



EFFECTS OF MALARIA PARASITEMIA ON HAEMATOLOGICAL PARAMETERS OF PREGNANT WOMEN ATTENDING GOMBE SPECIALIST HOSPITAL

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ABSTRACT

Malaria is a major public health problem in Sub-Saharan Africa. Most of the infections are asymptomatic, affecting mainly pregnant women and children. Blood samples were collected from 384 pregnant women. Data analysis was done using statistical package for social science version 20.0. Bivariate and Multivariate analysis were performed hence the P - value of less than 0.05 was considered significant. Out of the 284 (74%) pregnant women infected with malaria, 40.8% were within the age (21-25). Which has the highest rate of infection, whereas the lowest was ≥ 31 years (9.9%). The rate of infection base at the gestational age of pregnant women in the study tells that first trimester had the highest rate (41.9%) and third trimester had the lowest rate of infection (20.1%). In some of the hematological parameters, the total WBC, absolute lymphocytes and monocytes were significantly higher in the malaria infected patients than in non-infected pregnant women ($P < 0.05$). There was no significant difference in the basophil count between the malaria positive and the controls ($P > 0.05$). There was a significant difference in the levels of WBC, PLTC and MCV, MCH and MCHC; the insignificant difference between the first, second and third trimester of the positive cases and negative. In conclusion, Malaria infection can increase some of the physiological changes associated with pregnancy and should be prevented to save lives of the mothers and the babies.

keywords: Haematological, Infection, Malaria, Pregnancy, Women

INTRODUCTION

Malaria has been a major human health problem that threatens the lives of about 40% of the World's population causing morbidity and mortality worldwide (Gebremeskel and Krogstad, 2015). It is endemic in 100 countries making about half of the world's population to be at risk (Scuracchio *et al.*, 2011). About 50% of Nigerian population is reported to suffer from at least one episode of malaria each year (Imoru *et al.*, 2013). Nigeria has been reported to have the greatest burden of the disease among the endemic countries in the world. The tropical climate of Nigeria

accounts for the high prevalence of the disease, only south of Jos in Plateau State, Nigeria has lower incidence of malaria due to the low temperature of the area (FMH, 2008). Environmental and daily fluctuation of temperature is said to be associated with the infection rate and malaria parasite development (Paaijmans *et al.*, 2010). It was reported to be a common cause of miscarriage in pregnant women, premature delivery, low birth weight, maternal anemia, intrauterine growth retardation and intrauterine death (Aduloju *et al.*, 2013). Diagnosis of malaria in pregnancy using blood film detection technique becomes difficult when the parasite sequesters and

replicates in the placenta and therefore may not be found in the film (Public Health England PHE, 2014). Placenta malaria parasites can cross placenta wall either during pregnancy or at birth resulting into vertical transmission to the baby (Orogade, 2008). Malaria has resulted to about 11% of maternal and 30% of childhood mortality in Nigeria (CDC, 2012). Haematological parameters are used as indices to monitor the severity of malaria, the degree of changes in haematological parameters depend on the level of parasitemia, nutritional status, malaria immunity, and the endemicity of the disease (Maina *et al.*, 2010).

Malaria has been shown in many studies to worsen certain pregnancy outcomes (Rich *et al.*, 2009). These include an increased incidence of anaemia and spontaneous abortions. Others include intrauterine growth restriction (IUGR), stillbirths, prematurity, low birth weight, fetal distress and congenital malaria (Asa and Onayade, 2008). The biological basis for these adverse outcomes has been extensively studied. Erythrocytes infected with *Plasmodium falciparum* accumulate in the placental bed. This is through adhesion of the infected erythrocytes to molecules of Chondroitin a present in the placenta (Perlman and Troye, 2000). A prevalence of placental parasitaemia of between 10 and 45% in malaria endemic areas has been reported with significant *Plasmodium falciparum* dominance (Bruce, 1987). Pregnancy increases the frequency and severity of most infectious diseases but its effect on malaria seems worse (WHO, 2019).

Haematological changes are some of the most common complications in malaria and they play a major role in malaria pathogenesis. These changes involve the major cell types such as RBCs, leucocytes and thrombocytes (Ballem, 2018). Malaria infected patients tended to have significantly lower platelets, WBCs, lymphocytes, eosinophils, RBCs and Hb level, while

monocyte and neutrophil counts were significantly higher in comparison to non-malaria infected patients (Jensen *et al.*, 2017). One study showed patients with higher WBCs count compared with community controls, the most common complication during malaria infection is thrombocytopenia (Sullivan and Martin, 2015).

In Gombe State, Nigeria, about five million people are in the area of high malaria transmission. Diagnostic value of these haematological alterations may be easily obtained and useful in people living in malaria endemic areas. The present study was aimed to examine the effect of malaria on some haematological parameters in pregnant women in Gombe Specialist hospital. Haematological parameters including WBCs, RBCs, platelets count, PCV, haematocrit, differential leucocytes count, Mean corpuscular volume (MCV), Mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC). There is dearth of information on the effect of malaria parasitaemia on some haematological parameters in pregnant women in Nigeria particularly in Gombe North-Eastern Nigeria; perhaps the data acquired from this research will add value to the existing literature.

MATERIALS AND METHODS

Study Area

The study was conducted at the Gombe Specialist Hospital, located in the central part of Gombe town, Gombe State, North East of Nigeria (Figure 1).

Study Population and Design

The target population were consented pregnant women with malaria attending the hospital between May to July, 2019.

Study Design

A cross-sectional study was carried out among volunteering consented pregnant women with malaria attending specialist

hospital in Gombe State. A period of 2 month was used for sample collection before processing.

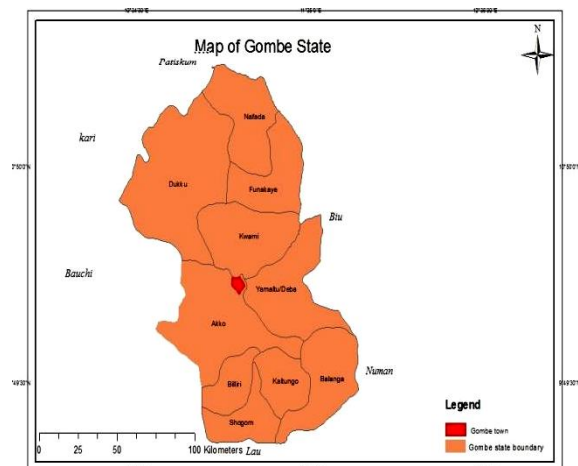


Figure 1: Map of Gombe State

Inclusion and Exclusion Criteria

Pregnant women with singleton pregnancies receiving antenatal care at the study centre participated in the study. Exclusion criteria were participants with pre-existing renal diseases, chronic kidney disease, hypertension and diabetes mellitus, human immunodeficiency virus, and acquired immune deficiency.

Ethical Approval and Consent

Ethical approval for the study was obtained from the Ethical Committee of the Gombe State Specialist Hospital. (Number: MOH/ADM/621/VOL.1/127) Consent from all participants was obtained prior to sample collection.

Sample Size Determination

In order to estimate the prevalence within 5% (or 0.05) allowable error and considering a 95% confidence level, a sample size of 384 (284 with gestational malaria as cases and 100 healthy pregnant women as controls) were used, as obtained through the following formula by Smith, (2013).

$$n = z^2 p (1 - p) e^2$$

Where $Z = 1.96$, $p = 50\%$ (0.5) i.e. probability of subject with desired characters and $e =$ standard error of the proportion, $e = 0.05$ Hence, A total Of 384 samples was collected.

Sample Collection

Blood samples were collected using phlebotomy procedure from each pregnant woman involved in this study and were subjected with a sterile needle and syringe. A total of 384 blood samples were collected from the Diagnostic service unit of Specialist Hospital Gombe

Procedure for Staining Thick Blood Film

This involved making thick blood films on clean grease free glass slides, allowed to air dry and stained with prepared Giemsa stain for 30 mintues. The Giemsa stain was prepared by diluting stock Giemsa stain in buffered water immediately before use. Stained slides were rinsed in clean water and allowed to air dry before examination under a microscope using X100 objective lens. Chromatin of malaria parasite was stained dark red and cytoplasm stained blue with Giemsa's stain. The presence of malaria parasite, identification of the species of human parasites and relative malaria parasite count in each blood sample was determined from the Giemsa stained thick films and Leishman stained thin blood films.

Malaria Parasitaemia was confirmed by microscopic examination using X100 objective lens (oil immersion lens). A slide was scored as negative when 100 high power fields had been examined for about 30 minutes without seeing any parasites. The amount of relative parasite count (Occurrence) in positive smears was done using a simple code from one to four crosses (+ - ++++), although none of the subjects had ++++. Malaria Parasitaemia occurrence was graded as; + = 1 – 10 parasites per 100 thick film field; ++ = 11–100 parasites per 100 thick film field; +++ = 1–10 parasites

per single thick film field; ++++ = more than 10 parasites per single thick film field after staining in 30 minutes as described by (Monica, 2005).

Procedure for Staining Thin Blood Film

Thin blood films were made on clean grease free glass slide and stained using Leishman staining technique as described by (Monica, 2005). The films were allowed to air dry and covered with Leishman stain for four minutes. The stain on the slides were diluted with buffered distilled water and allowed to stain for ten minutes. Slides were rinsed with water, allowed to air dry and examined under microscope using X100 objective lens.

Hematological Analysis

Immediately after the blood sample was collected, the following parameters were analysed using the automated blood Analyzer. Which include RBC, WBC, MCV, MCH, MCHC, Haematocrit, differential leukocyte and Platelet count?

Statistical Analysis

Data were entered into a computer and analysed using SPSS version 20.0 for Windows (SPSS Inc. Chicago, IL: USA). Simple percentages and description was used for the analysis. The results were presented in charts and tables where applicable.

RESULTS

Figure 2 below show the prevalence of malaria infection in various ages. The mean age of the participants was 28 years. Out of the total number of participants, 74% (284) had malaria confirmed by microscopy, whereas the rest tested negative 26%. The highest was observed at 21-25 years (40.8%) whereas the lowest was ≥ 31 years (9.9%). However, the mean age of the parasitemic and non-parasitemic pregnant women was 26.31 (± 9.94) years and 28.25 (± 10.14) years, respectively. Therefore, this close age range shows that age was not a confounding factor in our analysis.

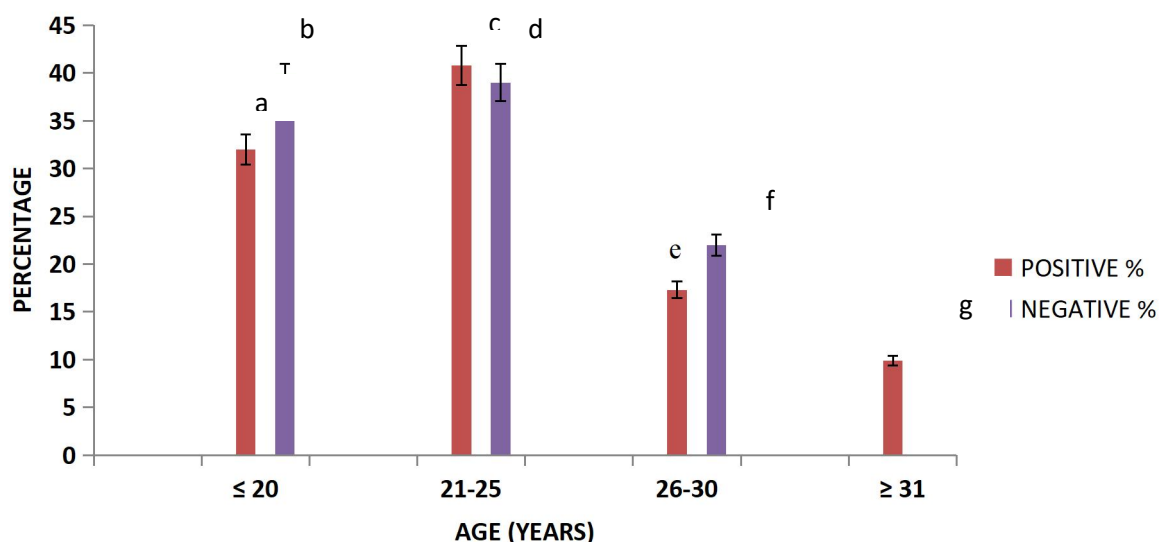


Figure 2: Association between malaria and age group of pregnant women in the study area. Different superscript letters are significant ($p < 0.001$) different compared across age group ($n = 384$).

Figure 3 below shows the prevalence in various gestational periods. The highest malaria infection among the women at their

first trimester 119 (41.9%) and the lowest was among third trimester 57 (20.1%).

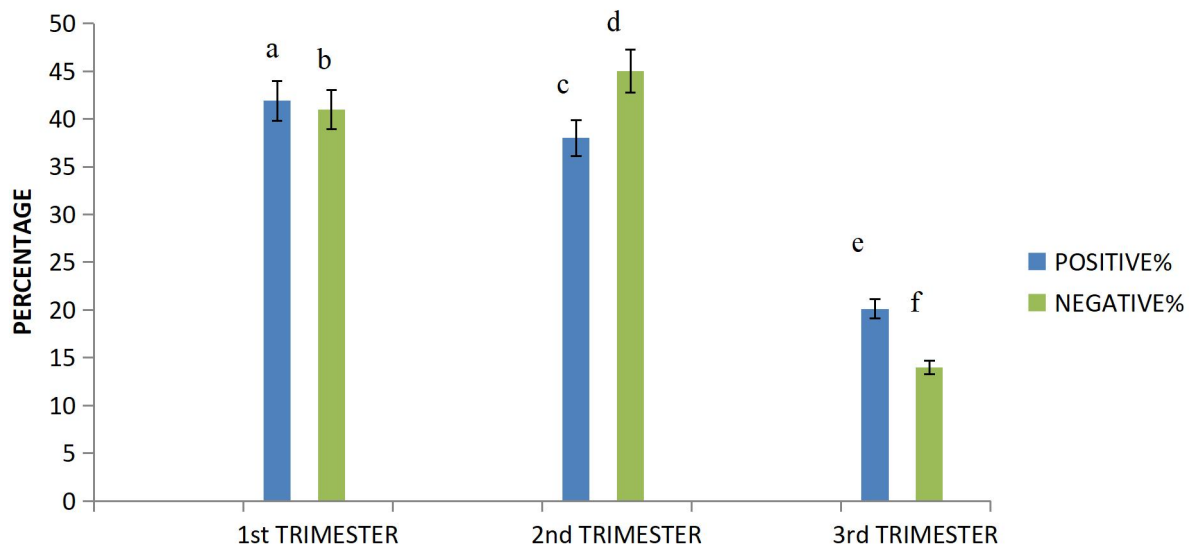


Figure 3: Association between malaria and gestational age of pregnant women in the study area.

Different superscript letters are significantly ($p < 0.001$) different compared across age group ($n = 384$).

Table 1 shows Effects of Malaria parasites on haematological parameters. The respective mean ($\pm$ SD) values of the total WBC count, lymphocytes, neutrophils, eosinophils, monocytes, RBC count, hematocrit, hemoglobin, RDW, platelets, and MPV in malaria parasitemic patients versus non-parasitemic patients are shown. The total WBC, the absolute lymphocytes and monocytes were significantly higher in the malaria infected patients than in the non-infected pregnant women ($p < 0.05$). However, the PCV, absolute neutrophils, eosinophil, and platelet count were lower significantly in the malaria patients than in the controls ($p < 0.05$). There was no significant difference in the basophil count between the patients and the controls

($p > 0.05$). The mean values for the platelet count and the differential percentage of lymphocytes were both significantly lower for the parasitic group compared with the non-parasitemic group.

There was a significant difference in the levels of PCV, WBC, PLTC, MCV, MCH and MCHC insignificant difference between the first, second and third trimesters of the positive cases and negative. A significant ($p < 0.005$) positive correlation using Pearson's correlation coefficient, was found between the PCV, RBC, WBC and PLTC. Parameters were affected by the gestational age and age of the pregnant women as shown in table 2 and 3.

Table 1: Effects of Malaria parasites on Haematological parameters

Parameter	Treatment		Test Statistics
	Positive Mean $\pm$ S.D	Negative Mean $\pm$ S.D	
PCV (%)	27.50 $\pm$ 0.41 ^a	30.57 $\pm$ 0.40 ^b	< 0.0001***
RBC($\times 10^{12}/L$)	4.04 $\pm$ 0.05 ^a	4.16 $\pm$ 0.06 ^c	< 0.0001***
MCV(fl)	75.62 $\pm$ 0.82 ^a	76.57 $\pm$ 1.28 ^b	0.025*
MCH(pg)	21.33 $\pm$ 0.51	25.11 $\pm$ 4.02	0.212ns

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MCHC(g/dl)	33.19±0.02	33.19±0.03	0.987ns
Platelet (x10 ⁹ /L)	164.94±6.34 ^a	172.86±6.14 ^c	< 0.0001***
PCT(ng/mL)	0.15±0.01 ^a	0.13±0.01 ^b	< 0.0001***
MPV	7.18±0.09 ^a	7.12±0.10 ^c	0.002*
PDW	8.48±0.25	8.61±0.27	0.177ns
Total WBC(x10 ⁹ /L)	4.82±0.29 ^a	5.45±0.23 ^b	< 0.0001***
Total Lymph	0.90±0.06 ^a	1.04±0.06 ^c	0.005*
Total Mono	0.34±0.02 ^a	0.33±0.01 ^b	0.001**
Total Grand	3.70±0.23 ^a	4.01±0.18 ^c	< 0.0001***
Lymphocyte (%)	22.70±1.22 ^a	25.02±1.01 ^b	< 0.0001***
Monocyte (%)	0.68±0.45	0.62±0.10	0.6602ns
Neutrophil (%)	74.46±1.57 ^a	74.24±1.09 ^c	< 0.0001***
Eosinophil (%)	1.94±0.20 ^a	0.26±0.06 ^b	< 0.0001***
Basophil (%)	0	0	---

Within parameter, Mean ± SD with different superscript are significantly different at $p < 0.05$.
a, b, c- indicates significant differences

PCV = Packed cell volume

Hb = Haemoglobin

Significant level = * $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$

ns = Not significant ($p > 0.05$)

Table 2: Effect of the interaction between gestational age and malaria parasite on haematological parameters (Mean ± SD)

MP results								
Gestational (trimester)		PCV (%)	WBC x10 ⁹ /L	RBC x10 ¹² /L	PLTC (x10 ⁹ /L)	MCV(fl)	MCH (pg)	MCHC (g/dl)
1 st	+ve	24.9±0.6	4.8±0.3	4.5±0.2	347±10	65.827±0.8	23.8±0.6	31.0±0.5
	-ve	32.1±0.6	8.4±0.3	9.6±0.2	198.9±10	84.4±0.8	32.1±0.6	32.9±0.5
2 nd	+ve	24.3±2.7	4.9±0.3	4.6±0.2	345.9±10	64.7±0.8	23.9±0.6	31.1±0.5
	-ve	31.7±2.6	7.9±0.3	7.9±0.2	208.7±10	84.7±0.8	31.6±0.6	33.1±0.5
3 rd	+ve	25.7±2.3	5.2±0.3	5.2±0.2	337.7±10	63.5±0.8	23.9±0.6	29.0±0.5
	-ve	32.8±1.5	8.8±0.3	8.8±0.2	204.8±10	85.6±0.8	32.5±0.6	33.3±0.5
Sig.	G. age	0.16(NS)	0.07(NS)	0.16(NS)	0.15(NS)	0.18(NS)	0.17(NS)	0.10(NS)
	Parasite	***	***	***	***	***	***	***
	Interaction	0.4 (NS)	0.9 (NS)	0.4 (NS)	0.9 (NS)	0.4 (NS)	0.9 (NS)	0.9 (NS)

Table 3: Effect of the interaction between age and malaria parasite on haematological parameters (Mean $\pm$ SD)

Age (Years)	MP results	PCV (%)	WBC $\times 10^9/L$	RBC $\times 10^{12}/L$	PLTC ($\times 10^9/L$)	MCV(fl)	MCH (pg)	MCHC (g/dl)
≤ 20	+ve	23.9 $\pm$ 1.9	4.6 $\pm$ 0.7	4.3 $\pm$ 0.7	344 $\pm$ 10	65.8 $\pm$ 0.8	23.5 $\pm$ 0.6	27.0 $\pm$ 0.5
	-ve	31.1 $\pm$ 1.8	8.3 $\pm$ 1.0	9.3 $\pm$ 0.9	346 $\pm$ 10	84.4 $\pm$ 0.6	32.1 $\pm$ 0.6	32.9 $\pm$ 0.5
21 – 25	+ve	22.8 $\pm$ 2.1	4.5 $\pm$ 0.8	4.1 $\pm$ 0.8	348.9 $\pm$ 0.6	64.7 $\pm$ 0.7	21.9 $\pm$ 0.6	30.2 $\pm$ 0.5
	-ve	32.4 $\pm$ 2.9	8.6 $\pm$ 1.9	9.4 $\pm$ 2.0	348.8 $\pm$ 0.6	84.7 $\pm$ 0.9	31.6 $\pm$ 0.6	33.1 $\pm$ 0.5
26 – 30	+ve	23.4 $\pm$ 2.9	4.7 $\pm$ 1.7	4.5 $\pm$ 1.8	349.8 $\pm$ 0.6	67.5 $\pm$ 0.5	23.1 $\pm$ 0.6	30.0 $\pm$ 0.5
	-ve	31.3 $\pm$ 1.9	8.3 $\pm$ 1.3	9.5 $\pm$ 0.9	347.7 $\pm$ 0.6	85.6 $\pm$ 0.4	32.5 $\pm$ 0.6	33.3 $\pm$ 0.5
Sig.	Age	***	***	***	***	***	***	***
	Parasite	0.19 (NS)	***	0.19(N S)	***	0.16 (NS)	***	0.16 (NS)
	Interaction	***	***	***	***	***	***	***

DISCUSSION

The prevalence rate of 74% found in this study is relatively high. There were results higher than the values obtained such as that of Aribodor, *et al.*, (2003) with 73%, 66.0%, respectively. However, Mvondo *et al.*, (2012) obtained lower values of 45.0%. The high prevalence rate recorded in this study area (Gombe) may be due to the fact that the climate and vegetation contributed to this prevalence. The seasonal rainfall is higher and longer which gives rise to much surface water to support the breeding of vectors. The period of study which is the rainy season also may have contributed to the high infection rate. High rate of malaria transmission during rainy season has been reported by Uneke *et al.*, 2006.

There was a higher prevalence of malaria among younger pregnant women between the ages of 21-25 years than older women. This agreed with the findings of Dicko *et al.*, (2008) who opined that adolescents and young adult pregnant women were more susceptible to malaria than older pregnant women; as a result of continuous development of malaria immunity. Pregnant women in their first trimester had the highest prevalence than those in second and third trimesters. This correlated with the work done by Brabin *et al.*, 2008 in western Kenya that prevalence was highest at 13–16 weeks' gestation (First trimester), and found similar number of recoveries in both groups

during the second and third trimesters. The loss of immunity in early pregnancy was equivalent to an 11-fold decrease in the rate of recovery from infection. The recovery seen in the late pregnancy suggests that the women mount a satisfactory immune response to malaria infection, re-acquiring their pre pregnancy immune status at about the time of delivery (Ingrid *et al.*, 2012). The observation could also be as a result of constant intermittent preventive treatment (IPT) given to these women during antenatal care visit which usually commence during second trimester.

However, this study found a progressive decline in Hb concentration from the first to the third trimester, but a drop from first to the second trimester. There was a slight rise in the PCV in the third trimester. These findings corroborate those of a similar study undertaken in Ibadan, south-western Nigeria, by Akingbola *et al.*, (2016) which reported exactly the same pattern the progressive decline in Hb concentration from the first to third trimester may be due to an increased demand for iron as pregnancy progresses. More iron is required to meet the expansion of maternal Hb mass and the needs of fetal growth. The additional progesterone and estrogen that are secreted by the placenta during pregnancy cause a release of renin from the kidneys. Renin stimulates the aldosterone-renin-angiotensin mechanism, leading to sodium retention and increased

plasma volume. The increase in plasma volume is relatively greater than the increase in red cell mass, which results in a fall in maternal Hb, hence the physiological anemia that occurs in pregnancy. Despite the physiological hemodilution associated with pregnancy, which also contributes to the drop in PCV in the first and second trimester, in late pregnancy, plasma volume increases at a slower rate, inducing a slight rise in hematocrit that may account for the slight rise in PCV in the third trimester (Shen *et al.*, 2010).

The increase observed in WBC count from the first to third trimester in this study is consistent with the findings of Akingbola *et al* (2016). The increase is primarily due to an increase in neutrophils and may represent a response to stress due to redistribution of the WBCs between the marginal and circulating pools. Pain, nausea, vomiting, and anxiety have been reported to cause leukocytosis in the absence of infection (Milhorat *et al.*, 2015). However a rising WBC count in pregnancy is not a reliable indicator of infection in subclinical chorioamnionitis; rather, clinical methods of detection such as maternal pyrexia, offensive vaginal discharge, and fetal tachycardia are better indicators, especially of preterm labor and membrane rupture. (WHO, 2019) This study also reported a gradual reduction in PLT count as pregnancy advanced, which is also consistent with (Akingbola *et al.*, 2016) study. Due to hemodilution secondary to expansion of plasma volume, the PLT count in normal pregnancies may decrease by approximately 10%, with most of this decrease occurring during the third trimester (McCrae, 2013; Ballem, 2018) although the absolute PLT count tends to remain within the normal reference range in most patients. (Burrows *et al.*, 2013; Sullivan and Martin 2017)

After anemia, thrombocytopenia is the second most common hematologic abnormality that occurs during pregnancy

(Magann and Martin, 2019). The overall incidence of thrombocytopenia in pregnancy is 8%, but when patients with obstetric or medical conditions are excluded, the incidence drops to 5.1% (Magann and Martin, 2019). MCV declined from the first to third trimesters in this study, while MCH remained relatively stable through all trimesters. MCHC was stable in the first and second trimester, but dropped in the third. Considered mildly depressed; from 50,000 to 100, 000 $\times 10^9/L$, moderately depressed; and of less than 50,000 $\times 10^9/L$, severely depressed (Magann and Martin, 2019). The overall incidence of thrombocytopenia in pregnancy is 8%, but when patients with obstetric or medical conditions are excluded, the incidence drops to 5.1% (Magann and Martin, 2019). MCV declined from the first to third trimesters in this study, while MCH remained relatively stable through all trimesters. MCHC was stable in the first and second trimester, but dropped in the third.

CONCLUSION

Malaria infection during pregnancy have adverse effects on maternal haematological parameters, particularly haemoglobin concentration, it is well established that anaemia is the most common consequence of *P. Falciparum* malaria infection. Malaria infection can increase some of the physiological changes associated with pregnancy and should be prevented to save lives of the mothers and the babies.

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