]. The result of this study is similar to a previous analytical (case-control) study in Kenya [7], which showed that travel within endemic regions is associated with higher malaria risk.

The findings in this study may be explained by the theory of parasite genetic variation and strain-specific immunity; which imply that exposure to new strains of P. falciparum for which immunity is lacking in those who travel is the actual underlying factor. [16, 24-27].

The primary outcome of this study which showed that semi-immune persons who travel to new areas with endemic regions are at higher risk for malaria could also have been influenced by more intense transmission at the travel destination which has documented by other studies in Kenya [7] and Brazil [32]. Resultantly, travel or change of locality may be responsible for the more serious cases of malaria that affect semi-immune individuals who appear to have acquired immunity due to perennial transmission of malaria and have previously been experiencing asymptomatic infections or mild clinical disease.

The higher mean parasite density observed among the relocated cohorts who had malaria fever would also appear to support an immunological explanation for the association identified in this study. Immunity to P. falciparum has been shown to be strain-specific and immunity is expected to be lacking in individuals exposed to new strains. Also parasitaemia is known to be higher in those who lack adequate immunity, e.g. non-immune travelers to malaria endemic regions, children and pregnant women [9].

A possible confounder to the effect of probable P.

falciparum genetic variability in this study is stressing from travel, as suggested by the report of a meta-analysis which associated stress with breakdown of immunity [28]. However, the level of stress said to be required to suppress immunity is high [28], and is believed to far exceed what is encountered in the journeys undertaken by participants in this study.

Other factors which could influence the outcome of the study beyond relocation or travel are the age of the subjects and the use of anti-malaria protection by the subjects. This was not found to be different in the relocated and resident study groups and was unlikely to have influenced the study outcome. In addition the proportions of subjects in both groups that regularly used protection against malaria were very small.

CONCLUSION

In view of the finding in this study that change of locality is a predisposing factor (risk factor) for malaria fever among semi-immune people, it would be considered appropriate for people moving or traveling to new locations with risk of exposure to infective bites of mosquitoes to be protected against malaria. This should be irrespective of their malaria immunity status (non-immune or semi-immune) and the endemicity of the travel destination.

It is therefore recommended that The National Malaria Control Programme should include health messages conveying this information as part of their Advocacy, Communication and Social Mobilization (ACSM) activities, targeting endemic residents (including Youth Corps members) who are likely to travel or occasionally change locality.

The National Malaria Control Programme should also extend the provision of health goods such as bed nets and insecticides for vector control to migrant workers and families. Larger scale and country wide studies are also recommended to provide more knowledge on the subject.

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