

# Malaria parasitemia and antimalaria prophylaxis in sickle cell anemia patients in steady state

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## ABSTRACT

Malaria parasitemia was assessed in 37 known sickle cell anemia patients attending the routine hematological clinic of the University of Benin Teaching Hospital, Benin-City, Edo State. Parasitemia was determined using the quantitative buffy coat analysis. The prevalence of malaria parasitemia among the population studied was 86.5%. There was no significant difference in the prevalence of parasitemia among the male and female sicklers ( $p=0.35$ ). Malaria parasitemia was significantly associated with hematocrit  $<0.20$  ( $p=0.03$ ). There was no statistically significant difference between the type of prophylaxis used and parasitemia. In conclusion, the role of malaria prophylaxis in preventing parasitemia seems negligible. It is therefore recommended that more emphasis.

**Key words:** Malaria, parasitemia, sickle cell, prophylaxis

## ÖZET

### Orak hücreli anemi hastalarında malarya parazitemisi ve anti-malarya profilaksisi

Orak hücre anemisi olduğu bilinene 37 hasta, Edo eyaleti Benin şehrinde Benin Üniversitesi Eğitim Hastanesi rutin hematoloji kliniğine başvurduklarında malarya parazitemisi açısından incelendi. Parazitemi kantitatif "buffy coat" incelemesi ile belirlendi. İncelenen hasta grubunda malarya parazitemi sıklığı %86.5 olarak bulundu. Erkek ve kadın orak hücre anemisi hastaları arasında parazitemi sıklığı açısından anlamlı bir fark yoktu ( $p=0.35$ ). Malarya parazitemisi hematokrit değerinin 0.20'den daha az olması ile anlamlı olarak ilişkiliydi ( $p=0.03$ ). Malarya profilaksi tipleri ile parazitemi arasında istatistiksel olarak anlamlı bir farklılık yoktu. Sonuç olarak, paraziteminin önlenmesinde malarya profilaksisinin rolü önemsiz gözükmemektedir. Bu nedenle, asıl olarak ilaçlı sivrisinek ağlarının kullanılması gibi diğer koruyucu önlemlere ağırlık verilmesi önerilmektedir.

**Anahtar kelimeler:** Malarya, parazitemi, orak hücre, profilaksi

## INTRODUCTION

Sickle cell anaemia (SCA), a chronic debilitating disorder of genetic origin, is common in Africans and the Afro Caribbean. The disorder is characterized by varying clinical manifestations, referred to as crises among others [1]. Crises could be precipitated by a number of conditions like stress, extremes of temperature, infections - bacteria, viral, protozoa, particularly malaria, and a host of others [2-5]. It is probably the recognition of infections like malaria as a potent inducer of crises that malaria prophylaxis is routinely given to SCA patients living in malaria-endemic regions. Malaria has the dual effect of initiating vaso-occlusive crises while at the same time triggering hemolysis of red cells that already have a markedly shortened life span [2]. Despite the prophylactic measures often embarked on by clinicians, malaria remains a relatively frequent reason for hospitalization among SCA patients.

The treatment and control of malaria is still a serious challenge in sub-Saharan Africa. As part of measures to combat malaria, focus is placed on prompt diagnosis and treatment [3-4]. Malaria and bacterial infections had been previously recognized as the most common problems of SCA patients presenting with severe anemia [5].

While protection against malaria is well established in individuals who are heterozygous for the sickle cell gene (HbAS) [6-9], the protection conferred by the HbSS gene on malaria is less well defined. Although there seems to be a general agreement among researchers on the protective nature of the HbS gene against malaria, the mechanisms through which this is achieved are controversial.

Various mechanisms postulated include an immune base protection occasioned by the enhancement of the host immune response by genetic trait, membrane oxidant injury, disruption of parasite metabolism and toxic heme production, among others [10-14].

Despite the widely reported protection against malaria by the HbS gene and the use of malaria prophylaxis, malaria is still a significant cause of morbidity and mortality among SCA patients [5,15,16].

While various studies [5-7,15,16] have been done to assess malaria parasitemia among sicklers, the role of various types of malaria prophylaxis used to our knowledge is yet to be ascertained. Our aim therefore was to assess the influence of malaria prophylaxis and the type of malaria prophylaxis on the level of malaria parasitemia among apparently healthy sicklers in Benin City.

## MATERIALS AND METHODS

**Subjects:** Thirty-seven SCA (HbSS) patients seen routinely in the hematology clinic of the University of Benin Teaching Hospital over a period of six months were recruited into the study. All the patients were in steady states and their full and informed consent was obtained before commencement of the study.

**Methods:** Blood (5 ml) was collected into an EDTA bottle for packed cell volume (PCV) (17) and malaria parasite estimation. Malaria parasitemia was determined using the quantitative buffy coat (QBC) analysis method as previously described [18]. Whole blood (50 µl) was drawn into a capillary tube coated with acridine orange and fitted with a cap. Spinning was done with a QBC microhematocrit centrifuge at 12000 rpm mounted on a small plastic holder and examined through an ordinary light microscope with customized fluorescence. The malaria parasite stained green (DNA: nucleus) and orange (RNA: cytoplasm), in reaction to acridine orange. The tube was examined in the region between the red blood cells and granulocytes and between granulocytes and mononuclear cell layer where parasites are most abundant. Parasite quantity in the blood sample was estimated using the "plus" system:

- +(1+) 1 parasite per QBC field
- ++(2+) 1-10 parasites per QBC field
- +++ (3+) 11-100 parasites per QBC field
- ++++ (4+) >100 parasites per QBC field.

Examination of malaria parasite was done by at least two lab scientists to avoid error that could arise from color blindness.

**Data Analysis:** Data collected were analyzed using INSTANT graph-pad, and the association between the use of anti-malaria prophylaxis and malaria parasitemia was established using Fisher's exact test. Statistical significance was set at 95% confidence limit.

## RESULTS

A total of 37 SCA patients (17 M, 45.9%, 20 F, 54.1%) aged 18-45 years (mean age 26.6 years, SD 5.6) were studied. Malaria parasitemia was demonstrated in 32 (86.5%) of the patients studied (Table 1). Sixteen (80%) of the females had malaria parasite in their blood film, while four were negative for malaria parasite. Sixteen (94.1%) of the males (n=17) had malaria parasitemia. However, there was no statistically significant difference between males and females infested ( $p=0.34$ ).

Malaria parasitemia and frequency of use of prophylaxis are shown in Table 2. Ten of the 12 patients (83.3%) using daily prophylaxis had malaria parasites, while 14 of the 17 (82.4%) using weekly prophylaxis and all 8 (100%) without prophylaxis were infested, but the difference was not found to be statistically significant ( $p=1.0$ ). Table 3 illustrates the PCV and malaria parasitemia. Twenty-one (95.5%) of the patients (n=22) with PCV <20% had malaria parasites in their

blood, while 10 (66.7%) of the patients (n=15) with PCV >20% were infested, and the association was found to be statistically significant ( $p=0.031$ ). The intensity of parasitemia between males and females is shown in Figure 1. Of the male population, 10/17 (58.8%) had 1+, 6/17 (35.3%) had 2+, while 1/17 (5.8%) was negative. Of the female population, 14 (70%), 2 (10%), and 4 (20%) had 1+, 2+, and nil malaria parasites, respectively. There was no statistically significant difference between males and females with 2+ parasitemia and those without malaria parasites ( $p=0.1026$ ).

## DISCUSSION

The sickle cell gene has been reported to confer some degree of protection against malaria. In this study, malaria parasitemia was found in 86.4% of the SCA patients studied, and this is in sharp contrast to the work done by Alouch<sup>10</sup>, who found a prevalence of 20% in SCA patients. The difference between our study and theirs could be

**Table 1. Prevalence of malaria parasitemia by sex**

Sex	Positive (%)	Negative (%)	Total (%)
Male	16 (94.1)	1 (5.9)	17 (100)
Female	16 (80.0)	4 (20.0)	20 (100)
Total	32 (86.4)	5 (13.5)	37 (100)

P = 0.35

**Table 2. Frequencies of prophylaxis use and parasitemia**

Prophylaxis use frequency	Positive (%)	Negative (%)	Total (%)
Daily	10 (83.3)	2 (16.7)	12 (100)
Weekly	14 (82.4)	3 (17.6)	17 (100)
None	8 (100)	0 (0)	8 (100)
Total	32 (86.5)	5 (13.5)	37 (100)

P>0.05

**Table 3. Packed cell volumes and malaria parasitemia**

Parasitemia	Packed Cell Volume		Total (%)
	PCV <20 (%)	PCV >20 (%)	
Positive	21 (95.5)	10 (66.7)	31 (83.8)
Negative	1 (4.5)	5 (33.3)	6 (16.2)
Total	22 (100.0)	15 (100.0)	37 (100)

P = 0.031

attributed to the number of patients studied and the methodology used. While we studied 37 SCA patients and used the QBC analysis, they studied 20 SCA patients and used the thick blood film method to detect malaria parasite in the blood.

The QBC analysis has been reported to be superior to Leishman staining technique in detecting low parasite density [18]. Again, our findings differ from those of Okuonghae *et al.* [16], who documented malaria parasites in 9% of the 166 children with SCA with pyrexia. While their study was performed on children presenting with fever, ours was conducted on adult SCA patients in apparent steady state. In this study, we also found that 10/12 (83.3%) of patients on daily prophylaxis and 14/17 (82.4%) of those on weekly prophylaxis had malaria parasites in their blood. It thus appears that malaria prophylaxis does not protect against parasitemia and that neither daily nor weekly prophylaxis seems to have an advantage over the other ( $p=1.000$ ). This had further corroborated the earlier work of Abjah and Aken'ova [19], who demonstrated a high mean malaria specific immunoglobulin G (pf-IgG) in 44 patients with SCA. The high level of pf-IgG found by Abjah *et al.* could be explained by the fact that malaria prophylaxis may reduce the parasite burden but is not sufficient to eliminate the parasite completely from the blood stream of these patients. The continuous presence of these parasites in the blood is expected to stimulate production of malaria antibodies. The large prevalence of malaria parasitemia obtained from our study could be a consequence of the ineffectiveness of the drugs in use as prophylaxis or the use of fake drugs as prophylaxis. Therefore, the efficacy of the malaria prophylaxis in current use needs to be re-evaluated, especially in light of the recent discoveries of large quantities of fake drugs in our country. This view is, however, contrary to that of Oniyangi and Omara [20] who had earlier reported reduced malaria episodes in patients on malaria prophylaxis.

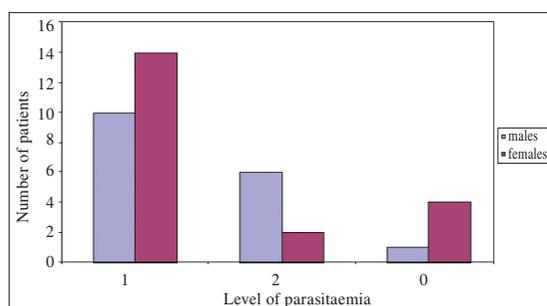
Expectedly, a significant association between PCV and malaria parasitemia was observed, with 59.5% of those with malaria parasitemia having PCV <20%, while only 27% of those with PCV >20% had malaria parasites. This agrees with the earlier work of Ambe *et al.* [6], who reported parasitemia in 66% of SCA patients with PCV <15% and concluded that malaria is a major contributor to the anemic crises seen in children. However, the role of malaria prophylaxis and degree of parasitemia were not addressed in their study. Again, the association of malaria parasitemia with PCV corroborates the earlier finding of Oniyangi and Omari [20] that chemoprophylaxis increases hemoglobin values.

In conclusion, we aimed to determine the role of malaria prophylaxis in malaria parasitemia using the QBC analysis to demonstrate malaria parasitemia. Thirty-two (86.4%) of the patients studied had malaria parasites in the blood despite adequate prophylaxis. The PCV was significantly low in those with malaria parasitemia. Despite the small number of patients studied, the role of malaria prophylaxis in preventing parasitemia seems negligible. We recommend that more emphasis should be placed on other preventive methods and that more work should be done on the efficacy of malaria prophylaxis in minimizing infestation.

Therefore, the efficacy of the malaria prophylaxis in current use needs to be re-evaluated, especially in light of the recent discoveries of large quantities of fake drugs in our country. This view is, however, contrary to that of Oniyangi and Omara [20] who had earlier reported reduced malaria episodes in patients on malaria prophylaxis.

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**Figure 1.** Level of malaria parasitaemia in SCA in patients

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