

Dikwa et al. Afr. J. Clin. Exper. Microbiol. 2021; 22 (3): 407 - 414

<https://www.afrcem.org>African Journal of Clinical and Experimental Microbiology. ISSN 1595-689X
AJCEM/2065. <https://www.ajol.info/index.php/ajcem>

Jul 2021; Vol.22 No.3

Copyright AJCEM 2021: <https://dx.doi.org/10.4314/ajcem.v22i3.12>**Original Article****Open Access**

Differences in haematological parameters and haemoglobin phenotypes in symptomatic and asymptomatic subjects with *Plasmodium falciparum* infection in parts of Kaduna metropolis, Nigeria

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Background: *Plasmodium falciparum* is the leading cause of malaria morbidity and mortality in Nigeria with varied symptoms and haematological consequences. The objective of this study is to assess the differences in haematological parameters and haemoglobin phenotypes in symptomatic *P. falciparum* infected and apparently healthy asymptomatic individuals in parts of Kaduna metropolis.

Methodology: A total of 1000 subjects; 500 symptomatic and 500 apparently healthy subjects asymptomatic for malaria, were recruited from selected hospitals and National Blood Bank in Kaduna metropolis. Blood samples were collected for thick and thin film microscopy to determine malaria parasitaemia and parasite species identification respectively. Haematological parameters were determined using automated blood analyser (KX-21N, Sysmex, Japan) and haemoglobin phenotypes by alkaline cellulose acetate electrophoresis.

Results: Of the 1000 subjects recruited, 347 (34.7%) were positive for *P. falciparum* on blood film, which included 226 (45.2%) of 500 symptomatic and 121 (24.2%) of 500 asymptomatic subjects ($p < 0.00001$). Of the 347 *P. falciparum* infected subjects, 275 (79.3%) had HbAA, 61 (17.6%) had HbAS, 1 (0.3%) had HbAC, 8 (2.3%) had HbSS, and 2 (0.6%) had HbSSf phenotypes. One hundred and sixty-three (72.1%) of the 226 symptomatic subjects had HbAA while 112 (92.6%) of the 121 asymptomatic subjects had HbAA, which indicated a significantly higher frequency of asymptomatic malaria in subjects with HbAA ($p < 0.00001$). Conversely, 53 (23.5%) of the 226 symptomatic subjects had HbAS while 8 (6.6%) of 121 asymptomatic subjects had HbAS, indicating a significantly higher frequency of symptomatic malaria in subjects with HbAS ($p = 0.000086$). The frequency of parasitaemia $> 3,000$ parasites/ μ L of blood was 100% for HbSSf, 25% for HbSS, 8.2% for HbAS and 2.2% for HbAA, which showed significantly higher frequency in subjects with HbSS ($X^2 = 7.5989$, $p = 0.0054$) and HbAS ($X^2 = 3.9627$, $p = 0.046519$) compared to HbAA. In symptomatic subjects, only MCHC value was significantly higher in subjects with HbAS (33.21 ± 2.430) compared to those with HbAA (32.09 ± 2.315) ($p = 0.003$), while all other haematological parameters were not significantly different ($p > 0.05$). In asymptomatic subjects, none of the haematological parameters was significantly different between subjects with HbAS and HbAA ($p > 0.05$).

Conclusion: Although the frequency of *P. falciparum* infection in this study is generally higher in subjects with HbAA, symptomatic infection and higher parasite density are associated with HbAS, HbSS and HbSSf. Effective utilisation of personal preventive measures by inhabitants, in addition to current malaria control and intervention strategies should be adequately implemented in Kaduna metropolis.

Keywords: Haematological parameters, haemoglobin, electrophoresis, *Plasmodium falciparum*, malaria

Received Aug 11, 2020; Revised Jan 31, 2021; Accepted Mar 27, 2021

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Différences dans les paramètres hématologiques et les phénotypes d'hémoglobine chez les sujets symptomatiques et asymptomatiques

atteints d'une infection à *Plasmodium falciparum* dans certaines parties de la métropole de Kaduna, Nigéria

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Abstrait:

Contexte: *Plasmodium falciparum* est la principale cause de morbidité et de mortalité liées au paludisme au Nigéria avec des symptômes et des conséquences hématologiques variés. L'objectif de cette étude est d'évaluer les différences de paramètres hématologiques et de phénotypes d'hémoglobine chez des individus symptomatiques infectés par *P. falciparum* et asymptomatiques apparemment en bonne santé dans certaines parties de la métropole de Kaduna.

Méthodologie: Un total de 1000 sujets; 500 sujets symptomatiques et 500 sujets apparemment sains asymptomatiques pour le paludisme ont été recrutés dans certains hôpitaux et dans la Banque nationale du sang de la métropole de Kaduna. Des échantillons de sang ont été prélevés pour la microscopie à couche épaisse et mince afin de déterminer respectivement la parasitémie du paludisme et l'identification des espèces de parasites. Les paramètres hématologiques ont été déterminés à l'aide d'un analyseur sanguin automatisé (KX-21N, Sysmex, Japon) et des phénotypes d'hémoglobine par électrophorèse sur acétate de cellulose alcaline.

Résultats: Sur les 1000 sujets recrutés, 347 (34,7%) étaient positifs pour *P. falciparum* sur frottis sanguin, qui comprenait 226 (45,2%) de 500 sujets symptomatiques et 121 (24,2%) de 500 sujets asymptomatiques ($p < 0,00001$). Sur les 347 sujets infectés par *P. falciparum*, 275 (79,3%) avaient HbAA, 61 (17,6%) avaient HbAS, 1 (0,3%) avaient HbAC, 8 (2,3%) avaient HbSS et 2 (0,6%) avaient des phénotypes HbSSf. Cent soixante-trois (72,1%) des 226 sujets symptomatiques avaient une HbAA tandis que 112 (92,6%) des 121 sujets asymptomatiques avaient une HbAA, ce qui indiquait une fréquence significativement plus élevée de paludisme asymptomatique chez les sujets avec HbAA ($p < 0,00001$). À l'inverse, 53 (23,5%) des 226 sujets symptomatiques avaient une HbAS tandis que 8 (6,6%) des 121 sujets asymptomatiques avaient une HbAS, indiquant une fréquence significativement plus élevée de paludisme symptomatique chez les sujets avec HbAS ($p = 0,000086$). La fréquence de parasitémie > 3000 parasites / μL de sang était de 100% pour l'HbSSf, 25% pour l'HbSS, 8,2% pour l'HbAS et 2,2% pour l'HbAA, ce qui a montré une fréquence significativement plus élevée chez les sujets atteints d'HbSS ($\chi^2 = 7,5989$, $p = 0,0054$) et HbAS ($\chi^2 = 3,9627$, $p = 0,046519$) par rapport à l'HbAA. Chez les sujets symptomatiques, seule la valeur MCHC était significativement plus élevée chez les sujets avec HbAS ($33,21 \pm 2,430$) par rapport à ceux avec HbAA ($32,09 \pm 2,315$) ($p = 0,003$), tandis que tous les autres paramètres hématologiques n'étaient pas significativement différents ($p > 0,05$). Chez les sujets asymptomatiques, aucun des paramètres hématologiques n'était significativement différent entre les sujets avec HbAS et HbAA ($p > 0,05$).

Conclusion: Bien que la fréquence des infections à *P. falciparum* dans cette étude soit généralement plus élevée chez les sujets atteints d'HbAA, une infection symptomatique et une densité parasitaire plus élevée sont associées à l'HbAS, l'HbSS et l'HbSSf. Une utilisation efficace des mesures de prévention personnelle par les habitants, en plus des stratégies actuelles de lutte antipaludique et d'intervention, devrait être mise en œuvre de manière adéquate dans la métropole de Kaduna.

Mots clés: Paramètres hématologiques, hémoglobine, électrophorèse, *Plasmodium falciparum*, paludisme

Introduction:

Although, global malaria burden has reduced, the burden is still high in the African region. According to the World Health Organization malaria report (1), the African region still accounts for the high global malaria burden in 2018, with an estimated 93% malaria cases and 94% deaths. *Plasmodium falciparum* accounted for 99.7% of estimated malaria cases in the region. Of the six countries that accounted for more than half of all malaria cases worldwide, Nigeria accounted for 25% of such cases and *P. falciparum* remained the dominant species (1). Several factors are responsible for the transmission and

spread of the malaria. These include climatic conditions such as rainfall pattern, temperature and humidity. These factors have been responsible for the seasonal transmission of malaria, with peak prevalence occurring during and immediately after rainy season (2,3,4,5).

Genetic factors have been shown to offer protection against malaria. These includes the possession of high concentration of haemoglobin F (HbF) in the red blood cells of new born infants (neonates) as well as individuals with sickled red cells containing abnormal haemoglobin (HbS). Sickle cell trait (HbAS) is also known to confers protection against severe falciparum malaria (2,6). The malaria-protective effect of HbAS or HbAC has been

hypothesized to include several innate immune mechanisms. Parasite growth and replication in the erythrocytes that contains HbAS or HbAC may be impeded in relative normal red cells when subjected to low oxygen tension. In addition, the proteins are the targets of specific antibodies may be more rapidly exposed in HbAS containing red blood cells resulting in an enhanced immune response to infection. There is also the possibility of unknown innate protection processes, which may up-regulate malaria-specific immune response and enhance non-specific immunity to malaria, thus, the optimal development of plasmodium in the deep organs where oxygen pressure is reduced may not be allowed in abnormal haemoglobin (7).

Malaria parasites grow and multiply in red blood cells with varied haematological consequences, resulting in changes in haematological parameters of the infected individuals (8). In previous studies, the effect of haemoglobin variants in *P. falciparum* infected individuals using haematological parameters were assessed with focus mainly on malaria infected individuals with clinical symptoms (7). In endemic regions, prolonged exposure confer immunity over time among adults, a condition in which resistance is acquired that is associated with continued asymptomatic parasitic infection (premunition).

There is need to examine individuals of different haemoglobin genotypes (variants) and determine the effect of *P. falciparum* infection on haematological parameters of both infected symptomatic and asymptomatic individuals. This research was carried out with aim of assessing the differences in haematological parameters and haemoglobin phenotypes in *P. falciparum* infected symptomatic and asymptomatic individuals in parts of Kaduna metropolis.

Materials and method:

Study area

This study was carried out in Kaduna metropolis, the capital of Kaduna State, Nigeria between March and November 2011. The state is located in North-western geopolitical zone and lies geographically within latitude $10^{\circ} 21' 23''$ N and longitude $7^{\circ} 26' 12''$ E, and is 608 meters above sea level. The state experiences both dry and rainy seasons. Dry season commences in the months of November to March and a rainy season usually from April through October and last between 4-5 months in the far and northern parts of the state and 5-6 months in the southern parts of the state, with vegetation typically of guinea savannah

type (9). Temperatures are high during the dry season, with annual average high temperature of 31.6°C , while relatively lower temperatures occur during the rainy season with annual low temperatures of 18.5°C (10).

The hospitals studied in the area were; Yusuf Dantsoho Memorial Hospital, Tudun Wada, Kaduna; Nigerian Army Reference Hospital (44), Kaduna; Gwamna Awang Hospital, Nassarawa, Kaduna; and St. Gerald Hospital, Kakuri, in Kaduna South LGA; and Barau Dikko Specialist Hospital, Kaduna; Barau Dikko Children Hospital; Kaduna; Nigerian Defence Academy Medical Centre, Ribadu Cantonment, Kaduna; and General Hospital, Kawo, Kaduna, in Kaduna North LGA.

Study population

The study population comprised of two subject categories; symptomatic malaria and asymptomatic apparently healthy individuals. Symptomatic subjects were persons manifesting aggregate of symptoms of falciparum malaria, which could either be mild uncomplicated or severe complicated malaria (11).

Ethical approval

Ethical approvals were obtained from Kaduna State Ministry of Health (MOH/ADM/744/T/9), the Federal Ministry of Health (NBTS/HQ/058/04), Nigerian Army Reference Hospital (44) (44/NARHK/GI/300/60) Kaduna, and confirmation was obtained from Nigerian Defence Academy Medical Centre and Saint Gerald Hospital.

Subject selection and recruitment

A sample size of 382 was obtained using a previous prevalence of 46.5% (12) in Kaduna State, and the formula described by Rothman et al., (13). However, a total of 1000 subjects comprising of 500 symptomatic and 500 asymptomatic subjects were randomly selected and recruited for the study.

Sample and data collection

During sample collection, biodata of all the subjects were collected with the aid of a questionnaire to obtain information on age, gender, occupation, socio-economic status, and daily recreational activities. In addition, information on malaria symptoms (mild or severe), type of anti-malaria drug intake, as well as the habitual use of mosquito net and insecticides by symptomatic individuals were recorded. Five millilitres of venous blood from each subject were collected into labelled tubes (vacutainer) containing Ethylene diamine tetra acetic acid (EDTA, sequestrene) anticoagulant (6). Medical personnel from selected hospitals

and the National Blood Transfusion Service (NBTS) assisted in sample collection.

Blood film microscopy for *P. falciparum*

Malaria parasite detection and parasitaemia level determination were carried out on thick blood films while parasite species were identified on thin blood film using the procedures described by Cheesbrough (6). Parasite density (parasitaemia) was estimated by counting number of parasites per 200 white blood cells (WBCs) assuming 8000 WBCs per μL of blood (5).

Haemoglobin electrophoresis (phenotypes)

The haemoglobin phenotypes of all subjects were determined by alkaline cellulose acetate electrophoresis (14), which was used to separate and identify the different haemoglobin types based on their migration within an electric field. Haemoglobin variants separate at different rates due to differences in their surface electrical charge as determined by their amino acids structure.

In performing the test, 100 ml of Tris-EDTA borate buffer was poured into each of the outer sections of an electrophoresis chamber. Cellulose acetate paper was impregnated with Tris-EDTA borate buffer and known control HbAA (normal adult haemoglobin phenotype), HbAS (sickle cell trait), HbAC, HbSS (sickle cell anaemia) and HbSSf (sickle cell anaemia with fetal haemoglobin) were placed at both ends of the cellulose acetate paper. Lysed blood samples were then placed between the controls using a Hb comb. The cellulose acetate paper was placed in the Hb electrophoresis tank containing Tris-EDTA buffer and run at 150 voltage for 15 min. Hb phenotypes were read according to their separation (14,15).

Haematological parameters

Haematological parameters were determined using automated blood analyser (Model KX-21N, Sysmex, Japan) on the blood samples. The following blood indices were determined; white blood cell (WBC) count and differentials

(neutrophil, monocytes and lymphocytes), platelets count, packed cell volume (PCV) or haematocrit, red cell counts, and red cell indices, which include mean corpuscular haemoglobin concentration (MCHC), mean corpuscular haemoglobin (MCH), and mean corpuscular volume (MCV) (14).

Statistical analysis

Data generated in this study were subjected to statistical analysis (SPSS version 17 statistical package). Association between *P. falciparum* infection in relation to different haemoglobin phenotypes of symptomatic and asymptomatic subjects was determined using Chi-square test. Means (\pm SD) of haematological parameters of *P. falciparum* infected symptomatic and asymptomatic subjects were compared using one way analysis of variance (ANOVA). Difference was considered significant at 95% confidence interval ($p < 0.05$).

Results:

Of the total 1000 subjects recruited for the study, 347 (34.7%) were positive for *P. falciparum* on blood film microscopy, which included 226 (45.2%) of 500 symptomatic and 121 (24.2%) of 500 asymptomatic individuals ($p < 0.00001$). Of the 347 *P. falciparum* infected subjects, 275 (79.3%) had HbAA, 61 (17.6%) had HbAS, 1 (0.3%) had HbAC, 8 (2.3%) had HbSS, and 2 (0.6%) had HbSSf phenotypes. Of the 226 symptomatic *P. falciparum* infected subjects, 163 (72.1%) had HbAA phenotype, while 112 (92.6%) of the 121 asymptomatic *P. falciparum* infected subjects had HbAA, which indicated a significantly higher frequency of asymptomatic malaria in subjects with HbAA ($p < 0.00001$). Conversely, 53 (23.5%) of the 226 symptomatic *P. falciparum* infected subjects had HbAS while 8 (6.6%) of 121 asymptomatic *P. falciparum* infected subjects had HbAS, indicating a significantly higher frequency of symptomatic malaria in subjects with HbAS ($p = 0.000086$) (Table 1).

Table 1: Prevalence of *Plasmodium falciparum* infection in relation to phenotypes of infected symptomatic and asymptomatic individuals

<i>Plasmodium falciparum</i> infection	No of subjects examined	No of subjects infected (%)	Haemoglobin phenotypes				
			HbAA (%)	HbAS (%)	HbAC (%)	HbSS (%)	HbSSf (%)
Symptomatic	500	226 (45.2)	163 (72.1)	53 (23.5)	0	8 (3.5)	2 (0.9)
Asymptomatic	500	121 (24.2)	112 (92.6)	8 (6.6)	1 (0.8)	0	0
Total	1000	347 (34.7)	275 (79.3)	61 (17.6)	1 (0.3)	8 (2.3)	2 (0.6)
<i>p</i> value		<0.00001	<0.00001	<0.000086	NA	NA	NA

NA = Not Applicable

Table 2: Distribution of *Plasmodium falciparum* parasitaemia level in relation to haemoglobin phenotypes of symptomatic and asymptomatic subjects

Haemoglobin phenotypes	No of subjects infected	Parasitaemia level (parasites/ μ L of blood)		
		<1000 (%)	1000-3000 (%)	> 3000 (%)
HbAA	275	199 (72.4)	70 (25.5)	6 (2.2)
HbAS	61	41 (67.2)	15 (24.6)	5 (8.2)
HbAC	1	0	1 (100)	0
HbSS	8	4 (50.0)	2 (25.0)	2 (25.5)
HbSSf	2	0	0	2 (100)
Total	347	244 (70.3)	88 (25.4)	15 (4.3)

The frequency distribution of *P. falciparum* parasitaemia among individuals of different haemoglobin phenotypes is presented in Table 2. Out of the 275 *P. falciparum* infected subjects with HbAA phenotype, 199 (72.4%) had parasitaemia level of < 1000 parasites/ μ L, 70 (25.45%) had parasitaemia level of <1000-3000 parasites/ μ L and 6 (2.2%) had parasitaemia level of >3000 parasites/ μ L. Of the 61 *P. falciparum* infected subjects with HbAS phenotype, 41 (67.2%) had parasitaemia level of <1000 parasites/ μ L, 15 (24.6%) had parasitaemia level of 1000–3000 parasites/ μ L, and 5 (8.2%) had parasitaemia level of >3,000 parasites/ μ L. Of the 8 *P. falciparum* infected subjects with HbSS phenotype, 4 (50.0%) had parasitaemia level of < 1000 parasites/ μ L, 2 (50.0%) had parasitaemia level of 1000–3000 parasites/ μ L, and 2 (25.0%) had parasitaemia level of > 3,000 parasites/ μ L. The frequency of parasitaemia > 3,000 parasites/ μ L of blood was 100% for HbSSf, 25% for HbSS, 8.2% for HbAS and 2.2% for HbAA, which showed significantly higher frequency in subjects with HbSS ($\chi^2=7.5989$, $p=0.0054$) and HbAS ($\chi^2=$

3.9627, $p=0.046519$) compared to HbAA phenotype. The only subjects with HbAC had parasitaemia level of < 3,000 parasites/ μ L but all the 2 subjects (100%) with HbSSf phenotype had parasitaemia level > 3,000 parasites/ μ L (Table 2).

The mean (\pm SD) haematological values of symptomatic *P. falciparum* infected subjects with HbAA and HbAS phenotypes are presented in Table 3. Significantly higher mean (\pm SD) value of MCHC was seen in HbAS (33.21 ± 2.430) compared to HbAA subjects (32.09 ± 2.315) ($p=0.003$). However, there were no statistically significant differences ($p>0.05$) in the mean (\pm SD) values of other haematological parameters between symptomatic *P. falciparum* infected subjects with HbAS and HbAA phenotypes (Table 3). The mean (\pm SD) haematological values of asymptomatic *P. falciparum* infected subjects with HbAA and HbAS phenotypes are presented in Table 4. There were no significant differences in the values of all the parameters between asymptomatic *P. falciparum* infected subjects with HbAS and HbAA phenotypes ($p>0.05$).

Table 3: Mean (\pm SD) haematological values of HbAA and HbAS phenotypes of infected symptomatic subjects

Haematological parameter	Haemoglobin phenotypes		p value
	HbAA (n=163) Mean (\pm SD)	HbAS (n=53) Mean (\pm SD)	
WBC $\times 10^9/L$	6.22 (\pm 2.987)	7.16 (\pm 4.228)	0.076
RBC $\times 10^{12}/L$	4.39 (\pm 0.807)	4.63 (\pm 0.869)	0.064
HB (g/dl)	12.11 (\pm 8.411)	12.45 (\pm 2.424)	0.772
PCV (%)	35.52 (\pm 6.492)	37.43 (\pm 6.904)	0.068
MCHC (g/l)	32.09 (\pm 2.315)	33.21 (\pm 2.430)	*0.003
MCH (pg)	26.17 (\pm 3.539)	27.00 (\pm 3.065)	0.128
MCV (fl)	81.73 (\pm 9.570)	81.23 (\pm 6.845)	0.727
LYM (%)	42.39 (\pm 15.383)	44.39 (\pm 16.514)	0.420
MONO (%)	10.51 (\pm 5.422)	9.67 (\pm 5.485)	0.333
NEUT (%)	46.71 (\pm 15.729)	45.93 (\pm 16.430)	0.756
PLATELETS ($\times 10^9/L$)	231.40 (\pm 128.844)	233.60 (\pm 97.855)	0.909

*Difference is significant ($p < 0.05$); WBC-White Blood Cells; RBC-Red Blood Cells; HB-Haemoglobin; PCV-Packed Cell Volume; MCHC-Mean Corpuscular Haemoglobin Concentration; MCH-Mean Corpuscular Haemoglobin; MCV-Mean Corpuscular Volume; LYM- Lymphocytes; MONO- Monocytes, NEUT-Neutrophils.

Table 4: Mean (\pm SD) haematological values of asymptomatic *Plasmodium falciparum* infected subjects with HbAA and HbAS phenotypes

Haematological parameters	Haemoglobin phenotypes		p value
	HbAA (n=112) Mean (\pm SD)	HbAS (n=8) Mean (\pm SD)	
WBC ($\times 10^9/L$)	5.12 (\pm 1.405)	5.50(\pm 2.014)	0.480
RBC ($\times 10^{12}/L$)	4.72(\pm 0.631)	4.68(\pm 0.680)	0.870
HB (g/dl)	14.04(\pm 0.811)	14.50(\pm 0.978)	0.131
PCV (%)	41.87(\pm 2.522)	43.18(\pm 4.302)	0.182
MCHC (g/l)	33.25(\pm 1.039)	32.89(\pm 1.066)	0.347
MCH (pg)	28.56(\pm 1.822)	28.59(\pm 0.985)	0.968
MCV (fl)	87.34(\pm 5.059)	86.95(\pm 3.513)	0.832
LYM (%)	36.76(\pm 8.851)	39.10(\pm 8.966)	0.472
MONO (%)	8.92(\pm 3.271)	10.83(\pm 6.387)	0.144
NEUT (%)	54.30(\pm 9.888)	50.08(\pm 12.864)	0.255
PLATELETS ($\times 10^9/L$)	213.19(\pm 62.359)	225.25(\pm 65.798)	0.599

WBC-White Blood Cells; RBC-Red Blood Cells; HB-Haemoglobin; PCV-Packed Cell Volume; MCHC-Mean Corpuscular Haemoglobin Concentration; MCH-Mean Corpuscular Haemoglobin; MCV-Mean Corpuscular Volume; LYM- Lymphocytes; MONO- Monocytes, NEUT-Neutrophils.

Discussion:

In this study, the prevalence of *P. falciparum* infection in both symptomatic and asymptomatic subjects examined was highest in those with HbAA phenotype, followed by those with HbAS phenotype. In a related study in Zaria, similar trend was also observed by Benjamin et al., (16) in which participants with HbAA phenotype had the highest percentage (76.9%) of malaria followed by those with HbAS (18.5%). The study by Onaiwu et al., (17) also revealed highest distribution of malaria infection among HbAA (66.7%) followed by HbAS (23.8%) among the study participants. This observation is similar to that of Albiti and Nsiah (18) who reported higher prevalence of *P. falciparum* among patients with HbAA phenotype than those with HbAS phenotype in Yemen. In another study in Nigeria, Esan (7), reported high frequency of

malaria attacks in persons with HbAA phenotype.

The susceptibility of individuals with haemoglobin phenotype AA to malaria infection is due to the low red cell membrane resistance to the invading parasite (19). Red cells are conducive for the growth and development of the parasite (17). However, the mechanism that cause reduction in the level of *Plasmodium* infection in heterozygous and homozygous sickle cell alleles (AS and SS), and confer resistance to *Plasmodium* infection was predicted to be due to distortion in the membrane of the cells as a result of which the morphology of the binding receptors on the surface of the red cell membrane cannot be recognized by the *P. falciparum* binding ligand (pfbl) (20).

The high parasitaemia level ($>3,000$ parasites/ μ L of blood) reported in subjects with HbSS (25%) and HbSSf (100%) phenotypes in this study is similar to the findings of Otajevwo

and Enabulele (19) who reported highest malaria infection rates of 71.4% among HbSS phenotype compared to others. This may be due to the non-protective nature of the HbS against severe falciparum malaria, and could be responsible for fatalities, especially in young infected children with sickle cell anaemia (2,6). The report of Daskum and Ahmed (21) showed that HbAS and HbSS do not impair parasite invasion of RBCs because high parasite densities are seen in *P. falciparum* infected RBCs of HbAS and HbSS *in vivo*. Despite their inability to impair parasite invasion, parasite growth was however proven to be impaired. According to Luoni et al., (22), phenotypes other than HbAC and HbCC are associated with reduced risk of clinical malaria and limited pathology, compared to severity of the disadvantaged HbSS and HbSC.

Significantly higher mean (\pm SD) value of mean corpuscular haemoglobin concentration (MCHC) was seen in HbAS compared to HbAA subjects in this study. This finding is in agreement with the study of Kosiyo et al., (23), who observed reduced MCHC among children with HbSS. MCHC is an index of red blood cells, derived from haemoglobin concentration and haematocrit, which are primary red cell measurements, and any factor affecting these parameters in either sickle cell or malaria patients would virtually affect MCHC (23).

Conclusion:

Although the frequency of *P. falciparum* infection in this study is generally higher in subjects with HbAA phenotype, symptomatic infection and higher parasite density are associated with HbAS, HbSS and HbSSf phenotypes. Effective utilisation of personal preventive measures by inhabitants, in addition to current malaria control and intervention strategies should be adequately implemented in Kaduna metropolis.

Acknowledgments:

The authors acknowledge the entire management and personnel of the hospitals sampled and the National Blood Transfusion Service (NBTS).

Contributions of authors

KBD conceived the study, carried out sample collection, sample analysis, data analysis and manuscript writing. DBM (deceased), YAU and ABS supervised and provided guidance on research conduct, manuscript

review and production. All authors read and approved the final version of the manuscript.

Conflicts of interest:

Authors declared no conflicts of interest

Funding:

This research was funded by the Nigerian Defence Academy Authority and the Tertiary Education Trust Funds (TETFUND) Nigeria.

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