EFFECT OF FALCIPARUM MALARIA ON HAEMATOLOGICAL PARAMETERS IN MALARIA INFECTED PATIENTS IN SOKOTO METROPOLIS

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ABSTRACT

Aim: This study was aimed at evaluating various effects of *falciparum* malaria on haematological parameters in malaria infected patients.

Study design: Hospital based cross-sectional study.

Place and duration of study: The study was conducted in Specialist Hospital, Sokoto Metropolis, Sokoto State Nigeria between May 2015 and November, 2015.

Methodology: Two hundred and fifty four (254) malaria suspected patients were recruited for the study. Thick and thin blood films were prepared for each patients and stained with Giemsa to aid the detection of malaria parasites. Patients haematological parameters were determined using hematology analyzer (Sysmex KX-21N).

Results: Out of the 254 patients, 167 (65.7%) had malaria. Significant differences in haematological parameters between *P. falciparum* malaria parasitemic patients and non parasitemic patients were only observed in mean (±SD) of the WBC (10.13±3.11x10³/µl versus 5.10±2.51x10³/µl, $P = .003$), Hb (12.54±2.15g/dl versus 8.13±1.68g/dl, $P= .001$) and the platelet count (262.67±112.13x10³/µl versus 125.67±41.70x10³/µl, $P = .005$). The mean (±SD) values of the red blood cells indices (MCV, MCH, MCHC) and differential lymphocyte and granulocyte count did not significantly differ between the two groups. Changes in haemoglobin, platelets and white blood cell count are the classical alterations.

Conclusion: Changes in haematological parameters are only indicators of probable malaria infection, but when used with other clinical and microscopy parameters, they can significantly improve malaria diagnosis and timely further treatment for malaria infection.

Keywords: Falciparum malaria, hematological parameters, Infection, Sokoto.

1.0 INTRODUCTION

Malaria, sometimes called the "King of Diseases", is a life-threatening, parasitic disease caused by protozoan parasites of the genus *Plasmodium*. It is transmitted from one person to another by the bite of infected female *Anopheles* mosquitoes. The most serious and sometimes fatal type of malaria is caused by *Plasmodium falciparum*. The other human malaria species, *P. vivax*, *P. ovale*, *P. malariae*, and sometimes *P. knowlesi* can cause acute, severe illness but mortality rates are low. Malaria is the most important infectious disease in tropical and subtropical regions, and continues to be a major global health problem, with over 40% of the world's population exposed to varying degrees of malaria risk in some 100 countries [1].

In Nigeria, malaria is endemic and stable, being a major cause of morbidity and mortality, resulting in 25% infant, 30% childhood and 11% maternal mortality [2]. It accounts for 300,000 deaths each year and about 60% of outpatient visits. It is estimated that about 100 children under one year and 203 children under-five years out of 1000, respectively, die annually [3]. In other words, one out of every five Nigerian children dies before his/ her fifth birthday [4].

Changes in hematological parameters are influenced by any disease condition which affects the haemopoetic physiology. This occurs with an endemic disease such as malaria [5]. 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 [6]. 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 [7]. The most common complication during malaria infection is thrombocytopenia [8]. The infection of red cells by malaria parasites, particularly *P. falciparum* results in progressive and dramatic structural, biochemical and mechanical modifications of red cells that can worsen into life-

threatening complications of malaria [9]. ~~While the vast majority of severe malaria and related mortality is caused by *P. falciparum* infection~~

2.0 MATERIALS AND METHODS

2.1 Study Design: The study was hospital based cross sectional and involved patients of all ages attending the outpatient clinics that were suspected of having malaria and referred by the resident clinician for blood examination at Specialist Hospital Sokoto (SHS) and Maryam Abacha Women and Children Hospital in the metropolis for initial diagnosis or follow-up of malaria.

2.2 Study Area

Sokoto is the capital city of Sokoto State, lies between latitude 13° 3' 490N, longitude 5° 14' 890E and at an altitude of 272 m the sea level above. It is located in the extreme North Western part of Sokoto North and South local government areas and also some parts of Kware LGA from the North, Dange Shuni LGA from South and Wamakko LGA to the West. Sokoto metropolis is estimated to have a population of 427,760 people [10] and by the virtue of its origin, the state comprises mostly Hausa/Fulani and other groups. Rainfall starts late that is in June and ends early in September but may sometimes extend into October. The highest temperatures of 45°C during the hot season are experienced in the months of March and April [11]

2.3 Sample Size Calculation

The sample size was determined using the following formula:

$$n = \frac{z^2pq}{d^2}$$

Where: n = Sample size, z = Standard normal deviates, p = Prevalence factor, q = Complementary proportion of p (1- p), d = Tolerable margin of error, d = Tolerable margin of error

Thus,

n = ?, z = 1.96,

p = (20.9%) (Abdullahi *et al.,* 2009)

q = (1- 0.209) = 0.791, d = (5%) = 0.05

$$n = \frac{(1.96)^2 \times 0.209 \times (1- 0.209)}{(0.05)^2}$$

= 254

2.4 Samples Collection:

Three (3) ml of venous blood was collected under sterile conditions from each individual into a labeled anticoagulant (EDTA) containers and stored immediately at -20˚C until needed for laboratory examination.

2.5 Sample Analysis

Thick and thin blood smears were prepared as described by the WHO standard method.

2.5.1 Staining thick and thin Blood Film

Giemsa stain

The thin film was fixed by briefly dipping it in methanol and allowed to air dried. Both the thick and thin film slides were placed on the staining rack. The stain was gently poured onto the slides and allowed to stained for 10 minutes. It was gently washed from the slide by adding drops of clean water and then placed in the drying rack, film side downwards, to drain and dry [12].

2.5.2 Analysis of Haematological Parameters Using Haematology Analyser (Sysmex KX-21N)

~~Sysmex machine was inspected (for instrument, reagents, waste bin and printer paper) before switch on the machine from power source, machine was calibrated before used and control sample run along each batches of sample analysis.~~ Well mixed EDTA blood sample was used for the analysis of full blood count, blood sample was aspirated through the sample probe one after another by pressing start switch on the machine, sample was analyzed, rinsed and the results were displayed on the LCD screen of the machine and also results were printed out. After the analysis, machine was shut down by aspirating cell clean which washed and rinsed the machine before finally shutdown and switched off from the power source [13].

2.6 Statistical Analysis

The data obtained were analyzed using SPSS version 20. The result were expressed as percentage and Mean ±SD. Group comparison were made using one way analysis of variance (ANOVA), paired comparison were carried out using the student t test and P-value of equal to or less than .005 ($P \leq .005$) was considered as significant.

3.0 RESULTS AND DISCUSSION

Out of 254 patients recruited in the study, there were 134 (52.8%) males and 120 (47.2%) females. 167 were positive by microscopy, thus giving a prevalence of 65.7%. The gender specific infection rate showed that males had the higher infection rate of 98(73.1%) than females who had a total of 69(57.5%) infection (Table 1). The study according to age showed that the age group 10-19 years had the highest infection rate 72% within the age group while the age group 40-49 years had the least infection rate of 52.8% (Table 2). Moderate infection (2+) represented

the highest percentage accounting for 50.3%, followed by scanty infection (1+) 35.9%. The percentage of infected subjects manifesting heavy infection (3+) was 9.6% while very heavy infection (4+) represented the least percentage accounting for 4.2% (Table 3).

Haematological parameters for the malaria parasitemic group were then compared with those of the non parasitemic group using the student's t test as shown in table 4. The respective mean (±SD) values of the total WBC Count, RBC Count, Hb, haematocrit, MCV, MCH, MCHC, Platelets, lymphocytes and granulocytes in malaria parasitemic patients versus non parasitemic patients are shown in table 4. The mean values for the total WBC count, platelets count, and Hb were significantly lower for the parasitemic group (5.10±2.51)x10^3/µl, (125.67±41.70)x10^3/µl, and (8.13±1.68)g/dl compared with non parasitemic group (10.13±3.11)x10^3/µl, (262.67±112.13)x10^3/µl, and (12.54±2.15)g/dl.

At present about 100 countries in the world are considered malarious. More than 2.4 billion of the world populations are still at risk. The incidence of malaria worldwide is estimated to be 300-500 million cases each year. Malaria is thought to kill between 1.1 to 2.7 million people worldwide each year. In Nigeria account for 300, 000 death each year and about 60% of out patients visit [14].

The high rate of malaria prevalence in the blood samples examined was quite worrisome. This is a reflection of the high rate of malaria parasitaemia in endemic malaria regions. The total prevalence of malaria infection in the study population was 65.7%. These results are higher than those of Abdullahi *et al.* [15] who in a similar research in Sokoto reported 27.29% prevalence rate, but lower than those of James *et al.* [16] who reported 70.6% prevalence in Northwestern Nigeria, and also lower than that of Adekunle *et al.* [17] who reported 71.1% prevalence in Ogun State. This result is also higher than the 40% annual prevalence rate found in Nigeria [18]. The

males had a relatively higher prevalence rate of 73.1% compared with their female counterparts that had prevalence rate of 57.5% that was statistically significant (*P = .002*).

This finding is in agreement with other study by Sethi *et al.* [19] who reported 59.5% prevalence in males and 40.5% in females. Similar reports had indicated a higher prevalence in males than females [14,20]. Studies had shown that females have better immunity to malaria and varieties of other parasitic diseases than males [21]. This may equally be attributed to the fact that males expose themselves to the bites of mosquitoes and other vectors more than females, especially when the weather is hot and during farm work [22]. Exception is found during pregnancy and reproductive ages, when females are more vulnerable to malaria attacks due to immune suppression [22].

Malaria prevalence was statistically significant in the various age groups (*P = .001*). The maximum numbers of cases were seen in the age group of 10-19 years and this compare favourably with the research by Chandrakanth [23] who reported the maximum cases in the age group of 10-20 years. This is in contrary to Sethi *et al.* [17] who reported the highest prevalence in the age group of 21-30 years.

Haematological abnormalities are considered a hallmark of malaria, and the one that have been reported to invariably accompany infection with malaria include anaemia, thrombocytopenia, splenomegaly, mild to moderate atypical; lymphocytosis and rarely disseminated intravascular coagulation (DIC) [24]. The results from this study showed that haematological parameters of patients with uncomplicated *P. falciparum* malaria are unreliable indicators for the presence of disease. Previous studies have revealed significant morphological and numerical changes in all the blood cell lines in malaria [1,2,25]. The changes observed however, were usually dependent on the parasite species [26,27], disease severity [3] and the immune status of an individual

[28,29], and therefore were found to vary from one person to another or from one region to another.

Leukocytes play a vital role in defense against malaria. Leukocyte changes in malaria are variable and depend on many factors such as acuteness of infection, parasitemia, disease severity, state of the host immunity to malaria and concurrent infections [30]. Majority of patients with acute uncomplicated *P. falciparum* malaria usually have their mean total leukocyte count (TLC) within normal range. However in some cases a mild leucopenia may occur especially in non immune adult or in case of complicated malaria [31]. The mean total leukocyte count in parasitemic patients in this study was 5.10±2.51x10/ul which is in agreement with results from prior studies [27]. Nevertheless despite the fact that the mean total leukocyte count in parasitemic patients was normal, it was significantly (*P = .003*) lower than that of the non parasitemic group (10.13±3.11 $x10^3/\mu l$). These findings are similar to those from a study by Haroon *et al.* [31] in which a significant decrease in mean TLC in the parasitaemic group was observed.

The finding in this study shown that in acute malaria, anemia (Hb< 11g/dl) is a common presentation, and this was in concordance with other studies [32,33]. In this study the mean Hb in parasitemic group (8.13±1.60g/dl) were significantly lower (*P = .001*) than that of the control group (12.54±2.15 g/dl). The pathogenesis of anemia in malaria is extremely complex, multifactorial and incompletely understood. It is thought to result from a combination of hemolysis of parasitized red blood cells, accelerated removal of both parasitized and innocently unparasitized red blood cells, depressed as well as ineffective erythropoiesis and dyserythropoietic changes [34]. Other factors include decreased red blood cell deformability,

splenic phagocytosis and /or pooling [35] so they have an increased rate of clearance from the circulation.

Platelets and coagulation factors are part of the extraordinary complex environment that surrounds flowing or sequestered parasitized RBCs and the enclosing tubular vascular endothelium [30]. Because of that, a lot of research work has been dedicated to determining the effect of malaria on platelets homeostasis. What is now apparent from those study is the fact that thrombocytopenia is major complication of malaria [5,26,27,36]. the magnitude of which is dependent on parasite species or disease severity.

In this study, the mean platelets counts in parasitemic group (125 (±41.70) x $10^3/\mu l$) were significantly lower than that of the non parasitemic group (262.67 (±112.13) x $10^3/\mu l$). These observations may imply that thrombocytopenia may be a marker *P. falciparum* infection. The association of platelets count and malaria infection has previously been described [5,37]. This is in conformity with previous study by Saravu *et al.* [25] who concluded that thrombocytopenia is observed in malaria.

The pathogenesis of thrombocytopenia is thought to involve a constellation of processes, some of which include splenic pooling of platelets, antibody (IgG) mediated platelets destruction, adenosine diphosphate (ADP) release following the haemolysis of parasitized RBC's, platelet aggregation and activation, parasite invasion of platelets, platelets phagocytosis, platelet adhesion to erythrocytes, dysmegakaryopoiesis and oxidative stress [30].

As observed elsewhere [38], the mean red blood cell indices (MCV, MCH, MCHC) of parasitemic group in this study were normal. This probably may be because uncomplicated malaria is associated with milder biochemical changes, for example, a lower production of

cytokines, less endothelial cell activation, milder changes in coagulation profile, less sequestration and less hemolysis as opposed to complicated/severe malaria.

Table 1: Prevalence of *P. falciparum* malaria with respect to gender

Gender	*P. falciparum* infection			
	Negative (%)	Positive (%)	Total (%)	*P-value*
				.002*
Male	36(26.9)	98(73.1)	134(52.8)	
Female	51(42.5)	69(57.5)	120(47.2)	
Total	87(34.3)	167(65.7)	254(100)	

*Values differ significantly (*P = .002*) between male and female

Table 2: Prevalence of *P. falciparum* malaria within age group

Age group (yrs)	*P. falciparum* infection			
	Negative (%)	Positive (%)	Total (%)	*P-value*
				.001*
≤ 9	5(35.7)	9(64.3)	14(5.5)	
10-19	7(28)	18(72)	25(9.8)	
20-29	25(32.1)	53(67.9)	78(30.7)	
30-39	18(28.6)	45(71.4)	63(24.8)	
40-49	17(47.2)	19(52.8)	36(14.2)	
≥ 50	15(39.5)	23(60.5)	38(15.0)	
Total	87(34.3)	167(65.7)	254(100)	

*Values differ significantly (*P = .001*) between male and female

Table 3. Distribution of infected subjects according to level of parasitaemia

Level of parasitaemia	Total	Percentage (%)
Scanty infection (1+)	60	35.9
Moderate infection (2+)	84	50.3
Heavy infection (3+)	16	9.6
Very heavy infection (4+)	7	4.2
Total	167	100

Table 4: Comparison of haematological parameters between parasitemic (smear positive) and non parasitemic (smear negative) patients.

Parameters	Smear Negative (n=87) Mean±SD	Smear Positive (n=167) Mean±SD	Mean difference	95% Confidence Interval (CI)	*P value*
Age (yrs)	33.51±14.69	30.28±15.20	-3.23	-10.26 – 3.79	.36
WBC ($10^3/\mu l$)	10.13±3.11	5.10±2.51	-5.03	-6.28 – 3.78	.003*
RBC ($10^6/\mu L$)	4.01±1.77	3.80±1.68	-0.21	-0.95 – 0.53	.57
Hb (g/dl)	12.54±2.15	8.13±1.60	-4.41	-5.22 – 3.60	.001*
PCV (%)	34.62±11.39	31.99±9.11	-2.63	-7.27 – 2.01	.26
MCV (fl)	80.34±11.32	81.17±15.19	0.83	-5.47 – 7.12	.79
MCH (pg)	30,92±16.51	35.01±18.97	4.09	-4.60 – 12.78	.35
MCHC (g/dl)	37.07±14.95	40.82±16.99	3.75	-4.06 – 11.56	.34

Plt ($10^3/\mu l$)	262.67±112.13	125.67±41.70	-137.00	-173.79 – 100.21	.005*
Lymphocyte (%)	49.98±20.89	58.05±63.75	8.06	-17.66 – 8.99	.51
Granulocyte (%)	42.40±24.03	38.07±22.75	-4.33	-6.33 – 30.54	.19

±± Values are Mean ± Standard Deviation of the Mean of parasitemic and non parasitemic patients.

* Values differ significantly ($P \leq .005$) between parasitemic and non parasitemic patients

WBC= White Blood Cell Count, RBC= Red Blood Cell Count, Hb= Haemoglobin, PCV= Packed Cell Volume, MCV= Mean Cell Volume, MCH= Mean Cell Haemoglobin, MCHC= Mean Cell Haemoglobin Concentration, Plt= Platelets.

CONCLUSION

Malaria parasitaemia has been shown to have effects on some haematological parameters from this study while some haematological parameters are more predictive of malaria infection than others. Anaemia (<11g/dl), thrombocytopenia ($<150x10^9$/l) and changes in total WBC count ($<4x10^9$/l) were identified as the key haematological indicators of malaria infection in the studied population. Although changes in haematological parameters are only indicators of probable malaria infection, when used with other clinical and microscopy parameters, they can significantly improve malaria diagnosis and timely further treatment for malaria infection. The major limitation of this study was the small number of patients with deranged hematological parameters especially in the parasitemic group, which created a slightly higher margin of error in the determination of the diagnostic relevance of the deranged parameters. Lack of previous

medical histories such as other diseases that may have analysis bias such as Hb diseases and anaemia, which could potentially affect the interpretation of the results. Subjective errors and manual errors cannot be excluded. It would be interesting and beneficial to study and compare the different reports discussing the haematological findings in patients living in endemic areas

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COMPETING INTERESTS

Authors have declared that no competing interests exist

AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. Authors NM and AS designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author MB and Author AA managed the analyses of the study and Author MU and NF managed the literature searches. All the authors read and approved the final manuscript.

CONSENT

Objectives and procedures of the research were explained to the subjects. Since this study involves invasive procedures, an informed consent was obtained from all the respondents and/or from their next of kin prior to blood sample collection.

ETHICAL APPROVAL

Ethical approval to conduct this study was obtained from the ethics and research committee of Specialist Hospital and that of Maryam Abacha Women and Children Hospital Sokoto in accordance with the clinical and university standard.

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