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Effect of Antimalarial Drugs on Haematological Indices of Malarial Patients

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Abstract: The possible effects of drug administration on haematological indices in blood of malaria positive individuals were evaluated in this study. A total of 100 individuals (consisting of 87 malaria positive patients and 13 malaria negative individuals used as control) were recruited for this study. The medical history of the patients such as the duration of illness, age, gender status, drug administered and social status were obtained. The degree of parasitaemia in the blood of malaria positive individuals was also determined. The results of this study showed a significant ($p<0.05$) decrease in total white blood cell (WBC) count in malaria positive individuals ($5.71\pm0.20\times10^3/\mu l$) compared to the control individuals ($9.05\pm1.68\times10^3/\mu l$). Also, there were significant ($p<0.05$) decrease in haemoglobin (Hb) concentration and packed cell volume (PCV) in malaria positive individuals (11.43±0.16g/dl,36.85±0.57%) compared to the control individuals (13.46±0.43g/dl, 40.33±0.70%) respectively. The decrease in WBC, Hb and PCV were observed to depend on degree of parasitemia, duration of illness, age range and sex of malaria patients. However, there were no significant ($p>0.05$) mean difference in the values of red blood cell, mean cell volume, platelet count, plateletcrit, mean platelet volume in malaria patients compared to the control patients, although, there were non-significant ($p>0.05$) decreases depending on the degree of parasiatemia, age range, sex and duration of illness of malaria positive individuals. However, the anti-malarial drugs significantly affected the WBC, Hb and PCV levels while the other haematological indices did not vary significantly. It can be concluded that the anti-malarial drugs should be used with caution in the management of malaria infection.

Key words: Malaria · Antimalaria drugs · WBC-white blood cell count · RBC-red blood cell count · Hb-haemoglobin concentration · PCV-packed cell volume · MCV-mean cell volume · PLT-platelet count · PCT-platelet crit · MPV-mean platelet volume

INTRODUCTION

Malaria continues to be a major health problem in some parts of the world. It is caused by protozoan *Plasmodium*, transmitted by female anopheles mosquitoes. Clinical presentation of malaria caused by various species (*P. vivax, P. falciparum, P. malariae, P. ovale*) resembles each other. Clinical features include fever, chills, sweating, headache, vomiting, diarrhea, abdominal pain, cough, splenomegaly and, hepatomegaly.

Malaria is the world's most common parasitic infection which poses major health challenges [1, 2, 3, 4]. The World Health Organisation (WHO) estimated that there were 219 million cases of malaria in 2010 resulting in 660,000 deaths based on documented cases [5]. This is equivalent to roughly 2000 deaths every day [6]. A 2012 study estimated that the number of documented and undocumented deaths in 2010 was 1.24 million. The majority of cases (65%) occur in children under 15 years old [7]. Pregnant women are especially vulnerable to the infection: about 125 million pregnant women are at risk of infection each year. In Sub-Saharan Africa, maternal malaria is associated with up to 200,000 estimated infant deaths yearly [8]. In Nigeria, there are over 100 million

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people at risk of malaria infection every year and it is estimated that about 50% of the adult population experience at least one episode yearly [9].

Haematological changes are some of the most common complications in malaria and they play a major role in malaria pathology. These changes involve the major cell lines such as red blood cells, leucocytes and thrombocytes. These blood cells are altered during malaria parasite infection because the entry of *P. falciparum* into erythrocytes usually leads to a marked increase in secretion of inflammatory cytokines (TNF-αβ, IL-1, IL-10 and IFN αβ) which may cause dyserythropoiesis, endothelial cell activation (due to over expression of cell adhesion molecules; ICAM-1, VCAM-1), activation of the coagulation cascade (due to platelet consumption and endothelial damage) and sequestration of parasitized RBCs (due to over expression of cell adhesion molecule, pfEMP, [10, 11, 12, 13 and 14]. These along with other mechanisms set in motion events that ultimately result in morphological and numerical changes in the different blood cell lines.

The treatment of malaria depends on the severity of the disease. The most effective strategy for *P. falciparum* infection is the use of artemisinins in combination with other anti-malarials (known as artemisinin-combination therapy, or ACT), which reduces the ability of the parasite to develop resistance to any single drug component [15]. These additional anti-malarials include amodiaquine, lumefantrine, mefloquine or sulfadoxine/pyrimethamine (also known as Fansidar). Chloroquine may also be used where the parasite is still sensitive to the drug [16].

This study was carried out to determine the possible effects of drug administration on haematological indices in malaria positive individuals to know if there is a reversal of the haematological indices in malaria patients following anti-malaria drug administration.

MATERIALS AND METHODS

Subjects: Patients admitted to Central Hospital, Benin City and a private clinic (Time Hospital) all in Benin City, Nigeria with diagnosis of malaria were recruited for this study. The study was conducted in compliance with the Declaration on the Right of the Patient (WMA, 2000) after approval by the Ethical Committee of the Central Hospital and Time Hospital, Benin City, Edo State, Nigeria. Before enrolment for the study, informed consent was obtained from the patients or their relatives. The study included a total of 100 patients, 87 tested malaria parasite positive (test patients), while 13 tested malaria parasite negative (control patients). Of the 87 malaria patients, 42 (48%) were males while 45 (52%) were females; the age of the patients ranged from 10 months to 65 years with mean age of 30 years. Maximum number (50%) of cases occur in 18-30 years age group. On admission, the medical history including; age, sex, social status, duration of illness and drug history of the patients were obtained and recorded.

Collection of Blood Sample: Blood samples were collected from patients by veinous puncture into 5ml ethylene diamine tetra-acetic acid (EDTA) anticoagulant bottles from the patients and delivered to the laboratory within 3hrs after collection. The samples were taken for haematological analysis and for the determination of the degree of parasitemia in the malaria patients.

Malaria Diagnosis: Malaria was diagnosed with blood smear staining method of Warhurst and Williams (1996). Malaria parasite detection was done by microscopic examination of thin blood films stained with 3% Giemsa stain. The parasitemia was graded as: += mild (1-999μL^{-1}), ++= moderate (1,000-9,999μL^{-1}) and +++ = severe (>10,000 μL^{-1}).

Haematological Indices Determination: Routine haematological parameters which included haemoglobin level (Hb), total white blood cell count (WBC), red blood cell count (RBC), packed cell volume (PCV), mean cell volume (MCV), platelet count (PLT), platelet crit (PCT) and mean platelet volume (MPV) were determined for all patients. These haematological parameters were obtained by subjecting the blood samples of the patients which were collected in ethylene diamine tetra acetic acid (EDTA) anticoagulant tubes to MS-9 Automatic Full Digital Cell Counter (Melet Schloesing Laboratories, Cergy Pontoise, France). This automated analyzer is a three part differential analyzer and works on the principle of impedance method.

Statistical Analysis: The results were expressed as mean±standard error of mean. The statistical analysis of data was performed using the one way ANOVA and student's t-test on SPSS version 16. Significant level was set at $p<0.05$. Also, correlation analysis and linear regression were presented for the haematological indices and the degree of parasitemia, duration of illness and age range of malaria patients.

RESULTS

The results obtained showed that the mean value of total white blood cell (WBC) count in malaria patients was significantly lower (5.71±0.20×10^3/µl) when compared to the control individuals (9.05±1.68×10^3/µl). Also, the haemoglobin concentration (Hb) and packed cell volume (PCV) mean values in malaria patients (11.43± 0.16g/dl, 36.85±0.57% respectively) were significantly lower compared to that of control individuals (13.46±0.43g/dl, 40.33±0.70% respectively). Although there were slight differences in red blood cell (RBC), mean cell volume (MCV), platelet count (PLT), platelet crit (PCT) and mean platelet volume (MPV) in malaria patients (4.42±0.08, 81.43±0.75, 186.55±6.13, 0.16±0.01 and 8.72±0.09 respectively) compared to the control individuals (4.72±0.19, 80.09±1.12, 200.62±15.09, 0.18±0.01 and 8.98±0.21 respectively), the differences were not statistically significant (Table 1).

Table 1: Haematological indices of malaria patients

Analytes/ Patients	WBC (×10^3/µl)	RBC (×10^6/µl)	Hb (g/dl)	PCV (%)	MCV (fl)	PLT (×10^3/µl)	PCT (×10^3/µl)	MPV (fl)
Control	9.05±1.68^a	4.72±0.19^a	13.46±0.43^a	40.33±0.70^a	80.09±1.12^a	200.62±15.09^a	0.18±0.01^a	8.96±0.21^a
Malaria Patients	5.71±0.20^b	4.42±0.08^a	11.43±0.16^b	36.85±0.57^b	81.43±0.75^a	186.55±6.13^a	0.16±0.01^a	8.72±0.09^a

Values represent mean ± SEM. Values in the same column with different superscript alphabets differ significantly (P<0.05).

Table 2: Effect of degree of parasitemia on some haematological indices in malaria patients

Degree of parasitemia	WBC (×10^3/µl)	RBC (×10^6/µl)	Hb (g/dl)	PCV (%)	MCV (fl)	PLT (×10^3/µl)	PCT (×10^3/µl)	MPV (fl)
Control	9.05±1.68^a	4.72± 0.19^a	13.46± 0.41^a	40.33± 0.71^a	80.09 ±1.12^a	200.62 ±15.09^a	0.18 ±0.01^a	8.96±0.21^a
Mild(+)	5.68±0.24^b	4.71± 0.09^a	11.57± 0.19^b	36.58± 0.57^b	81.49± 0.85^a	189.02±7.39^a	0.17±0.01^a	8.72±0.11^a
Moderate (++)	6.01±0.40^b	4.47± 0.18^a	10.75± 0.25^c	35.72±0.92^b	82.28±1.52^a	182.90±13.54^a	0.16±0.01^{a,b}	8.64±0.14^a
Severe (+++)	3.73±0.86^c	3.28± 0.51^b	8.71± 0.96^d	29.87±7.38^c	71.50±4.81^b	138.67±48.47^b	0.15±0.04^b	8.47±0.79^a

Values represent mean ± SEM. Values in the same column with different superscript alphabets differ significantly (p<0.05)

Table 3: Effect of duration of illness on some haematological indices in malaria patients

Duration of Illness	WBC (×10^3/µl)	RBC (×10^6/µl)	Hb (g/dl)	PCV(%)	MCV (fl)	PLT (×10^3/µl)	PCT (×10^3/µl)	MPV (fl)
Control	9.05± 1.68^a	4.72±0.19^a	13.46±0.41^a	40.33±0.71^a	80.09±1.12^a	200.62±15.09^a	0.18±0.01^a	8.96±0.20^a
1-4 days	5.62± 0.29^b	4.30±0.17^a	10.92±0.30^b	34.26±1.13^b	80.26±1.24^a	190.93±9.53^a	0.17± 0.01^a	8.83±0.17^a
5-8 days	5.61± 0.32^b	4.60±0.11^a	11.70±0.27^c	37.62±0.65^a	82.65±0.91^a	183.15±9.40^a	0.16±0.01^a	8.78± 0.14^a
9-12 days	5.55± 0.86^b	4.26± 0.17^a	11.52±0.30^{b,c}	35.08± 1.67^b	85.6± 3.57^a	154.50±27.01^b	0.14±0.02^a	8.33±0.20^a
13days and above	6.01± 0.61^b	4.24±0.29^a	10.95±0.32^{b,c}	36.69±0.87^{a,b}	79.25±2.62^a	209.18±17.28^a	0.18±0.02^a	8.43±0.23^a

Values represent mean ± SEM. Values in the same column with different superscript alphabets differ significantly (p<0.05)

Table 4: Gender consideration on some haematological indices in malaria patients

SEX	WBC (×10^3/µl)	RBC (×10^6/µl)	Hb (g/dl)	PCV (%)	MCV (fl)	PLT (×10^3/µl)	PCT (×10^3/µl)	MPV (fl)
Control-male	8.25± 1.53^a	4.73± 0.24^a	13.08±0.52^a	40.54±0.84^a	81.16±1.25^a	203.50±21.66^a	0.17±0.01^a	8.64±0.25^a
Test-male	5.29± 0.21^b	4.50± 0.12^a	11.55±0.24^b	37.75±0.81^a	80.54±1.05^a	185.48±8.67^b	0.16±0.01^a	8.58±0.13^a
Control-female	10.52±3.78^a	8.66±3.95^a	12.05±2.10^a	39.92±1.34^a	77.22±1.62^a	181.60± 19.41^a	0.15± 0.02^a	9.28±0.33^a
Test-female	6.11± 0.32^b	6.42± 0.32^b	11.22±0.21^a	35.69±0.74^b	82.26±1.06^a	183.78±8.54^a	0.16±0.01^a	8.75±0.13^a

Values represent mean ± SEM. Values in the same column with different superscript alphabets differ significantly (p<0.05).

Table 5: Relationship between age and some haematological indices of malaria patients

Age Range (years)	WBC (×10^3/µl)	RBC (×10^6/µl)	Hb (g/dl)	PCV (%)	MCV (fl)	PLT (×10^3/µl)	PCT (×10^3/µl)	MPV (fl)
Control	9.09± 1.68^a	4.71±0.19^a	13.46±0.41^a	40.33±0.71^a	80.09±1.12^a	200.64±15.09^a	0.18± 0.01^a	8.96±0.20^a
1-10	5.29±0.51^b	3.65±0.34^b	9.17±0.52^b	26.97±2.07^b	76.31±2.08^b	150.56±15.46^b	0.14±0.01^a	8.64±0.26^a
11-17	5.98±0.81^b	4.22±0.32^{a,b}	10.08±0.31^{a,b}	32.37±0.72^{b,c}	76.80±1.12^b	171.56±23.64^b	0.17±0.01^a	8.83±0.52^a
18-30	5.97±0.24^b	4.58±0.11^a	11.41±0.21^{a,b}	37.15±0.63^c	81.86±0.98^a	191.05±7.17^{a,b}	0.17± 0.01^a	8.77±0.13^a
31 years & above	5.41± 0.43^b	4.47±0.12^a	13.08±1.11^a	38.34±1.01^{a,c}	82.77±1.39^a	191.03±13.38^{a,b}	0.16±0.01^a	8.72±0.15^a

Values represent mean ± SEM. Values in the same column with different superscript alphabets differ significantly (p<0.05).

Table 6: Effect of drug administration on some haematological indices of malaria patients

DRUGS	WBC ($\times10^3$/µl)	RBC ($\times10^6$/µl)	Hb (g/dl)	PCV (%)	MCV (fl)	PLT ($\times10^3$/µl)	PCT ($\times10^3$/µl)	MPV (fl)
Control	9.05±1.68^{a}	4.72±0.19^{a}	13.46± 0.41^{a}	40.33±0.71^{a}	80.09±1.12^{a}	200.62±15.09^{a}	0.18±0.01^{a}	8.96±0.20^{a}
ACT	5.06± 0.42^{b}	4.29±0.20^{a}	11.36± 0.35^{b}	36.93±1.00^{b}	82.72±1.77^{a}	179.62±15.80^{a}	0.16±0.01^{a}	8.69±0.22^{a}
CQ	6.68±0.82^{a,b,c}	4.81±0.33^{a}	11.33±0.72^{b}	37.11±1.97^{a,b}	79.2±1.77^{a}	215.25±21.54^{a}	0.18±0.02^{a}	8.53±0.30^{a}
Fansidar	5.43±0.78^{c}	4.84± 0.29^{a}	12.07±0.27^{a,b}	39.47±2.20^{a,b}	79.70±5.81^{a}	189.33±28.50^{a}	0.18±0.03^{a}	9.73±0.09^{a}
No drug	5.77± 0.28^{b,c}	4.33± 0.10^{a}	10.88±0.26^{b}	36.04±0.86^{b}	81.45± 0.93^{a}	186.40±8.26^{a}	0.16±0.01^{a}	8.61±0.11^{a}
Others	5.54±0.32^{b,c}	4.71± 0.22^{a}	12.03±0.23^{a,b}	36.34±1.36^{b}	81.45±3.05^{a}	176.10± 13.07^{a}	0.16±0.01^{a}	8.96±0.36^{a}

Values represent mean ± SEM. Values in the same column with different superscript alphabets differ significantly ($p<0.05$)

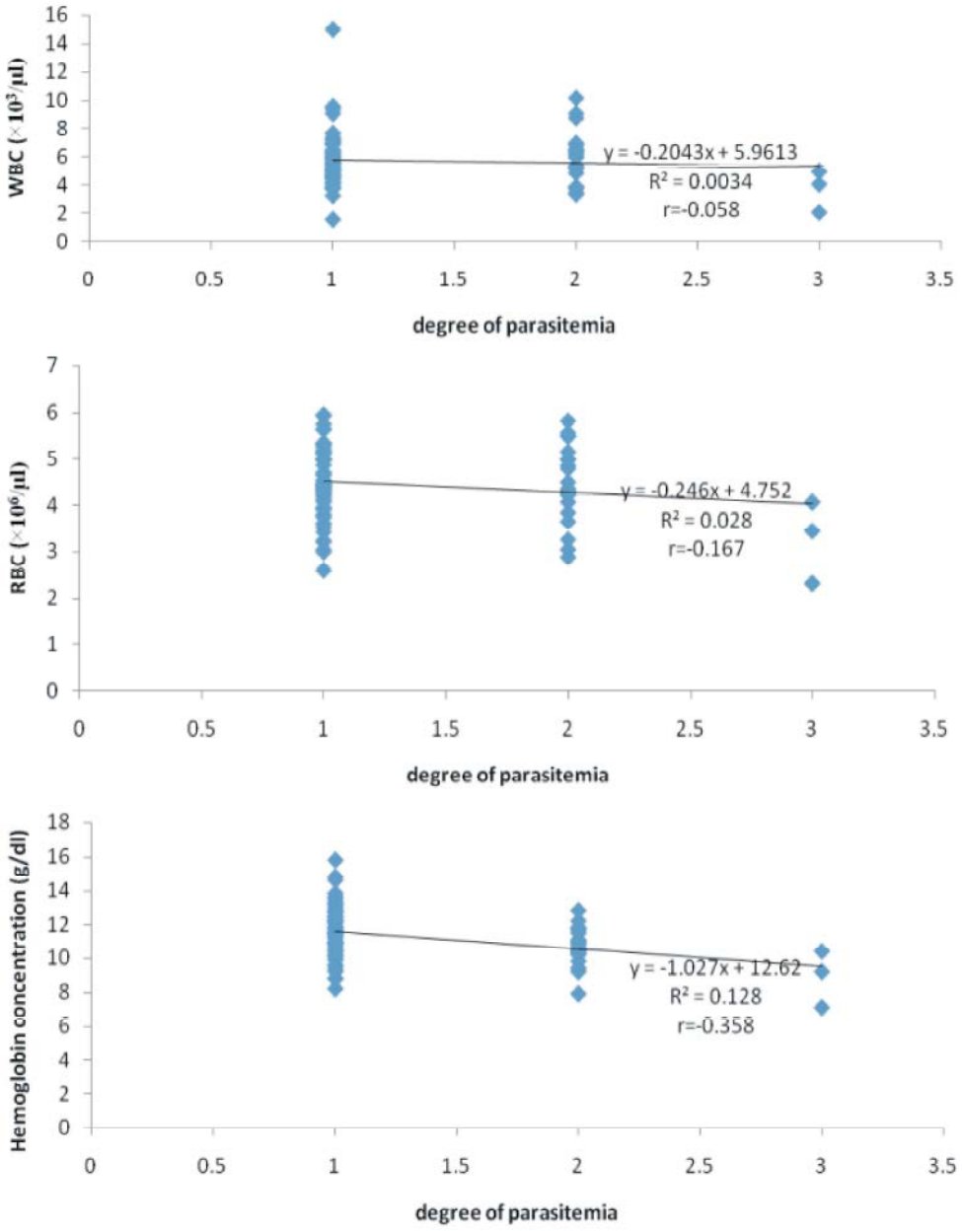

Fig. 1: Plot showing non-significant negative correlation (r=0.-058) for WBC against degree of parasitaemia and also significant negative correlation (r=0.-167, r=-0.358) for red blood cell (RBC) and hemoglobin respectively

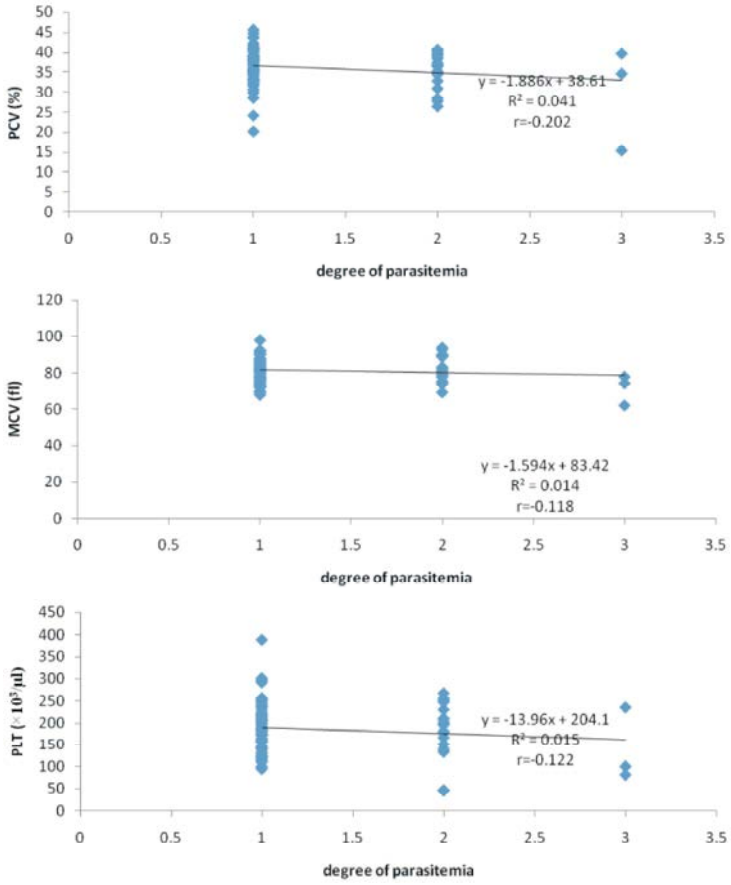

Fig. 2: Plot showing significant negative correlation (r=-0.202, r=-0.118, r=-0.122) for packed cell volume (PCV), mean cell volume (MCV) and platelet count respectively against degree of parasitemia

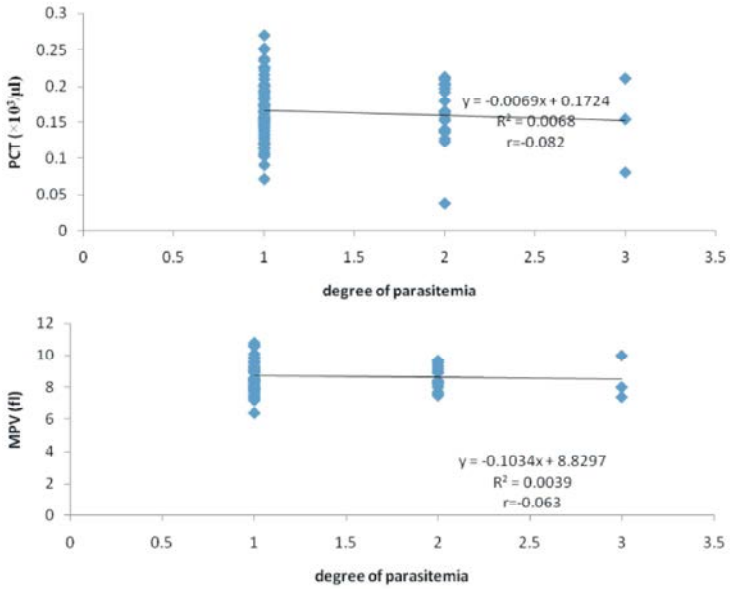

Fig. 3: Plot showing non-significant negative correlation (r=-0.082, r=-0.063) for platelet crit and mean platelet volume respectively against degree of parasitemia

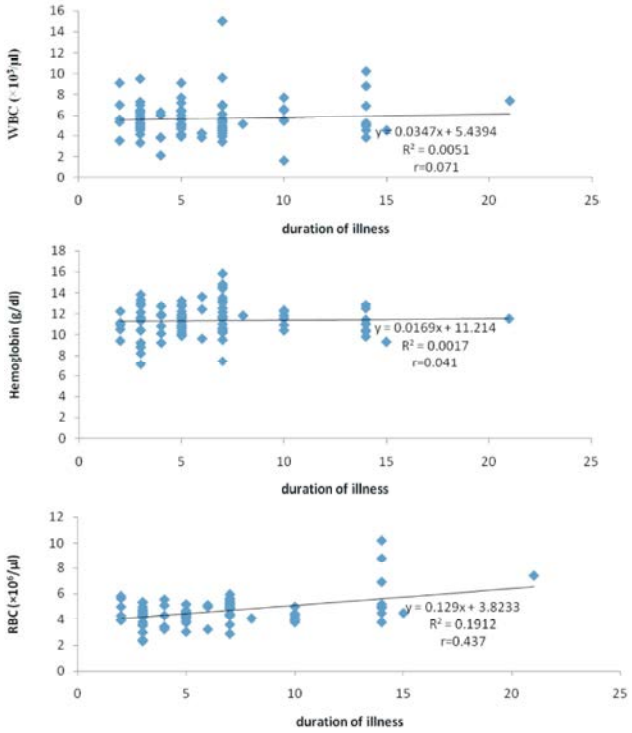

Fig. 4: Plot showing non-significant positive correlation (r=0.071, r=0.041) for white blood cell (WBC) and haemoglobin respectively against duration of illness and significant positive correlation (r=0.437) for red blood cell

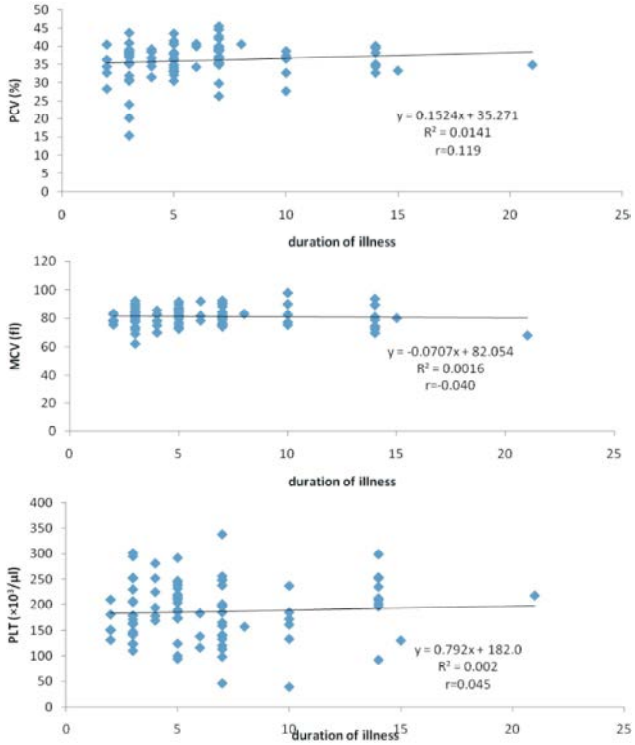

Fig. 5: Plot showing significant positive correlation (r=0.119) for packed cell volume (PCV) against duration of illness and non-significant negative correlation (r=-0.040) for mean cell volume (MCV) and non-significant positive correlation (r=0.045) for platelet count (PLT)

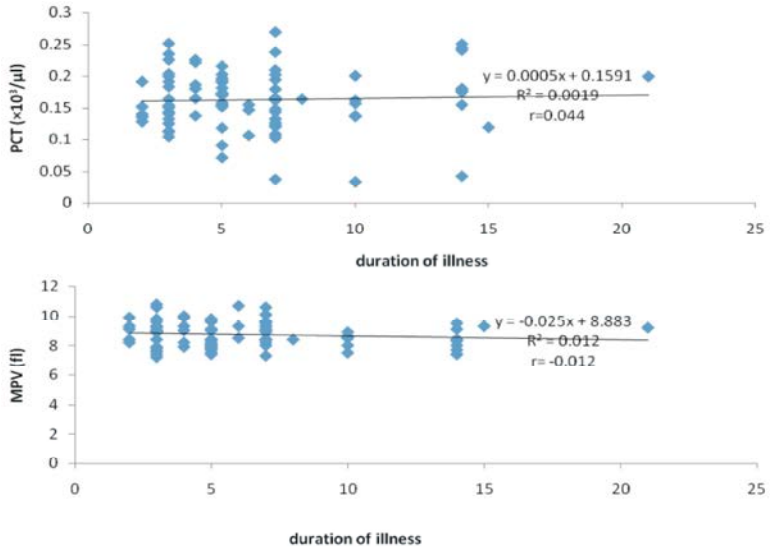

Fig. 6: Plot showing non significant positive correlation (r=0.044) for platelet crit (PCT) against duration of illness and non significant negative correlation (-0.012) for mean platelet volume (MPV)

It was also observed that there was a significant ($p<0.05$) decrease in mean value of WBC of malaria patients with respect to their degree of parasitemia. However, the mean value of WBC in mild and moderate patients were not statistically significantly ($p>0.05$) different (5.68±0.24 and 6.01±0.40 respectively). Also, the mean RBC value for the control patients were not significantly ($p<0.05$) different from the mild and moderate (4.72±0.19, 4.76±0.09 and 4.47±0.18 respectively), but were significantly ($p<0.05$) higher than severe malaria patients (3.28±0.05). The haemoglobin (Hb) concentration were all statistically significantly ($p<0.05$) lower in mild, moderate and severe parasitaemia with severe cases recording the least value (8.71±0.96). The mean packed cell volume (PCV) also follow the same pattern as that of Hb for all the degrees of parasitaemia except for mild and moderate patients in which the mean value were not statistically significantly ($p<0.05$) different from each other. The mean values of MCV, PLT, PCT and MPV for all the degrees of parasitaemia were not statistically significantly ($p<0.05$) different from each other except in severe cases where the values were significantly reduced ($p<0.05$) when compared to the control (Table 2).

The other indices, mean RBC, MCV, PLT, PCT and MPV of the malaria patients were not significantly different when compared to that of the control individuals (Table 3). The WBC, Hb and PCV were all significantly reduced ($p<0.05$) with duration of illness especially in severe parasitaemia. The same observation was made when the malaria patients were divided into different sexes (Table 4) and age (Table 5).

Similarly, the WBC, Hb and PCV levels of the malaria patients were also significantly reduced ($p<0.05$) when undergoing anti-malarial drug therapy (Table 6). The results obtained also show that the mean values of RBC, MCV, PLT, PCT and MPV of the malaria patients are not significantly different ($p>0.05$) when compared to control individuals in the different drug treatments (Table 6). It is interesting to note that the haematological indices of those patients not yet on drugs did not vary significantly ($p>0.05$) from those on anti-malarials.

The degree of parasitaemia was observed to correlate negatively with some haematological parameters, with haemoglobin concentration having strong significant negative correlation (r=-0.358). However, RBC. PCV MCV and PLT have weak negative correlation (r=-0.160, r=-0.202, r=-0.118 and r=-0.122 respectively), while WBC, PCT and MPV have non-significant negative correlation (r=-0.058, r=-0.082 and -0.063 respectively). (Figures 1, 2 and 3).

The duration of illness was observed to correlate positively with some haematological parameters, with RBC having the highest significant positive correlation (r=0.437). However, PCV have low positive correlation (r=0.119) while other haematological parameter does not have any significant correlation with duration of illness (Figures 4, 5 and 6).

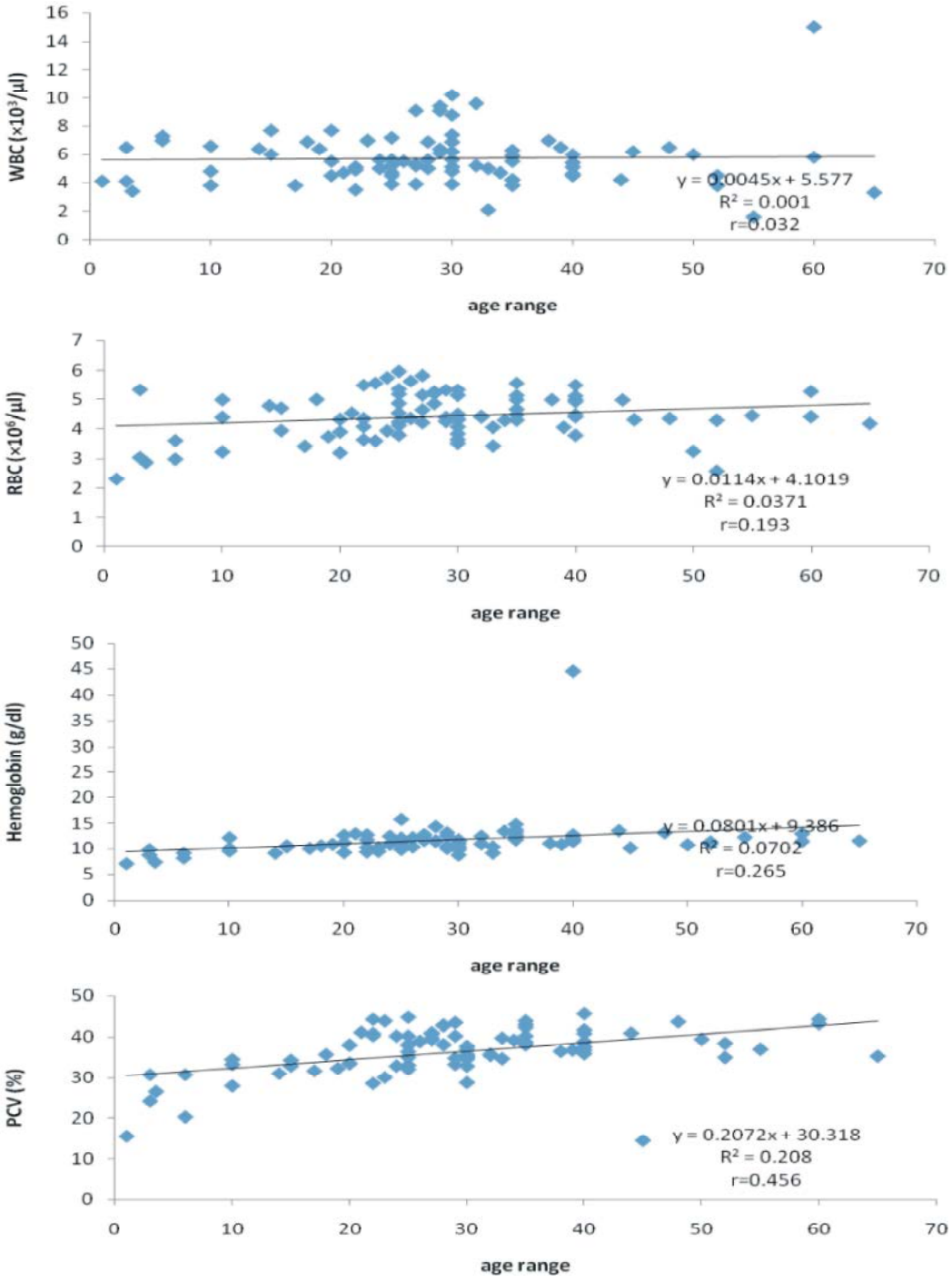

Fig. 7: Plot showing non-significant positive correlation (r=0.032) for WBC against age range and significant positive correlation (r=0.193, r=0.265, r=0.456) for RBC, haemoglobin and packed cell volume (PCV) respectively

Also, there is a positive correlation in relation to the ages of the patients with PCV and haemoglobin having the highest significant positive correlation (r=0.456 and r=0.265), while RBC, MCV and PLT have weak positive correlation (r=0.193, r=0.189 and r=0.105 respectively). However, WBC, PCT and MPV have non-significant positive correlation (r=0.032, r=0.065 and r=0.010 respectively) (Figures 7 and 8).

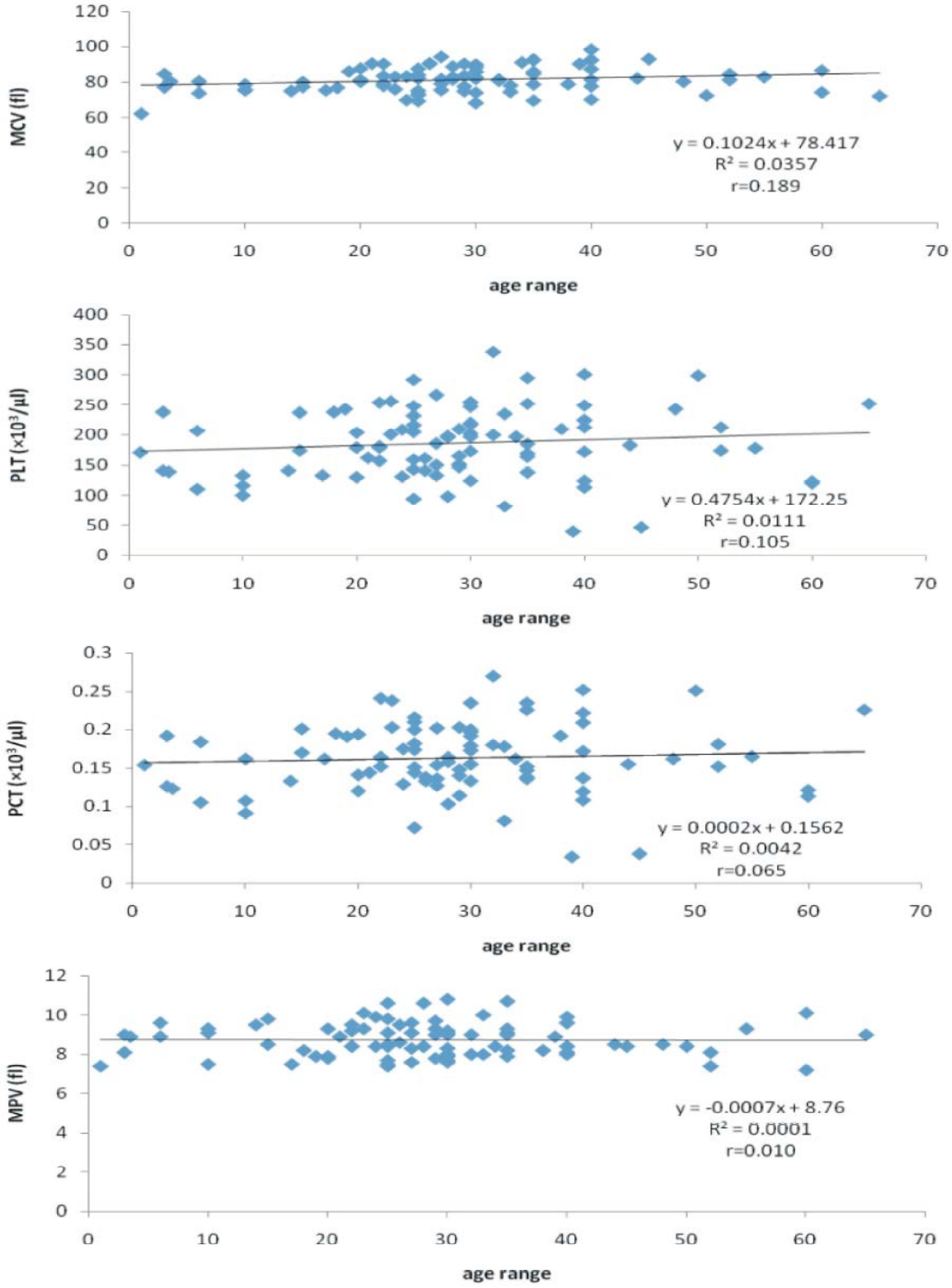

Fig. 8: Plot showing significant positive correlation between mean cell volume (MCV) and platelet count (PLT) and non-significant positive correlation between platelet crit and mean platelet volume(r=0.189, r=0.105, r=0.065, r=0.010) respectively against age range

DISCUSSION

Malaria causes high incidence of morbidity and mortality in people living in the highly affected zones of Sub-Sahara. *Plasmodium falciparum* is the widest spread species found in Nigeria. The disease causes alteration in different body components among which are the haematological indices [17, 18, 19, 20].

In the present study, it was observed that there was significant ($p<0.05$) decrease in total white blood cell (WBC) count in the malaria patients compared to the control individuals. The decrease in the total WBC is more significant with the increase in degree of parasitemia, duration of illness and age of malaria patients. This decrease in total white blood cell count is indicative of likely leukopenia in the malaria patients. This is in agreement with the report of Igbeneghu and Odaibo (2013) [21]; these authors in their study reported leukopenia in some malaria patients. However, this result is different from the report of Rojanasthien and Surakamolleart (2012) [22] who found no decrease in total leucocyte count in malaria patients. The likely leukopenia in malaria patients has been linked with depletion in the lymphocyte subset of the total leukocyte through fas-induced apoptosis [23] and due to sequestration of the cells in the lymph nodes or other body tissue during malaria parasite infection. Although the mechanism involved in both process have not been fully elucidated.

Also, the decrease in the RBC indices such as RBC count, Hb and PCV observed in malaria patients with respect to their degree of parasitemia, duration of illness and age may suggest likelihood of anemia. Abdalla and Pasvol (2004) [24] reported that malaria causes decrease in RBC indices including haemoglobin concentration and packed cell volume, mean cell volume (in severe cases) and this is the common cause of anemia in malaria endemic regions. Anemia in acute malaria have been demonstrated to be due to increase in hemolysis and decrease in the rate of production of red blood cells, increased destruction of parasitized red blood cells and accelerated removal of both parasitized and non-parasitized red blood cells [25], ineffective erythropoiesis due to increase circulating TNF-α [26]. In malaria endemic areas, the prevalence and severity of anemia are usually determined by a number interacting factors; these include among others, the parasite species, degree of parasitemia, age of host, sex, etc. The unchanged mean cell volume (MCV) of malaria patients (including patients with mild and moderate parasitemia) compare to the control is in support of the report of Haruna, *et al*. [27], which reported that the mean red blood cell indices (MCV, MCH, MCHC and RDW) of uncomplicated malaria patients does not change significantly from control individuals. This could probably be that uncomplicated malaria is associated with milder biochemical changes, for example, lower production of cytokines, less endothelial cell activation, less hemolysis as compared to severe malaria which have more altered biochemical changes which was also observed in this study to decrease the mean cell volume (MCV) in severe malaria patients.

In the present study, it was observed that there were no significant ($p>0.05$) changes in the mean platelet count (PLT), platelet crit (PCT) and mean platelet volume (MPV) of the malaria patients when compared to the control individuals. However, these parameters were significantly decreased in severe malaria patients which may likely indicate thrombocytopenia in severe malaria patients. This is in support of the study by Haruna, *et al.* [27], which reported that acute uncomplicated malaria is not associated with a marked reduction in platelets count as compared to severe malaria patients. Also, the platelet indices in this study were significantly lowered in malaria patients with age range 1-10 years when compared to the control patients. This result is in agreement with the earlier report by Maina, *et al.* [28] which reported that decrease in total platelet count and hence thrombocytopenia is hallmark of malaria in children due to depletion of platelet count and other platelet indices. The likely cause of thrombocytopenia during malaria is complex and may be related to coagulation disturbances, splenomegaly and platelet destruction by macrophages, bone marrow alterations, antibody-mediated platelet destruction, oxidative stress and platelets aggregation [29].

This study showed that some of the haematological indices of malaria patients were close to the same level with the control individuals with respect to the anti-malaria drug administered. From this study, the most potent anti-malaria drug capable of restoring the haematological indices to that of the control individuals is ACT and chloroquine. This is in support of the report of Sreeviski *et al.* [30], which reported reversal of major haematological indices upon administration of anti-malaria drugs among which is ACT. The reason for this reversal of some haematological indices upon drug administration may be due to the decrease in degree of parasitemia caused by these drugs which help to restore the processes in the blood cell production in the bone marrow

which had been altered by the parasite. However, among the haematological indices the total white blood cell count in malaria patients does not appear to be restored to the same level with control individuals upon administration of an anti-malaria drug.

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