Haematological Parameters of Individuals Infected with *Plasmodium falciparum* in Parts of Kaduna Metropolis, Kaduna State, Nigeria

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Abstract: Malaria remained a major public health problem in Nigeria, *Plasmodium falciparum* account for most malaria cases, changes in haematological parameters are main features of *P. falciparum* infection. The aim of this study is to assess changes in haematological parameters of *P. falciparum* infected symptomatic and asymptomatic individuals. Five hundred blood samples from each category were collected. Parasites detection and parasitaemia level determination were performed on thick blood films, parasites were identified on thin film. Complete Blood Counts (CBCs) of all blood samples were performed using automated blood analyser (Model KX-21N. Sysmex, Japan). Results shows significantly lower mean (±SD) values of neutrophils, RBC, Hb, PCV, MCHC, MCH and MCV in symptomatic individuals compare to asymptomatic individuals (P<0.05). Packed Cell Volume and MCH were significantly lower (P<0.05) in symptomatic individuals with high level of parasitaemia. Significant increase in lymphocytes and monocytes was observed in symptomatic and asymptomatic individuals with high parasitaemia, Platelets level was significantly lower in asymptomatic individuals. Reduced PCV values recorded are features of anaemia, reduced red cell indices are features of iron deficiency anaemia. Significant increase in lymphocytes observed in this study may be attributed to antimalarial drugs intake by symptomatic individuals.

Keywords: Haematological Parameters, *P. falciparum* Infection, Symptomatic, Asymptomatic, Individuals

1. Background

Blood plays vital role in protecting the body against infectious and foreign bodies including parasites. Malaria parasites *Plasmodium* invade and reside in the red blood cells causing enormous destruction of the parasitized red blood cells [1]. Malaria is one of the leading cause of high morbidity and mortality rates in the world. The burden imposed by malaria on the society and the nation at large is enormous. It has adverse effect on the physical and social well being of people and has been reported to be one of the most economically significant diseases of humans. It is one of the leading cause of high morbidity and mortality rates in the world [2].

It was estimated that about 198 million cases of malaria occurred worldwide in 2013, with an estimated 584,000 deaths. In addition, 3.2 million people were at risk of being infected with malaria and developing disease, while 1.2 billion others are at high risk of infection; Africa was estimated to have the heaviest burden accounting for 90% of all malaria deaths, 78% of which occurred among children aged less than five years [3]. Malaria is endemic in Nigeria, with transmission occurring throughout the year, approximately 97% of the population are at risk of infection [4, 5].

*Plasmodium falciparum* is by far the most important
malaria parasite in Africa, it accounts for over 90% of malaria cases, with cases untreated resulting in ill health and death, particularly in young children, pregnant women and non-immune adults. Infection with *P. falciparum* may result in wide variety of symptoms, ranging from mild to severe disease, and could be described as uncomplicated and severe malaria [1, 6, 7].

Uncomplicated malaria is defined as symptomatic malaria without signs of severity or evidence of clinical or laboratory evidence of vital organ dysfunction. The signs and symptoms of uncomplicated malaria are nonspecific and usually accompanied with fever. Severe malaria results from ineffective or delayed treatment of *P. falciparum* infection. In both cases, infection progresses to severe malaria with manifestations of complications. Severe falciparum infection is one of the major causes of anaemia in humans [8].

The invasion of red blood cells by malarial parasites results in changes in haematological parameters, although such changes may vary depending on the level of disease endemicity, nutritional status, genetic factor, socio-demographic condition, and host immunity [9, 10, 11].

Several studies have been carried out to determine the effect of *P. falciparum* infection on the haematological parameters of infected and non-infected individuals [12, 10, 11]. Malaria has been reported to be the cause of childhood morbidity which is associated with varied haematological consequences. The haematological parameters of malaria-infected and non-infected children evaluated showed significantly lower values of platelets, lymphocytes, eosinophils, red blood cell counts and haemoglobin in malaria-infected children while absolute monocytes, neutrophils counts and mean platelets volume (mpv) were comparatively higher than in the non-malaria infected children. The study further showed that children with platelets counts of < 150,000/µL were 13.8 times more likely to have malaria [11].

The relevance of haematological parameters in predicting malaria in patients with signs and symptoms of malaria in Uganda showed a significant difference in the haematological parameters of *falciparum* malaria parasitaemic patients and non parasitaemic patients. These parameters include the Mean (±SD) of the differential monocytes counts (10.89±6.23% versus 8.98±5.02%) and the platelets counts (172.43±80.41 cell/µL versus 217.82± 95.96 cells/µL), Mean (±SD) values of the Red Blood Cells indices, Haemoglobin counts, MCV, MCH and MCHC, the differential Neutrophils and Lymphocytes counts and the Mean Platelets Volume (MPV) did not significantly differ between the two groups [13].

In Nigeria, previous studies conducted showed differences in malariumetric indices of asymptomatic carriers, the investigation revealed that children in the rural communities had the highest mean pcv of 34.2%, the malariumetric indices among the asymptomatic carriers were high, especially in the urban slum [14]. Similar work was carried out on malaria infected children. The haematological parameters of 695 children with acute uncomplicated malaria studied showed significantly lower mean haematocrit values (28.4%±4.8) observed in children <5 years than that observed in older children (32.8% ± 4.8) (P<0.001) [15].

An understanding of changes or abnormalities in haematological parameters of *Plasmodium falciparum* infected symptomatic and asymptomatic individuals is essential, an important tool for detecting complications such as anaemia associated with *Plasmodium falciparum* infection. The aim of this study is to assess changes in haematological parameters of *Plasmodium falciparum* infected symptomatic and asymptomatic individuals in parts of Kaduna Metropolis, Kaduna State.

2. Materials and Methods

2.1. Study Area

The study was conducted in Kaduna metropolis, Kaduna state, Nigeria. Kaduna metropolis is the capital of Kaduna State, it is located in North-western geopolitical zone and lies geographically within latitude 10°21’23”N and longitude 7°26’25”E, and is 608 meters above sea level. The State was characterised by two distinct seasons viz: Dry season, which 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 [16]. Relatively high temperatures are recorded during 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 [17].

2.2. Ethical Approval

Ethical approvals were obtained from Kaduna State Ministry Of Health (MOH/ADM/744/T/9) for the sampling of symptomatic and asymptomatic individuals in the selected hospitals within the state. Approval for the sampling of asymptomatic individuals in the National Blood Transfusion Service was obtained from the Federal Ministry Of Health (NBTS/HQ/058/04). Approvals were also obtained from the 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 respectively.

2.3. Sample Collection

Blood specimens were collected from the study population. The study population comprised of two categories of people viz: symptomatic and asymptomatic individuals. A total of 1000 blood samples were collected and examined between March and November, 2011. This comprised of 500 blood samples from symptomatic patients collected in selected hospitals within the metropolis, and 500 asymptomatic blood samples collected from apparently healthy blood donors in some of the selected hospitals within the metropolis and from the National Blood Bank Kaduna. Sample collection commenced after ethical approval was obtained from the Federal Ministry of Health, Kaduna State.
Ministry of Health and other hospitals sampled. Hospitals where blood samples were collected are as follows: Kaduna South L.G.A: Yusuf Dantsoho Memorial Hospital, Tudun Wada Kaduna; Nigerian Army Reference Hospital (44), Kaduna; Gwamna Awang Hospital, Nassarawa Kaduna; St. Gerald Hospital, Kakuri. Kaduna North L.G.A: Barau Dikko Specialist Hospital, Kaduna; Barau Dikko Children Hospital; Kaduna; Nigerian Defence Academy Medical Centre, Ribadu Cantonment, Kaduna; General hospital Kawo, Kaduna.

Venous blood sample was collected from each person into labelled tubes (vacutainer) containing Ethylene diaminetetraacetic acid (sequestrene) anticoagulant [1, 18]. During blood sample collection, bio data of the individuals sampled was obtained to establish age, sex, occupation and socio-economic status of all individuals sampled, in addition, information on malaria history and type of anti-malarial drug intake by symptomatic individuals were recorded. Medical personnel’s from the respective sampled hospitals and the National Blood Transfusion Service (NBTS) assisted during sample collection.

2.4. Sample Analysis

Plasmodium falciparum detection

Blood samples were screened for P. falciparum separately. Parasites detection and parasitaemic level determination were carried out on thick blood films, while parasite was identified on thin film [1, 7]. Parasite density (parasitaemia) was estimated by counting number of parasite in 200 white blood cells (wbcs) assuming 8000wbcs per µL of blood [1, 7].

2.5. Haematological Analysis

Complete Blood Counts (CBCs) of all blood samples collected were performed using automated blood analyser (Model KX-21N. Sysmex, Japan) the protocol as described by the manufacturer was adopted. The analyser provide the following information: Haemoglobin (Hb), Packed Cell Volume (PCV)/ Haematocrit, Red blood Cell Counts and Red Cell Indices; Mean Corpuscular Haemoglobin Concentration (MCHC), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Volume (MCV), White Blood Cell Count and Differential White Blood Cell Count (Lymphocytes, Monocytes and Neutrophils), in addition, platelets counts of infected individuals was also obtained.

2.6. Data Analysis

Data generated in this study were analysed using SPSS version 17 statistical package. Significant difference in means (±SD) of haematological parameters of symptomatic and asymptomatic individuals was determined using Analysis of Variance (ANOVA).

3. Results

Results of the haematological parameters investigated showed changes in haematological parameters of symptomatic and asymptomatic individuals. The mean (±SD) values of the various indices vary in the symptomatic and asymptomatic individuals examined. Table 1 presents the mean (±SD) values of haematological indices of infected symptomatic and asymptomatic individuals. Most of the values were significantly lower in symptomatic individuals: Neutrophils=46.52±15.870; RBC=4.41±0.845; Hb=12.07±7.286; PCV=35.65±6.882; MCHC=32.35±2.407; MCH=26.32±3.490; MCV=81.45±9.006 compared to asymptomatic individuals: Neutrophils=54.02±10.10; RBC=4.71±0.631; Hb=14.07±0.827; PCV=41.96±2.670; MCHC=33.22±1.041; MCH=28.56±1.776; MCV=87.31±4.961 (P<0.05).

However, a few of the haematological indices showed significantly higher values in the symptomatic individuals, such as WBC=6.70±3.635; lymphocytes=42.74±15.588 and monocytes=10.46±5.441, compared to asymptomatic individuals: WBC=5.15±1.445 lymphocytes=36.92±8.840; monocytes 9.05±3.550 (P<0.05). Although the value of platelets was higher in symptomatic than asymptomatic individuals, the difference was not significant (P>0.05).

Table 1. Mean (±SD) of haematological indices of infected symptomatic and asymptomatic individuals.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symptomatic (n=226)</th>
<th>Asymptomatic (n=121)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>6.70 (±3.635)</td>
<td>5.15 (±1.445)</td>
<td>0.000</td>
</tr>
<tr>
<td>RBC</td>
<td>4.41 (±0.845)</td>
<td>4.71 (±0.631)</td>
<td>0.001</td>
</tr>
<tr>
<td>HB</td>
<td>12.07 (±7.286)</td>
<td>14.07 (±0.827)</td>
<td>0.003</td>
</tr>
<tr>
<td>PCV</td>
<td>35.65 (±6.882)</td>
<td>41.96 (±2.670)</td>
<td>0.000</td>
</tr>
<tr>
<td>MCHC</td>
<td>32.35 (±2.407)</td>
<td>33.22 (±1.041)</td>
<td>0.000</td>
</tr>
<tr>
<td>MCH</td>
<td>26.32 (±3.490)</td>
<td>28.56 (±1.776)</td>
<td>0.000</td>
</tr>
<tr>
<td>MCV</td>
<td>81.45 (±9.006)</td>
<td>87.31 (±4.961)</td>
<td>0.000</td>
</tr>
<tr>
<td>LYM</td>
<td>42.74 (±15.588)</td>
<td>36.92 (±8.840)</td>
<td>0.000</td>
</tr>
<tr>
<td>MONO</td>
<td>10.46 (±5.441)</td>
<td>9.05 (±3.550)</td>
<td>0.011</td>
</tr>
<tr>
<td>NEUT</td>
<td>46.52 (±15.870)</td>
<td>54.02 (±10.102)</td>
<td>0.000</td>
</tr>
<tr>
<td>PLATELETS</td>
<td>233.31 (±120.330)</td>
<td>213.99 (±62.378)</td>
<td>*0.101</td>
</tr>
</tbody>
</table>

*Note: Difference not significant (P > 0.05)

Key: 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 2 also shows the Mean (±SD) of haematological indices by parasitaemic level in infected symptomatic individuals. The Mean (±SD) values of PCV and MCH were found to be significantly lower in symptomatic individuals with high level of parasitaemia (>5000 parasites/L) compared to those with low level of parasitaemia (<5000 parasites/L and <1000 parasites/L) (PCV = 34.467±8.5597; MCH = 25.637±3.4346 and PCV = 36.504±5.7317; MCH = 26.726±3.4760) respectively (P<0.05). In addition, the mean (±SD) values of RBC, Hb, MCV and lymphocytes were also found to be lower in this group, though the difference was not statistically significant (P>0.05).

Significantly high mean (±SD) values of WBC (9.547±5.0219) was also found in those with high level of parasitaemia (>5000 parasites/L) compared to 7.179±4.1425 for those with low levels of parasitaemia (<5000 parasites/L and <1000 parasites/L) respectively (P<0.05). Although, the mean (±SD) values of monocytes, neutrophils, platelets and MCHC were also found to be higher in this group, the difference was not statistically significant (P>0.05).

The Mean (±SD) of haematological indices by parasitaemic level in infected asymptomatic individuals is presented in Table 3. The mean (±SD) values of lymphocytes (41.14±7.795) and monocytes (10.32±2.426) were found to be significantly higher in the high parasitaemia level (>5000 parasites/L blood) (P<0.05), compared to those (35.80±8.799 and 8.71±3.730 respectively) with low parasitaemia level (<1000 parasites/L blood). Significantly lower mean (±SD) values of neutrophils (48.54±7.608) and platelets (172.24±60.504) respectively were found in the high parasitaemia level group (>3000 parasites/L blood) compared to those (55.46±10.214 and 224.9±58.357) with low level of parasitaemia (<1000 parasites/L blood) (P<0.05). No significant difference was observed in the Mean (±SD) values of the following values; WBC, RBC, Hb, PCV, MCHC, MCH, and MCV in asymptomatic individuals with low parasitaemic level (P>0.05).

Result further shows that 67% of symptomatic individuals take oral anti-malarial drugs, 25% takes anti-malarial drugs orally or parenteral (injectable) and 2% takes antimalarial drugs parenteral. Previous malaria history of symptomatic individuals revealed that 88% had mild symptoms while only 12% had severe symptoms of malaria.

Table 3. Mean (±SD) of haematological indices by parasitaemic level in infected asymptomatic individuals.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parasitaemia &lt;1000parasites/µL blood (n=96)</th>
<th>Parasitaemia &gt;3000parasites/µL blood (n=25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>5.18±1.398</td>
<td>5.02±1.639</td>
<td>0.629</td>
</tr>
<tr>
<td>RBC</td>
<td>4.73±0.638</td>
<td>4.67±0.616</td>
<td>0.681</td>
</tr>
<tr>
<td>HB</td>
<td>14.06±0.874</td>
<td>14.12±0.626</td>
<td>0.773</td>
</tr>
<tr>
<td>PCV</td>
<td>41.96±2.828</td>
<td>41.92±2.004</td>
<td>0.942</td>
</tr>
<tr>
<td>MCHC</td>
<td>33.25±1.016</td>
<td>33.12±1.146</td>
<td>0.564</td>
</tr>
<tr>
<td>MCH</td>
<td>28.71±1.797</td>
<td>28.02±1.615</td>
<td>0.088</td>
</tr>
<tr>
<td>MCV</td>
<td>87.57±5.201</td>
<td>86.33±3.847</td>
<td>0.269</td>
</tr>
<tr>
<td>LYM</td>
<td>35.80±8.799</td>
<td>41.14±7.795</td>
<td>*0.007</td>
</tr>
<tr>
<td>MONO</td>
<td>8.71±3.730</td>
<td>10.32±2.426</td>
<td>*0.044</td>
</tr>
<tr>
<td>NEUT</td>
<td>55.46±10.214</td>
<td>48.54±7.608</td>
<td>*0.002</td>
</tr>
<tr>
<td>PLATELETS</td>
<td>224.9±58.357</td>
<td>172.24±60.304</td>
<td>*0.000</td>
</tr>
</tbody>
</table>

*Note: Difference is significant (P < 0.05) 
Key: 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.
4. Discussion

The significantly lower values of neutrophils, RBC, Hb, PCV, MCHC, MCH and MCV observed in symptomatic individuals (P<0.05) compare to asymptomatic individuals and also lower values of Hb, PCV and MCH observed in symptomatic individuals with high level of parasitaemia (P<0.05) in this study shows that changes or abnormalities in haematological indices are common in malaria infection. Changes in haematological parameters are some of the most common complication in malaria, and play a major role in malaria pathology. Such changes involved the major cell types such as red blood cells (erythrocytes), white blood cells (leucocytes), platelets (thrombocytes), and packed cell volume (PCV) and haemoglobin [9, 10].

Changes in haematological parameters may also vary depending on the level of disease endemicity, nutritional status, genetic factor, socio-demographic condition, and host immunity [9, 10]. Destruction of the red blood cells by malaria parasites has been attributed to the reproduction of malarial parasite in the red blood cells which results in rapid destruction of the target red blood cells and thus an accelerated removal of both parasitized and non-parasitized cells occur [12], this bring about changes in haematological indices [9, 13].

The increase destruction of red blood cells by malarial parasites (haemolysis) leads to decrease in major cells such as red blood cells, Hb, PCV and red cell indices, which results in anaemia. Anaemia is the most common red blood cell disorder that occurs as a result of decrease in the concentration of haemoglobin below the normal limit (<11g/dL) for a person’s age, gender and environment, resulting in the reduction of the oxygen carrying capacity of the blood. Anaemia in malaria is usually microcytic hypochromic type due to iron deficiency [1]. Reduced PCV values are features of anaemia, while reduced red cell indices such as MCHC, MCH and MCV as observed in the present study are features of iron deficiency anaemia (microcytic hypochromic anaemia) [1]. In a related study in India, Hussain et al. [10] also recorded significantly lower PCV in malaria infected individuals. Significantly lower values of Hb, PCV and red cell indices were also observed among malaria infected individuals studied.

The significant increase in values of lymphocytes (lymphocytosis) and monocytes (monocytosis) observed among symptomatic and asymptomatic individuals with high parasitaemia (<3000 parasites/µL) and also the significant increased in white blood cells in symptomatic individuals with high level of parasitaemia (>5000 parasites/µL) could be due to the vital role played by white blood cells (leucocytes) in defence against malaria. Leukocytes are known to be involved in body’s immune defence by producing antibodies in response to infection. Changes in leucocytes counts in malaria depends on factors such as acuteness of infection, parasitaemia, disease severity, state of the host’s immunity and presence of concurrent infections. This finding is similar to that observed by others [4], where significant increase in WBC counts was also recorded among P. falciparum infected patients.

An increase or decrease in differential white blood cells count affects the changes in the total lymphocyte count in malaria [13]. Although, decrease in lymphocytes counts (lymphopenia) have been reported to be the most commonly observed situation in falciparum malaria, antimalarial drugs intake has also been associated with decrease lymphocytes counts. Lymphocytosis has been shown to replace lymphopenia in a matter of few days after an initiation of drugs therapy, before gradually normalising over the next couple of weeks [21]. According to Cheesbrough [1], increased lymphocytes (lymphocytosis) and monocytes (monocytosis) are associated with malaria and are commonly observed in prolong duration of illness.

Significant increase in values of lymphocytes observed in this study therefore could be due to antimalarial drugs intake by majority of the symptomatic individuals prior to sampling. This finding is in line with the work of Ifeanyi and Esan [22] who observed an increase in lymphocytes in post-malarial treated patients than pre-treated patients. This however is contrary to the previous reports which showed decreased in lymphocyte population [11, 13, 12].

The significantly lower platelets count observed among asymptomatic individuals with high level of parasitaemia (<3000 parasites/µL) could be associated with increase destruction or consumption of platelets in malaria due to entry of parasites into red blood cells which leads to activation of the coagulation cascade and endothelial damage as observed by previous worker [13].

Changes in haematological parameters observed in P. falciparum infected symptomatic and asymptomatic individuals in this study is common in malaria [4, 5, 20, 23], although, such changes may occur with other viral and bacterial infections, early detection of such changes may assist in taking measures to prevent progression to severe malaria.

5. Conclusion

The findings in this study has shown that haematological parameters of Plasmodium falciparum infected symptomatic individuals were significantly lower than that of asymptomatic individuals, significantly lower values of neutrophils, RBC, Hb, PCV, MCHC, MCH and MCV observed in symptomatic individuals (P<0.05) compare to asymptomatic individuals. Reduced PCV values recorded are features of anaemia, reduced red cell indices are features of iron deficiency anaemia. Significant increase in lymphocytes observed in this study may be attributed to antimalarial drugs intake by symptomatic individuals. Haematological parameters are important tool for diagnosis and detecting changes or abnormalities in Plasmodium falciparum infected individuals at an early stage and this may prevent...
complications associated with severe malaria.

Limitation of the study included lack of medical history and anti-malarial intake by asymptomatic individuals which could no doubt affect the interpretation of the results.

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Competing Interest

Authors have no competing interest.

Author’s Contribution

KB Dikwa was the lead researcher, conceived the study, carried out sample collection, sample analysis, data analysis and manuscript writing. DB Maikaje, YA Umar and AB Suleiman supervised and provided guidance on research conduct, manuscript review and production.

Availability of Data

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Consent of Publication

Not applicable.

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