Short Term Outcome of Malaria at Rwanda Level 2 Hospital Bria in Central African Republic: A Cross-Sectional Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author JBB, Principal investigator, designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author John Byimana, Principal investigator, corrected the protocol and the draft of the manuscript. Authors AN, Justin Bayisenga and JMR managed the literature search and read the manuscript. Authors AG, EN and SR collected the data and read the manuscript. All authors read and approved the final manuscript.

Original Research Article	

ABSTRACT

Background: Malaria has been recognized as a disease affecting peacekeeping forces serving in malaria endemic countries. We wanted to determine the short term outcome of malaria at Rwanda Level 2 hospital.
Methods: Malaria cases were prospectively reviewed and followed at Rwanda Level 2 hospital Bria

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in Central African Republic from 4th April to 14th July 2017. Clinical, laboratory, treatment and short outcome findings were analyzed.

Results: Patients (102 in subjects) with positive rapid diagnostic test and blood smear were reviewed, prevalence rate was 14.97%, mean age of 37.77±8.39 years and male presented with 91.20%, male sex ratio of 10:1. Headaches, body weakness, joint aches, muscle aches, chills and fever presented respectively 98%, 89.20%. 84.30%, 81.40%, 61.80% and 49%. Digestive symptoms were presente anorexia, nausea, abdominal discomfort and vomiting 41.20%, 37.20%, 31.40% and 8.80% respectively. *Plasmodium falciparum* was found in 98%, associated with vivax in 1% and isolated vivax in 1%. High parasitemia of 1 to 10 parasites per thick field and more was found in 8.80%. Malaria recurrence rate was 13.70% with a duration period mean of 38.92 days (range 20-82 days). 35.71% had recurrent within thirty days. 82.40% of patients received tablets Artemether-lumefanthrine. This High parasitemia was associated respectively with nausea p=0.013, OR=5.9, 95% (1.3 - 26.93) and anorexia p=0.003 OR=11.43, 95% (1.43-87.99). Clinical and laboratory findings post treatment showed a strong statistical association.

Conclusion: Malaria is prevalent at Bria; multitudes of symptoms and sign have been documented. Post treatment clinical and laboratory findings showed efficacy of treatment.

1. INTRODUCTION

Malaria is a life-threatening disease caused by parasites that are mainly transmitted to people through the bites of infected female *Anopheles* mosquitoes, the most deadly, and it predominates in Africa. It remains an important health threat to non-immune travelers with the explosive growth of global travel and affecting peacekeeping forces serving in malaria endemic countries [1-4].

The human-pathogenic *Plasmodium* species shows preponderance of *P. falciparum* in tropical Africa, while *P. vivax* prevails over *P. falciparum* in South America. Both *P. falciparum* and *P. ovale* are prevalent in South-Eastern Asia and Western Pacific. Although *P. malariae* may occur in all malarious areas, its prevalence is generally low. *P. ovale* is widespread principally in tropical Africa whereas *P. knowlest* infection occurs in certain forested areas of South-Easter Asia [5].

Although severe malaria is more often seen in cases of *P. falciparum* infection, complications and even death have been reported in non-falciparum malaria as well [6].

It is manifesting as a multitude of symptoms, degrees of severity and indirect morbid consequence and accuracy of a clinical diagnosis varies with the level of endemicity, malaria season, and age group [7-9].

WHO estimates that 212 million cases of malaria occurred worldwide in 2015 (uncertainty range: 148–304 million) and about 429 000 people died from the disease (uncertainty range: 235 000–639 000), mostly children under five years of age in sub-Saharan Africa. Africa WHO region accounted for 90% and 92% of malaria cases and deaths respectively [1].

The Security Council established the United Nations Multidimensional Integrated Stabilization Mission in the Central African Republic (MINUSCA) by its resolution 2149 (2104) on 10 April 2014 [10]. Rwanda Level 2 hospital is the UN hospital, which serves UN personnel based in Eastern headquarter. It is staffed with surgeons, anesthetists, gynecologist, internist physician, pediatrician, general practitioners, nurses, dental therapeutists, psychologist and physiotherapist.

2. MATERIALS AND METHODS

This was a cross-sectional prospective study on malaria cases received from outpatient department and admitted at Rwanda Level 2 Bria hospital from 4th April to 14th July 2017. Were included all patients whom clinical and laboratory findings confirmed malaria infection using blood smear test among people having facility to this hospital within the period of the study. Patients were recruited prospectively and followed for a short period; patients were reviewed after antimalarial treatment for clinical and laboratory examinations. This follow up was a formal review in outpatient clinic. The sample size was all patients who met inclusion criteria within the period of study. The consent form was obtained from all patients who participated in the study. The "plus system" was used in laboratory to

quantify parasites [11]. The follow up was set after finishing treatment and patient was reviewed once after introduction of anti malaria treatment (after finishing anti malaria drugs) for clinical evaluation and for laboratory control, patients put on coartem the control blood smear test was done on fourth day, those who had Artesunate for 24 h completed then coartem; the test was done after artesunate dose, those on quinine completed seven days of treatment and the test was done forty eight hours after intravenous dose of quinine and seven days after for the one who had quinine per os. Parasitemia was categorized in high or low and patients presenting parasitemia of 1 to 10 parasites per field and more were considered having high parasitemia.

Proposal was submitted and approved by Rwanda Level 2 ethical committee.

Data were entered in the computer programme Statistical Package for the Social Sciences (SPSS) software version 16.0 and were analyzed both with the aid of the computer programme SPSS and Microsoft Excel.

Descriptive statistics were used for frequencies, mean, and analytical statistics being used for cross tabulations, 95% confidence intervals applied as necessary. Comparison of means and proportions were done.

The statistical test Pearson's Chi-square was computed only for 2x2 tables with cells which had expected count more than 5 and those having expected count less than 5, Fisher's Exact Test was used. McNemar test was applied for qualitative variables and Paired Samples t-test used on quantitative variables for comparison and the limit of significance was established at $p < 0.05$.

3. RESULTS AND DISCUSSION

3.1 Results

In total, 102 patients met our inclusion criteria with a prevalence rate of 12.22%. Male sex ratio of 10:1. The median was 38 years and minimum age was 22 years, maximum being 60 years.

The Table 1 shows summarized characteristics of participant.

Table 2 shows association p=0.013 between presenting high parasitemia of 1–10 per thick field parasites and more with nausea and anorexia. Those presenting nausea had a risk of 5.9 times. Those with anorexia had a strong association also with p=0.003 and OR=11.43.

This study showed that 13.7% had another malaria episode after recruitment due to *P. falciparum*.

According to the treatment, 82.4% were treated with Artemether 20 mg and Lumefanthrine 120 mg, four tablets bid for 72 hours, 12.7% had IV artesunate for 24 hours; then complete with Artemether 20 mg and Lumefanthrine 120 mg four tablets bid for 72 hours. 3.9% had IV quinine for 48 hours; then complete with quinine per os for five days. One patient had quinine per os.

A morbidity of three days counted for coartem, four days for artesunate and coartem and seven days for quinine was noted. The mean was 3.32 days which patient spent taking treatment for a total of 339 days.

This study proved that after completing anti malaria drugs, patients followed had 67.6% of headaches, 53.9% of body weakness, anorexia of 27.5%, abdominal discomfort of 4.9%, nausea of 3.9%. 100% of patients had no chills neither vomiting.

Fourteen patients had recurrent malaria where 35.71% had malaria before completing thirty days, 37.71% got it between 30-45 days. The mean days of recurrence were 38.92 days.

There was significance proportions and mean regression of symptoms and sign of malaria after the period of follow up, where some symptoms completely disappeared after immediate treatment. And the temperature 1 which is mean of measured fever before treatment was more than 37.5°C and the control temperature mean was normal at 36.4170 C.

3.2 Discussion

In this study, hundred and two malaria cases have been diagnosed, treated and followed at Rwanda Level 2 hospital Bria in Central African Republic for a short period.

This study found male sex ratio of 10:1 where males represented 91.2%.

In the different other studies, authors found also high prevalence in males. Fernando SD et al. [12] found 98.4%, Barbara E et al. [13] found 84%, Muhammad I et al. [14] found 88.6%,

Fabien Sauvet et al. [15] found 97.39%. These findings show that the number of females deployed in peacekeeping missions compared to males is still low.

Table 1. Table of base line characteristics of participants

Variable	Categories	Number	Percent	Mean
Sex	Male	93	91.2	
	Female	9	8.6	
Age group (Years)	<37.8	50	49	37.77 ± 8.396
	>37.8	52	51	
Headaches	Yes	100	98	
	No	2	2	
Body Weakness	Yes	91	89.2	
	No	11	10.8	
Joint aches	Yes	86	84.3	
	No	16	15.7	
Muscle aches	Yes	83	81.4	
	No	19	18.6	
Chills	Yes	63	61.8	
	No	39	38.2	
Fever (°C)	< 37.5	52	51	
	≥37.5	50	49	
Anorexia	Yes	42	41,2	
	No	60	58.8	
Nausea	Yes	38	37.3	
	No	64	62.7	
Abdominal discomfort	Yes	32	31.4	
	No	70	68.6	
Vomiting	Yes	9	8.8	
	No	93	91.2	
Plasmodium	Falciparum	100	98	
	Falciparum+Vivax	1	1	
	Vivax	1	1	
Parasitemia	1–10 per 100 thick fields	81	79.4	
	11-100 per 100 thick fields	12	11.8	
	1–10 per thick field	3	2.9	
	>10 per thick field	6	5.9	

Table 2. Association between symptoms and parasitemia

		Parasitemia	Grouped	P-value	OR 95% CI
		≤ 2+	> 2+		
Nausea	Yes	31	7	0.013	5.9 (1.3 - 26.93)
	No	62	2		
Anorexia	Yes	34	8	0.003	11.43 (1.43-87.99)
	No	59	1		

Table 3. Comparison of symptoms and sign before and after malaria treatment

Variables	Group 1a	Group 1b	Diff. of proportions	Chi-square	P-value
Headaches	98%	67.60%	0.3	29.032	p<0.001
Body Weakness	89.20%	53.90%	0.35	21.814	p<0.001
Joint aches	84.30%	2.90%	0.81	81.012	p<0.001
Muscles aches	81.40%	2%	0.79	79.012	p<0.001
Chills	61.80%	0%	0.62	61.016	p<0.001
Anorexia	41.20%	27.50%	0.14	4.024	0.045
Nausea	37.30%	3.90%	0.33	32.029	p<0.001
Abdominal discomfort	31.40%	4.90%	0.26	21.806	p<0.001
Vomiting	8.80%	0%	0.09	Binominal distrib.	0.004
Blood smear	Positive	Negative	1	100.01	p<0.001

				95% CI of difference				
Variable	Mean 1	Mean 2	Diff. of Means	Lower	Upper	t	df	p-value
Temp.1-Temp.2	37.604	36.417	1.1873	1.0106	1.3639	13.332	101	p<0.001

Our patients' age was between 22 and 60 years old with a mean of 37.77 ± 8.396. These results demonstrate that our population was young adult and are similar to results found by below other authors [14] found that peacekeepers with skin diseases were aged form 20 to 60 years. Regarding our mean age of 37.77 years, [9] found that troops aged between 20-40 years constituted 96.3%.

In this study, symptoms and signs dominated by headaches, body weakness, joint aches, muscles aches were quietly comparable to those found by L. Sanchez et al. [16]. The difference being due to sample size.

Plasmodium falciparum was prevalent at 98% and associated or not with *P. vivax* in 2%. These results are similar to those found by [12] where descriptive statistics of the malaria attacks during deployment of military in endemic overseas territories found a rate of (n=44); where *P. falciparum* was found to be prevalent with 22.7% and *P. vivax* with 13.6%; they found also that not recorded of 63.7% in 44 malaria attacks.

In this study, patients had a minimum time of treatment of three days up to seven days. A morbidity of 3.22 days loss (out of work) was found during this study for a total of 339 days. These results are comparable to the result found by [3] in the last century, malaria historically caused greater loss of manpower than combat-related injuries during deployments to tropical regions. This study found that there is no association between sex and parasitemia neither age with parasitemia p=0.407 and p=0.939 respectively. These results are similar to those found by Hassan Ali et al. [17] where they found that malaria parasite density was not related to age, gender and hepatosplenomegaly.

This study found a malaria recurrence mean of 38.92 days (range 20-82 days), where 35.71% had malaria before 30 days, 37.71% got it between 30-45 days, 14.29% got it between 46 to 60 days and 14.29% had it after 60 days. These results are superposable to those of Yehenew A. Ebstie et al. [18], where it is reported that only 1.5% of participants were shown late parasitological failure between seventh and 14th day follow up and 1.3% were free from anemia at the end of follow-up.

The study found an association between parasitemia of more than 1–10 parasites per thick field, p=0.013, OR=5.9 95% CI (1.3 - 26.93). There is a relative risk of 5.9 to have this parasitemia when patient having malaria presente nausea at arrival. There was also association between presenting anorexia due to malaria with parasitemia of more than 1–10 parasites per thick field p=0.003, OR= 11.43 95% CI (1.43-87.99).

Regarding comparison of clinical manifestations of malaria before and after the treatment, this study found that all symptoms and sign of our patients had significantly decreased with positive proportions, means and significant probabilities less than 0.05 as shown in the comparative table. These results are similar to those found by [18], among 130 participant in the study, 60% were males and 96.1% participants were free from parasitemia at day 3. At the end of the study, 98.5% of participants showed adequate clinical and parasitological response of the drug.

Artemisinin derivatives were used in 95.1% in this study, and showed a good outcome from clinical and laboratory control results. These findings are similar to those of Houston S, Houston A [19], where Artemisinin derivatives are currently the mainstay of antimalarial treatment throughout the world. Their implementation, along with expanded use of insecticide-treated bed nets, accounts for a large part of the reduction in malaria deaths in Africa over the past decade.

This study found that two patients had malaria while were on prophylaxis of Lariam and doxycycline. These findings are correlated to this statement where Prophylactic and clinical failures of doxycycline against *P. falciparum* have been associated with both inadequate doses and poor patient compliance. However, resistance can also explain failures of prophylaxis [20].

4. CONCLUSION

Malaria is still considered as global morbidity health problem and major killer. It is prevalent in Bria area; where multitude of symptoms and sign some associated with parasitemia and mixed species of *Plasmodium* have been documented.

The association between parasitemia of 1–10 parasites per thick field, nausea and vomiting has been documented. Artemisinin derivatives showed good clinical and laboratory outcome. There was a significant immediate decrease of

symptoms and sign after malaria treatment. An average of 3.32 days malaria morbidity was found.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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