African Journal of Microbiology Research Vol. 6(4), pp. 770-778, 30 January, 2012
Available online at http://www.academicjournals.org/AJMR
DOI: 10.5897/AJMR11.911
ISSN 1996-0808 ©2012 Academic Journals

Full Length Research Paper

Frequency and complications of *falciparum* malaria among febrile staff members of UN deployed to Northern Sudan

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Accepted 15 December, 2011

Malaria is a mosquito-borne parasitic disease, common around the globe especially in poorest countries. It is inevitable and remediable, yet it is still killing many people every year, 90% of them are in Africa. Malaria is an important threat to tourists, soldiers and employees travelling or working in endemic areas. The present study was carried out among UN staff members working in regions of Damazin, AL Obayid, kosti and areas of Blue and White Nile States. Study period comprised five years from Jan 2006 to Dec 2010. Febrile patients both males and females were screened for malaria. Thereafter, the malaria positive patients were further screened for *Plasmodium falciparum* and *Plasmodium vivax*. *P. falciparum* was found in 80% of febrile patients. Most of the patients (63.6%) presented in the first two days of febrile illness and the largest number of *Falciparum* malaria cases was reported from July to October each year. Mean index of *falciparum* malaria at presentation was a major factor in determining hematological and liver functions derangements and the time taken for fever to settle after starting either of two antimalarial drugs, that is, quinine or artemether.

Key words: *Plasmodium falciparum, plasmodium vivax*, quinine, artemether, *falciparum* Index.

INTRODUCTION

World malaria report 2010 estimates 225 million cases of malaria worldwide last year with largest number (78%) from Africa. The estimated malaria related deaths in 2009 were 7, 81000 (WHO, 2010). In Sudan (having a coast line along Red Sea), northern Africa due to climate models, it is estimated that 75% of the population (37 millions) are at risk of endemic malaria, while 25% are at risk of epidemic malaria. Malaria is endemic in southern states with high transmission rate while parts of the north are exposed to epidemics following the heavy rains or floods from River Nile (Malaria Prevalence and Indicator Survey Sudan, 2005).

Plasmodium falciparum is the dominant parasite with more than 90% of all morbidity except for the border regions with Ethiopia whereas *Plasmodium vivax* does also cause malaria episodes although the exact proportion of these infections is not yet known (Hay et al., 2000).

Malaria affects soldiers and employees travelling or working in endemic areas. Non-immune civilians and military personnel traveling in malaria-endemic areas are at risk of getting malaria and may become clinically ill during or after their travel. Approximately 25-30 million travelers from non-tropical regions visit malaria-endemic countries annually, and about 30,000 cases of travel-associated clinical malaria occur each year (Leder et al., 2004). The risk of malaria for travelers varies notably between endemic areas and periods of exposure (Machault et al., 2008).

In the present study, we summarize frequencies, trends, and demographic characteristics of all cases of malaria that were diagnosed and reported among members of the UN staff deployed in northern region of

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Table 1. Frequency and percentage of incidence malarial cases in different age and gender groups.

Age	Gender		Frequency	Percent
	Male	Female		
20-30	22	46	68	32.1
30-40	24	68	92	43.4
40-50	8	31	39	18.4
>50	2	11	13	6.1
Total			212	100.0

Sudan mainly in Blue and White Nile states between 2006 and 2010.

MATERIALS AND METHODS

Patient's selection criteria

This study was carried out among UN staff members working in regions of Damazin, AL Obayid, kosti and areas of Blue and White Nile States along with few team sites in North Sudan from Jan 2006 - Dec 2010 before the independence of South in July 2011. Patients were enrolled on volunteer basis after providing information about the blood test for malaria and use of two established anti malarial drugs, that is, qunine and artemether. All adult male and female staff members of UN working in regions of Damazin, AL Obayid and Kosti having fever and other clinical features of malaria like headache, vomiting, rigors and body aches were included in this descriptive study. Approval was taken from administrators of medical facilities and team sites. Ethical committee of base hospital at Damazin approved as this was an observational study.

Drugs selection

Two anti malarial drugs quinine and artemether were selected as they were available at medical facilities. No randomization could be done as adequate stocks of these drugs could not be maintained due to lack of infrastructure and long distances. The choice was thus much based on doctor's preference taking into consideration the monitoring facilities available and quantity of each drug. Time taken for fever to settle after use of two drugs was noted separately.

Biochemical parameters

Malaria parasite detection

Adults with acute onset of fever were tested for malaria parasite by preparing thick and thin films and staining with giemsa stain. Of those found to be positive for *falciparum* malaria, parasitemia was calculated by counting number of asexual parasites per 200 WBCs and multiplying by 40 (Assumes a WBC count of 8000 /µl).

Hematological profile

Hematological parameters including hemoglobin, platelet counts were estimated using Sysmex Pouch 100i Semi automated Chemical Analyzer using reagents Cell Pack 20 L (Sysmex) and Stromatolyzer WH 500 (Sysmex). Prothrombin time and activated partial thromboplastin time was estimated by using commercially available reagents.

Liver function tests

Alanine aminotransferase (ALT) and total bilirubin were determined before start of treatment by using the commercially available reagents. Fibrinogen degradation products (FDPs) were done in all cases during prospective period, that is, Jan 2010 – Dec 2010 as this investigation was not uniformly available at all facilities in previous years. Microlab 300 was used for liver function tests. The reagents used are ALT (Merck) and Total Bilirubin (Merck).

Statistical analysis

All data was analyzed by SPSS statistics 17. Descriptive statistics including frequency, mean and standard deviation was used for describing age, gender and number of *falciparum* cases. Linear regression model was utilized for describing the relationship between *falciparum* index and derangement in hematological parameters.

RESULTS

Total number of fever cases observed from Jan 2006 – Dec 2010 was 1529 out of which malaria positive cases were 265 (17.3%). High depicted 43.4% of patients of age group between 30-40 years with only 6.1% patients greater than 50 years.

High prevalence of malaria incidence cases was observed among the patients of age group between 30-40 years (Table 1). *Falciparum* malaria was noted in 212 cases (80%) with 156 (73.56%) males and 56 (26.41%) females. Number of malaria positive and *falciparum* cases among febrile patients during the study period is distributed year wise in Figure 1.

Most of the patients (63.6%) presented in the first two days of febrile illness and the largest number of *falciparum* malaria cases was reported from July to October each year (Figure 2, Table 2).

The mean value for total *falciparum* malaria cases over 60 months was 3.53 (SD 3.301) while that for vivax was 0.88 (SD 0.804) with females made up 26.4% of *falciparum* cases while 73.56% were males.

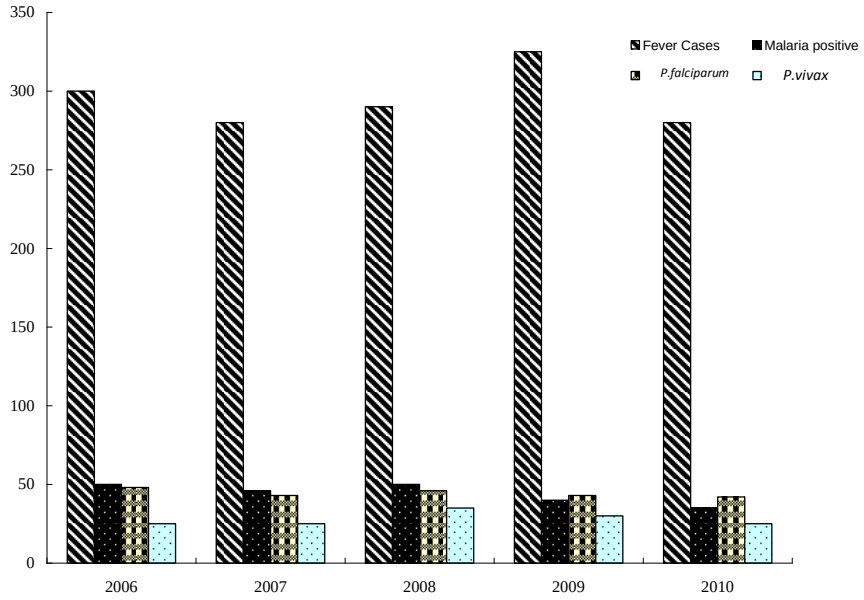

Figure 1. Year wise malaria positive cases among febrile patients.

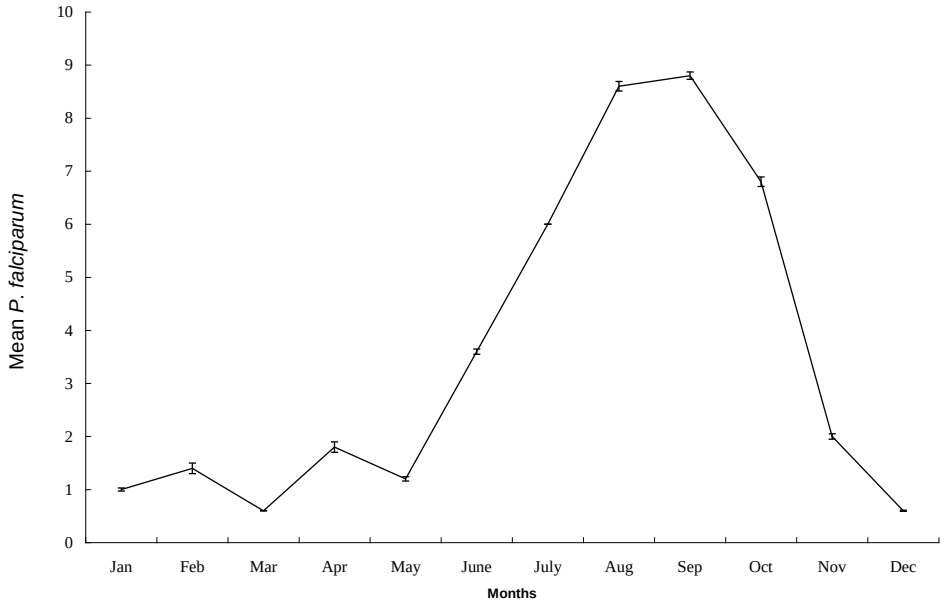

Figure 2. Seasonal variability observed among *P. falciparun* malaria cases.

Table 2. Year wise distribution of *falciparum* cases.

Year	Mean	Std. Deviation
2006	4.33	3.892
2007	3.58	3.175
2008	3.92	3.232
2009	3.08	3.370
2010	2.75	3.108
Total	3.53	3.301

Hematological profile

Hematological parameters observed for *falciparum* malaria includes hemoglobin, platelets, PT, PTTK, and showed the following trends (Table 3).

Applying linear regression model (Figure 3) it was noted that there was a linear relationship between *falciparum* index and derangement of hematological parameters keeping index as independent variable. The mean index for minimum hemoglobin value of 9.4 g/dl

Table 3. Hematological parameters.

Parameter	Hb (g/dl)	PLT	PT (s)	PTTK (s)
Mean	14.397	150.38	17.41	35.84
S.D	2.1582	67.246	4.435	5.080
Minimum	9.4	39	14	32
Maximum	18.2	298	39	54

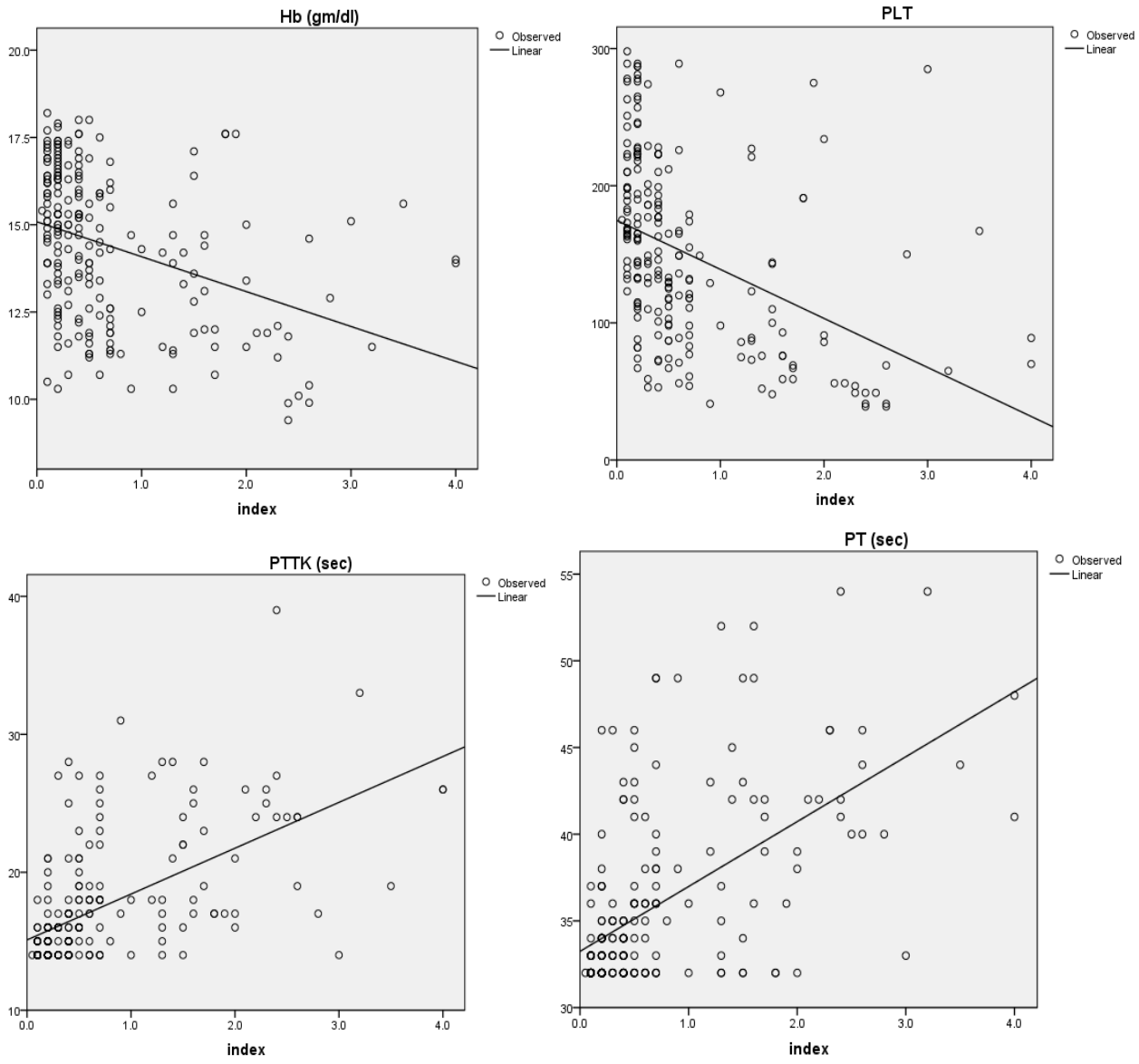

Figure 3. Linear regression curve for hematological parameters verses index.

was 2.4% and mean hemoglobin level of 18.2 g/dl at presentation showed index of 0.1%. Mean platelets count of 39 × 10^9 /L had index of 2.5% and PT, PTTK were abnormal above mean index of 0.318 and 0.395%, respectively.

Linear regression curve for hematological parameters verses index coefficients for platelets, hemoglobin, PT, PTTK, were obtained after applying Linear Regression Model showing statistically significant relationship ($p < 0.05$) between index and hematological parameters as shown in the Table 4. Derangement of liver functions also showed similar trends with maximum values of ALT and

Table 4. Coefficients of hematological parameters among *falciparum* positive cases.

Coefficients	Parameter	Unstandardized coefficients		Standardized coefficients	t	Sig.
		B	Std. Error	Beta		
Platelets	index	-36.208	5.392	-0.420	-6.715	0.000
	(Constant)	175.612	5.636		31.158	0.000
Hemoglobin	index	-1.008	0.178	-0.365	-5.675	0.000
	(Constant)	15.099	-.186		81.337	0.000
PT	index	3.330	-.318	0.586	10.487	0.000
	(Constant)	15.085	-.332		45.445	0.000
PTTK	index	3.750	0.367	0.576	10.222	0.000
	(Constant)	33.226	0.383		86.652	0.000

Table 5. Mean index of ALT and bilirubin among *falciparum* positive cases.

Parameter	ALT (U/L)	BIL (µmol/L)
Mean	14.397	45.89
S.D	2.1582	14.752
Minimum	9.4	13
Maximum	18.2	112

Table 6. Coefficients of ALT and Bilirubin among *falciparum* positive cases.

Coefficients		Unstandardized coefficients		Standardized coefficients	t	Sig.
		B	Std. Error	Beta		
ALT	index	11.169	1.052	0.591	10.621	0.000
	(Constant)	38.103	1.099		34.667	0.000
Bilirubin	index	11.402	1.313	0.514	8.682	0.000
	(Constant)	12.657	1.373		9.221	0.000

bilirubin seen at mean index of 4.0% (Table 5).

Initial index also predicted the fever settling time after starting treatment as represented by regression curve (Figure 5). Patients with mean index of 0.233 (SD 0.0577) responded to treatment in six hours while it took 120 h in cases of mean index having value of >1. Coefficients for ALT and bilirubin were obtained after applying linear regression model (Table 6) showing statistically significant relationship ($p < .05$) between index and hematological parameters as shown in the Figure 5.

Fibrinogen degradation products (FDPs) were not uniformly done in all cases from Jan 2006 – Dec 2009 mostly due to non availability. From Jan 2010 this test was performed in all *falciparum* cases on admission and following results were obtained (Table 7). Number of *falciparum* cases having positive FDPs was 32 (15.15%) and 43 (20.3%) cases tested negative. Positive and negative test results with increasing *falciparum* index are shown in Box Plot (Figure 6).

Hundred Individuals found positive for *falciparum* were given artemether combination and hundred and twelve were prescribed Quinine. Fever settling time for artemether was minimum of 6 and maximum of 96 h (SD 26.695) for quinine it was 12 and 120 h, respectively (SD 30.096). The mean time in hours for artemether was 40.62 h for Quinine it was 50.81 h. Most cases responded in 48 h after starting treatment (Figure 7).

DISCUSSION

Major cause of morbidity and mortality in Sudan is *falciparum* malaria. About 20–40% of outpatient clinic visits and approximately 30% of hospital admissions are due to this disease. The entire country of Sudan is at risk,

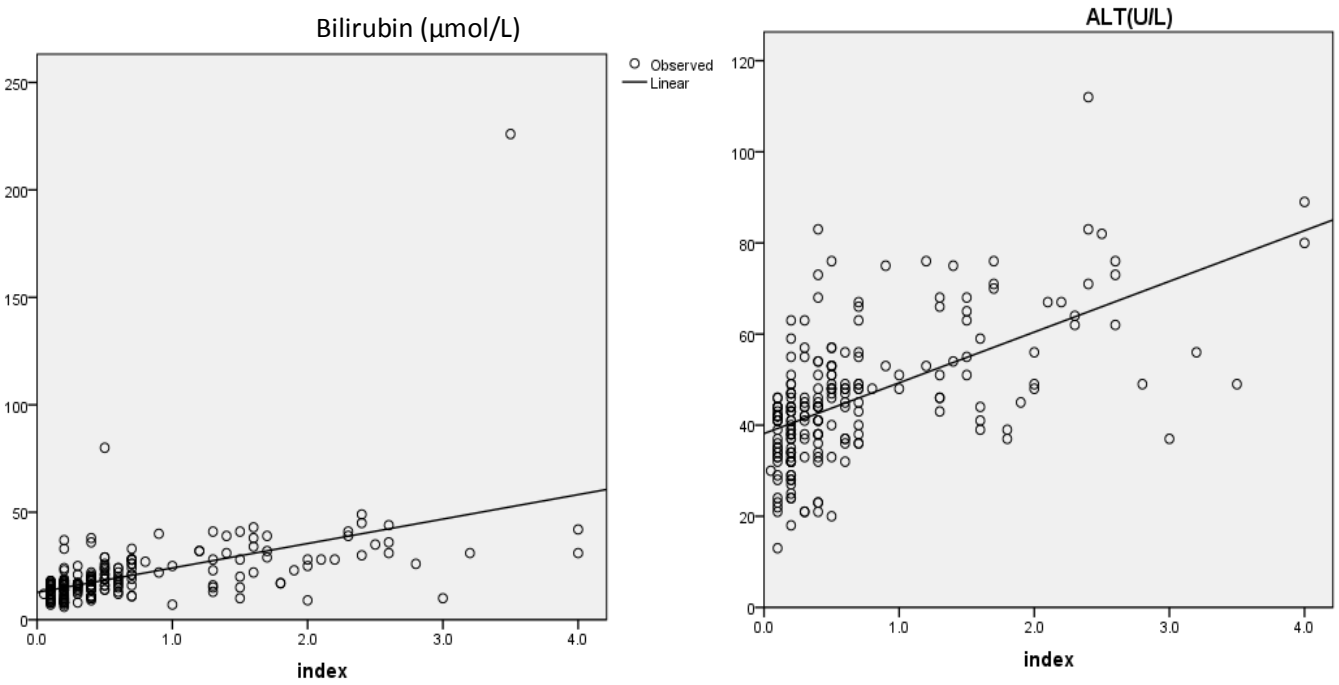

Figure 4. Linear regression curve for ALT and total bilirubin.

Table 7. Results of fibrinogen degradation products among *falciparum* malaria cases.

FDPs	Year					Total
	2006	2007	2008	2009	2010	
Positive	0	12	8	0	12	32
Negative	0	10	12	0	21	43
Total	52	43	47	37	33	212

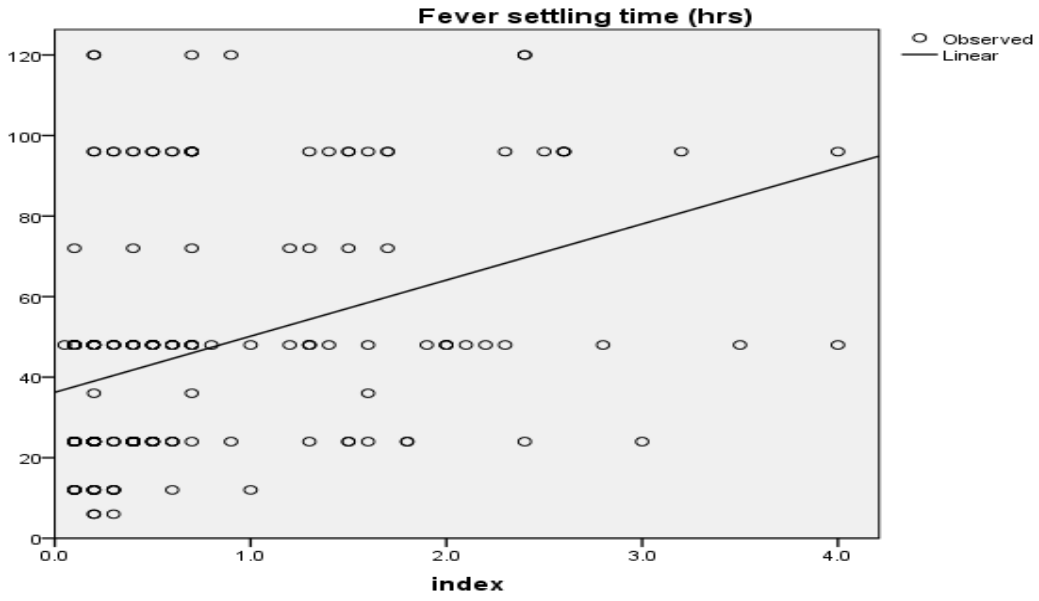

Figure 5. Linear Regression Curve for fever setting time.

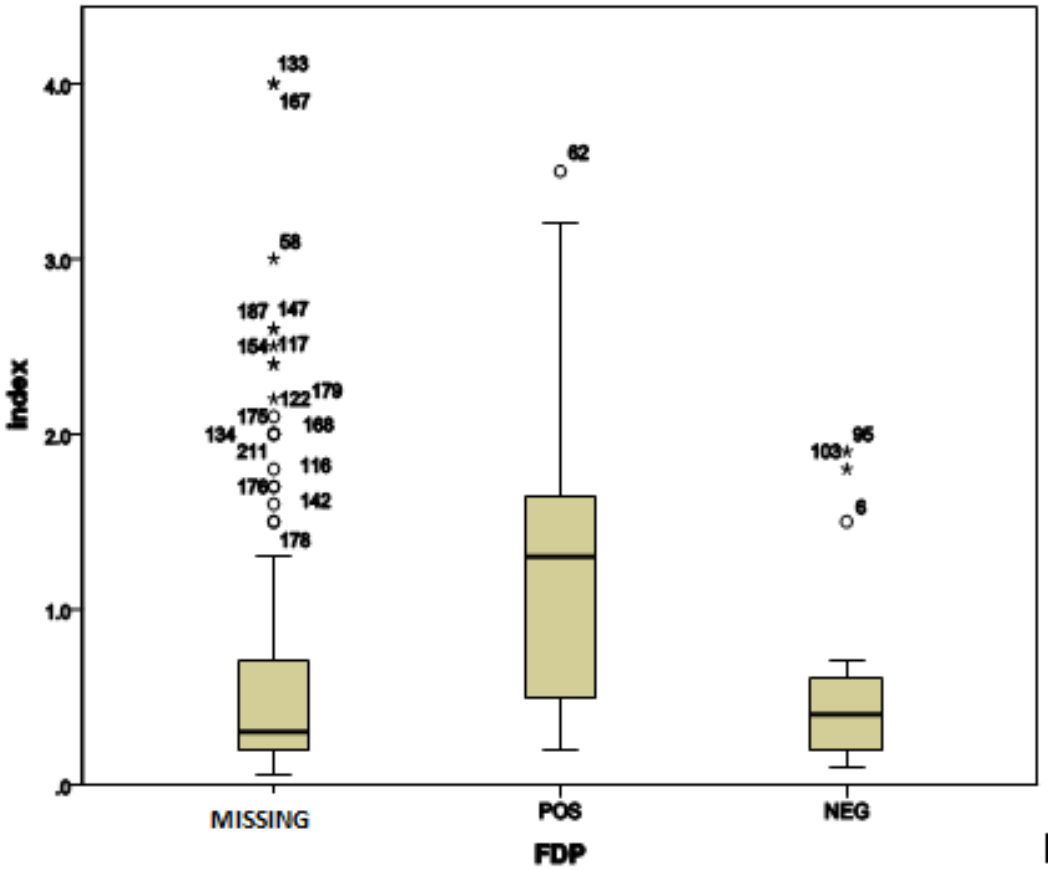

Figure 6. Box plot showing trends in FDPs result with Varying *falciparum* Index.

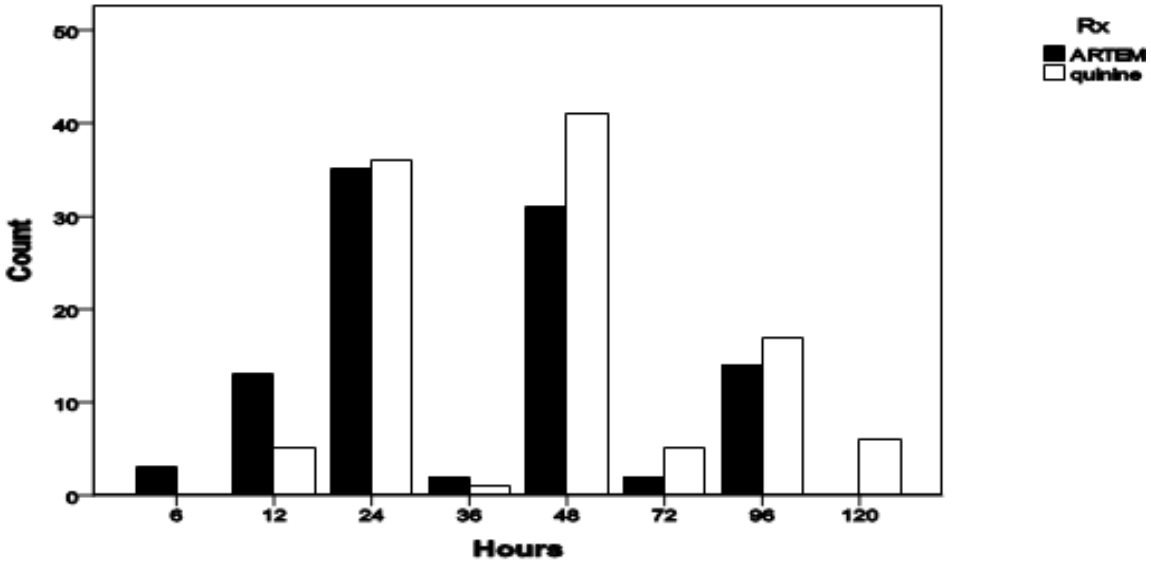

Figure 7. Fever settling time after start of antimalarials.

population living in the northern, eastern and western states have low to moderate risk of acquiring malaria with predominantly seasonal transmission and epidemic outbreaks. In southern Sudan, malaria is moderate to high or highly intense, generally with perennial transmission. *P. falciparum* is by far the predominant

parasite species. Rural areas other than irrigated schemes in Greater Darfour, Kordofan, Blue Nile, White Nile, Sinnar, Gezira, Gedarif, Kassala and Khartoum have seasonal transmission (Haider et al., 2000).

This study highlighted that non immune UN staff members showed seasonal variability with respect to frequency of *falciparum* cases with maximum cases observed from July to October each year for five years This observation was made despite of the fact that vector control, personal protection and prophylaxsis were in place in most of the residential and working areas of staff members. Thus besides having good malaria control as compared to locals, UN staff still suffered, the rainy season took its toll over all other factors. Breakdown in road communication, slips at personal level and overall increase in vector density might have contributed to this outcome.

In another study in neaby Democratic Republic of Congo the prevalent Malarial type was *falciparum* with trasmission seen between April to September among UN troops. Thirty six percent of all hospitalizations were due to Malaria and 98% were due to *P. falciparum* (Er-Rami et al., 2011).

Haider and colleagues in the study titled "The epidemiology of febrile malaria episodes in an area of unstable and seasonal transmission" reported the risk of *falciparum* malaria was significantly lower in individuals aged 20–88 years than in the 5–19 years age-group. Serological data showed that among local population the difference in incidence among various age groups was not due to differences in exposure alone. Ages between 5-19 years might have been affected more because of lack of immunity.

The present study showed that 43.4% of patients were in the age group of 30-40 years with 73.56% of all malaria cases being males. UN Staff both males and females came from non endemic areas and might have suffered because of previous non exposure. In a study done at United Nations hospital in Freetown, Sierra Leone, a Jordanian Medical Level III Hospital, 89.1 % of cases were males with mean age of 34.4% (Kawar et al., 2003).

The derangement in hematological parameters and liver functions in this study depended on *falciparum* index. Anemia and thrombocytopenia was observed with increasing mean index as shown in linear regression model. As the mean *falciparum* index reached 2.4-2.5%, mean hemoglobin dropped to 9.4 g/dl and platelets counts were seen at 39×10^9 /L. The linear relationship between increasing *falciparum* index and low hemoglobin and platelet counts was statistically significant ($p<.05$). Regarding liver functions similar trend was seen. Again significant results were obtained using regression model. Mean value for ALT was 45.89 IU/L with maximum of 112 IU/L. Bilirubin mean value was 19.66 µmol/l with maximum measurement at 80 µmol/l. A study at Royal Free Hospital found that levels of serum bilirubin, aspartate transaminase and alkaline phosphatase in adults with *P. falciparum* malaria were out of reference range in 63% of patients, these parameters were also abnormal in our study with maximum levels at mean index of 4% (Davies et al., 1996).

Fibrinogen degradation Products (FDPs) were done in all patients from Jan 2010 – Dec 2010. Earlier due to non availability this test was not uniformly performed. The minimum *falciparum* index at which FDPs were positive was 0.2% and the range was up to 3.5%. Future testing of this parameter will help understanding the association.

In the present study patients were treated either with artemether (Intramuscular artemether plus doxycyclin or artemether lumefantrine oral tablets) or qunine. Physicians choice, availability of medicines, duration of fever and clinical toxicity were the deciding factors for choosing either of the two medicine. The mean fever settling time for artemether was 40.62 h, for Quinine it was 50.81 h.

At University of Khartoum a study done on treatment of *falciparum* malaria showed that artemether cleared parasitaemia within five days and patients were free of symptoms within 48 h after starting treatment. Artemether and quinine showed equal parasite clearance time (Ibrahim et al., 1993).

Artemisinin combination was found to be effective in a number of other studies in Africa. A study in Papua New Guinea artemisinin combination with naphthoquine showed adequate clinical and parasitological response (Francis et al., 2009).

Likewise a study in Cameroon, Senegal and Ivory Coast, more than 96% of patients who received treatment with dihydroartemisinin - piperaquine phosphate - trimethoprim were apyrexial after 48 h and 83.5% of patients receiving artemisinin - lumefantrine were asymptomatic in the same period (Hervé et al., 2011).

Thus the response to either of the two established anti malarials was good among UN staff members both males and female of all ages in the present study.

Conclusion

This study showed that clinical pattern of *falciparum* malaria among UN staff members deployed in North Sudan follow seasonal transmission with peak incidence during and after rainy season, that is, from July to October. Middle aged males and females belonging to age groups thirty to forty were mostly affected. There was a linear relationship between derangements in hematological parameters, fever settling time and *falciparum* index at presentation which was statistically significant.

Future prospective studies that could include both local population and deployed members at the same time, taking into account factors for malaria transmission and studying epidemiology of malaria among UN staff members both males and females stationed in different

geographical areas of Africa might help to explain the observed differences further.

ACKNOWLEDGEMENTS

We acknowledge the United Nations medical facilities of Blue Nile state for providing all types of facilities.

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