Evaluation of Blood Cells and Platelets in *Plasmodium Falciparum* Malaria Infected Individuals

Ifeanyichukwu M.O[1], Esan A.J[2,*]

[1]Immunology Department, Nnamidi Azikiwe University, Nnewi Campus
[2]Haematology Department, Federal Medical Centre, Ido-Ekiti, Ekiti State Nigeria, Immunology
*Corresponding author: ayodelejacob4u@gmail.com

Abstract The aim of this study was to evaluate blood cells and platelets in Plasmodium falciparum malaria infected individuals. The study was conducted at Federal Medical Centre Ido-Ekiti, Nigeria. Two hundred and two blood samples were collected twice from each of the subjects; after obtaining informed consent and grouped as pre and post anti-malaria drug treatment samples. Thick blood film was made and stained with Giemsa's staining technique for malaria parasite detection and malaria parasite count as described by Monica Cheesbrough, blood cell parameters were analysed using Haematology Analyser. Data obtained was analysed using SPSS version 16. The result of this present study showed that, the mean±SD of malaria parasite count, mean platelet volume, total white blood cell count, relative and absolute neutrophil count, relative monocyte count, relative eosinophil count, in pre treatment were significantly (p<0.05) higher compared to post anti-malaria treatment and control. However, the mean±SD of absolute platelet count, relative lymphocyte count in pre treatment were significantly (p<0.05) lower compared to post treatment and control. The prevalence of Plasmodium falciparum malaria infection in male was higher compared to female. The study showed that, high parasite density was associated with severe clinical illness and complications which significantly reduced after taking anti-malaria drug. Thrombocytopaenia is one of the haematological abnormalities observed in patients with malaria parasite infection which usually disappears with the treatment of malaria infection, changes in the white blood cells were less dramatic in this study.

Keywords: malaria parasite, blood cells and anti-malaria drug

Cite This Article: Ifeanyichukwu M.O, and Esan A.J, "Evaluation of Blood Cells and Platelets in *Plasmodium Falciparum* Malaria Infected Individuals." *International Journal of Hematological Disorders*, vol. 1, no. 1 (2014): 49-54. doi: 10.12691/ijhd-1-1-10.

1. Introduction

The aim of this study was to evaluate blood cells and platelets parameters in *Plasmodium falciparum* malaria infected individuals. Malaria is a serious public health problem in most countries of the tropics. It is a major cause of mortality and morbidity, between 300 and 500 million people suffer acute cases of malaria in 100 developing countries each year, and the majority of the victims are children [1]. In Nigeria about 96 million people are exposed to malaria, and out of these 64 million people get infected and almost 300,000 deaths are being reported annually in the general population, of which over 100,000 deaths are of children [2]. Malaria parasite counts is the most important aspects of reporting malaria infections, it is used to estimate the level of parasitemia present in the blood, assessment of malaria parasites morphological is also critical for accurate interpretation. Assessment of the parasite density provides a useful indicator of severity of infection, particularly in non-immune patients, and the level of parasitaemia (parasite burden or load) correlates generally with clinical features and prognosis. A clinical malaria was defined as

Plasmodium falciparum parasitaemia >2,500 parasites/μl and axillary temperature ≥37.5°C or reported fever over the previous 24 hours. Haematological changes are some of the most common complications in malaria and they play a major role in malaria pathology [3,4]. These changes involve the major cell lines (red blood cells, leucocytes and thrombocytes). An understanding of these hematological changes will help in diagnosis and treatment and may also serve to predict and prevent various complications [3,4]. White blood cell differential measures the percentage of each type of white blood cells (WBC) that is in the blood. It reveals if there are any abnormal or immature cells. White blood cells are an important part of body's defense which buildup the body immune system. Other hematological reactions to malaria infection that have been reported include neutropenia, eosinophilia, neutrophilia and monocytosis [5,6]. Among the various haematological changes in malaria infection; thrombocytopaenia is the most consistent one, which occurs in more than half of the patients [7,8]. In endemic areas, malaria has been reported as the major cause of low platelet counts [9]. This is so characteristic of malaria, that in some places, it is used as an indicator of malaria in patients presenting with fever [8]. Platelet counts of less than 150 x 109/ L increase the likelihood of malaria by

12–15 times [10]. Thrombocytopaenia was seen in about 85% of the patients with uncomplicated malaria and in all the patients with severe *falciparum* malaria [8]. Faseela reported that, 82.8% patients had thrombocytopaenia whereas 17% patients had a normal platelet count. Malaria parasite was found to exert a significant reduction in platelet count in parasitized subjects. An inverse relationship was established between parasite density and platelet count [11,12]. The mechanisms leading to thrombocytopenia in malaria is thought to include immune mechanisms, oxidative stress, alterations in splenic functions, and a direct interaction between *plasmodium* and platelets [13]. The precise mechanism behind thrombocytopenia, however, remains unclear. Both the immunological as well as the non immunological destruction of platelets have been implicated [7,8,13,14,16].

2. Materials and Methods

2.1. Subjects, Study Design and Sample Collection

This study was conducted at Federal Medical Centre, Ido-Ekiti, Ekiti State Nigeria; between November 2012 and March 2013. Subjects were *Plasmodium falciparum* malaria infected adult individuals; presented with signs and symptoms of malaria infection. This was confirmed using malaria rapid kit test and microscopy detection of malaria parasite. Two hundred and two blood samples were collected twice from each malaria infected individuals; grouped as pre-treatment (at presentation) and post anti-malaria drug treatment using Artemisinins combination therapy, (artesunate and artemether). One hundred and two blood samples from apparently healthy adult individuals negative to malaria infection was collected for control; both *Plasmodium falciparum* malaria infected subjects and controls were within the age 15-64 years. Patient's consent was sort for through an informed consent form; also ethical approval was obtained from the hospital. Structured questionnaire was used to obtained demographic characteristic and other relevant information for the study.

2.2. Methodology

Thick blood film was made from EDTA blood sample and stained with Giemsa's staining technique for malaria parasite detection and malaria parasite count as described by Monica Cheesbrough, (2005). Blood cell parameters which includes absolute platelet count, mean platelet volume, platelet distribution width, total white blood cell count, relative and absolute differential white blood cell count were analysed using haematology analyser (Sysmex Automated Haematology Analyser Model kx-21n, manufactured by Sysmex Co-operation Kobe, Japan)

3. Statistical Analysis

Data obtained were analysed for mean and standard deviation; to compare the mean and standard deviation in each of the groups (pre, post treatment and control group).

Significance test was done by ANOVA and t-test. Level of significance was considered as <0.05.

4. Results

Table 1: showed comparisons of mean±SD of *Plasmodium falciparum* infected blood cell parameters in pre treatment, post anti-malaria treatment and control. The parameters includes malaria parasite count (per μl), absolute platelet count $(XI0^9)$, platelets distribution width (%), mean platelet volume (pL), white blood cell count $(XI0^9)$, relative neutrophil count(%), relative lymphocyte count(%), relative monocyte count(%), relative eosinophil count(%), absolute neutrophil $(XI0^9)$, absolute lymphocyte $(XI0^9)$ and absolute monocyte$(XI0^9)$. The mean±SD of malaria parasite count 2628.20±415.22 in pre treatment was significantly (p<0.05) higher compared to 2305.20±538.62 in post treatment (F = 1369.00; P = 0.00). The mean ± SD of absolute platelet count 168.62 ± 30.05 in pre treatment was significantly (p<0.05) lower compared to 179.78± 57.41 and 285.65 in post treatment and control respectively. (F=184.38; P=0.00).The mean ± SD platelet distribution width 12.01 ± 1.75 in control was significantly (p<0.05) lower compared to mean ± SD of platelet distribution width 13.60 ± 2.44 and 13.76 ± 2.46 in pre and post treatment respectively.(F = 20.81; p = 0.00). The mean ± SD of total white blood cell count 6.69± 1.67 in pre treatment was significantly (p<0.05) higher compared with 5.85 ± 1.96 and 4.42 ± 0.33 in post treatment and control respectively (F = 65.26 p = 0.00). The mean ± SD of relative neutrophil count 57. 43 ± 1.67 in pre treatment and 57. 28 ± 4.66 in controls were significantly (p<0.05) higher in each case compared with 52.90 ± 8.56 in post treatment (F = 15.50 p = 0.00). The mean ± SD of relative lymphocyte count 38.27 ± 9.34 in pre treatment was significantly (p<0.05) lower compared to 44.80 ± 7.98 and 41.56 ± 4.44 in post treatment and control respectively. (F = 33.55 p = 0.00). The mean ± SD of relative monocyte count 3.67 ± 2.18 in pre treatment was significantly (p<0.05) higher compared to 1.81 ± 1.51 and 0.93 ± 1.05 in post treatment and control respectively (F = 101.14; p= 0.00)   The mean ± SD of relative eosinophil count 0.96 ± 1.36 in pre treatment was significantly (p<0.05) higher compared to 0.49 ± 0.89 and 0.31 ± 0.67 in post treatment and control respectively (F = 15.53; p=0.00). The mean ± SD of absolute neutrophil count 3.89 ± 1.37 in pre treatment was significantly (p<0.05) higher compared to 3.14 ± 1.31 and 2.54 ± 0.29 in post treatment and control respectively (F = 45.69; p= 0.00). The mean ± SD of absolute lymphocyte count 1.84 ± 0.23 in control was significantly (p<0.05) lower compared to 2.49 ± 0.70 and 2.57 ± 0.35 in pre treatment and post treatment respectively (f = 40.32; p= 0.00) The mean ± SD of absolute monocyte count 0.11 ± 0.12 in post treatment was significantly (p<0.05) lower compared to 0.24 ± 0.18 and 0.42 ± 0.47 in pre treatment and control respectively (F = 88.98; p= 0.00). However, in between comparison between pre treatment and post treatment show that pre treatment had higher mean ± SD of malaria parasite count, total white blood cell count, relative neutrophil count, relative monocyte count, relative eosinophil count, absolute neutrophil count and absolute monocyte count compared to mean ± SD in post treatment

while post treatment had higher mean ± SD of relative lymphocyte compared to mean±SD in pre treatment. However, the mean±SD of absolute platelet count, platelet distribution width (PDW) and absolute lymphocyte were higher in post treatment compared to pre treatment while mean platelet volume (MPV) mean ± SD in pre treatment compared to post treatment, show no statistical significant difference (p>0.05). In between comparison between pre treatment and control show that pre treatment had higher mean ± SD of malaria parasite count (MPC), platelet distribution width (PDW), platelet volume (MPV), white blood cell count (WBC), relative monocyte, relative eosinophil, absolute neutrophil and absolute lymphocyte compared to mean ± SD in control; while control had significantly (p<0.05) higher mean ± SD of absolute platelet, relative lymphocyte and absolute monocyte compared to mean ± SD in pre treatment. The mean ± SD of relative neutrophil in pre treatment was higher when compared to mean ± SD of relative neutrophil in control, comparisons show no statistical significant difference (p>0.05). Multiple comparison between post treatment and control show that post treatment had significantly (p<0.05) higher mean ± SD of malaria parasite count (MPC), platelet distribution width (PDW), white blood cell count (WBC), relative lymphocyte, relative monocyte, absolute neutrophil and absolute lymphocyte compared to mean ± SD in control while control had significantly (p<0.05) higher mean ± SD of absolute platelet, relative neutrophil and absolute monocyte compared to mean ± SD

in post treatment. The mean ± SD of relative eosinophil was higher in post treatment compared to control; comparisons show no statistical significant difference (p>0.05). However, Figure 1 showed the prevalence of *P. falciparum* malaria parasite infection in sex distribution for both malaria infected subjects and control. The frequency for male and female were 129 and 73 respectively in malaria infected subjects while the frequency of control (non malaria infected individual) were 58 and 44 for male and female respectively.
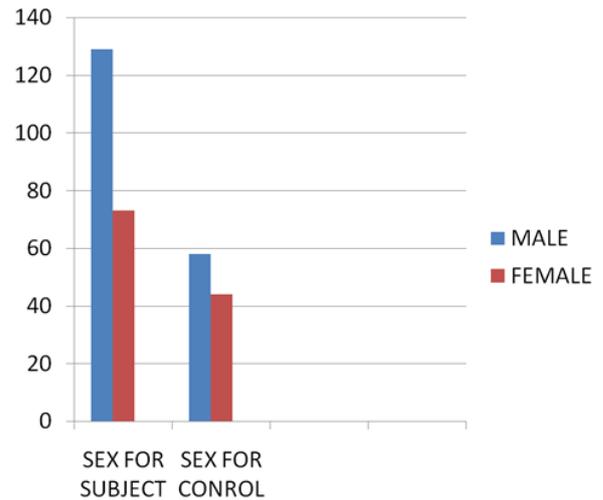

Figure 1. Sex Distribution of Malaria Infected Subject and Control

Table 1. Mean ± Sd Of Blood Cells and Platelet Parameters in Pre, Post Anti-Malaria Treatment in Malaria Infected and Control

Groups	MPC μ/L	PLT X10^9/L	PDW	MPV pL	WBC X10^9/L	NEU %	LYMP %	MONO%	EOSIN %	NUE X10^9/L	LYM X10^9/L	MONO X10^9/L
Pre- Treatment (N=202)	2628.20 ± 415.22	168.62 ± 50.05	13.60± 2.44	9.77 ± 0.80	6.69± 1.67	57.43± 9.99	38.27± 9.34	3.67± 2.18	0.96± 1.36	3.89± 1.37	2.49± 0.76	0.24± 0.18
Post Treatment n = (202)	2305.20 ± 538.65	179.78 ±57.41	13.74± 2.46	9.61± 0.65	5.85± 1.96	52.90± 8.56	44.80± 7.98	1.81± 1.51	0.49± 0.89	3.14± 1.31	2.57± 0.38	0.11± 0.12
Control N= (102)	-	285.65 ±47.81	12.01± 1.75	9.51± 0.25	4.42± 0.33	57.28± 4.66	41.56± 4.44	0.93± 1.05	0.31± 0.67	2.54± 0.29	1.84± 0.23	0.42± 0.47
F (p-value) (Pre Treatment)	1369.00 (0.00*)	184.38 (0.00*)	20.81 (0.00*)	5.97 (0.00*)	65.26 (0.00*)	15.50 (0.00*)	33.55 (0.00*)	101.14 (0.00*)	15.53 (0.00*)	45.69 (0.00*)	40.32 (0.00*)	88.98 (0.00*)
VS (Post Treatment) p-value	0.00*	0.10	0.84	0.06	0.00*	0.00*	0.00*	0.00*	0.00*	0.00*	0.60	0.00*
(Pre Treatment) VS (Control) P-value	0.00*	0.00*	0.00*	0.00*	0.00*	0.98	0.00*	0.00*	0.00*	0.00*	0.00*	0.00*
(Post Treatment) VS (Control) P-value	0.00*	0.00*	0.00*	0.19	0.00*	0.00*	0.00*	0.00*	0.13	0.00*	0.00*	0.00*

P<0.05 significance, P>0.05 no Significant, F (P-value) = mean ± SD of parameters compared using ANOVA
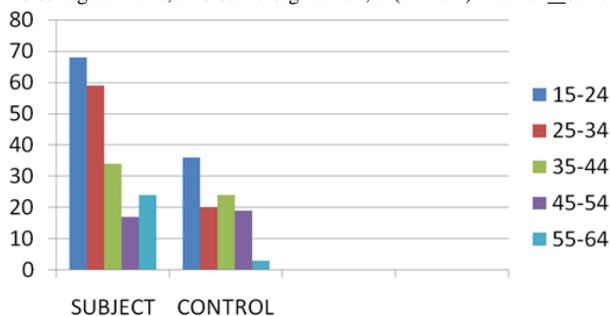

Figure 2. Age Disribution for Malaria Infected Subject And Control

5. Discussion

Malaria parasite counts is the most important aspects of reporting malaria infections, it estimate the level of parasitemia present in the blood. In this present study, the mean value of malaria parasite count in pre-treatment was significantly higher compared to post- treatment; this was due to effect of anti-malaria drug used during treatment. McElroy *et al.,* [17] and Murthy *et al.,* [18] supported that, patients with high parasite count have more severe and complicated course, also stated that the level of parasitaemia is useful as one of the criteria in defining "severe *P. falciparum* malaria" and to monitor the effect of anti-malarial therapy. Blood cell parameters which include absolute platelet counts, platelet distribution width, mean platelet volume, total white blood cell count, relative and absolute neutrophil, lymphocyte, monocyte and

eosinophil were significant in pre-treatment, post-treatment and control subject. The mean values of absolute platelet counts, platelet distribution width, relative and absolute lymphocyte in pre-treatment were lower compared to post-treatment while mean platelet volume, total white blood cell count, relative and absolute neutrophil, monocyte and eosinophil were higher compared to post-treatment; the blood cell parameters in control subjects were within normal range. Among the various haematological changes in malaria infection; thrombocytopaenia is the most consistent one, which occurs in more than half of the patients [7,8]. In endemic areas, malaria has been reported as the major cause of low platelet counts [9]. In this present study, thrombocytopenia was observed in the patient at presentation; a decrease in thrombocytopenia was observed in post-treatment. Increase in absolute platelet count observed in this present study during malaria treatment was supported by Dhanashri *et al.*, [19], who stated that absolute platelet count rises rapidly during the recovery of the patient after the anti malaria treatment. In other study, thrombocytopaenia usually disappears with the treatment of malaria infection and requires no treatment for it [20]. However, contrary to this fact, Sumbele *et al.*, [21] reported a decrease in platelet count was observed following treatment. Mechanism of thrombocytopaenia in malaria infection stated that platelets engulf malaria parasites, in the process of engulfing platelets are damaged and thus being removed from circulation [22]. Reduced platelet counts during malaria infection result from platelet activation; splenic pooling and the clumping of platelets have also been suggested as the reasons for thrombocytopaenia [7,12,23]. Mean platelet volume (MPV) vary with platelet production; younger platelets are larger than older ones, low mean platelet volume (MPV) indicates average size of platelets; older platelets are generally smaller than younger ones; also low mean platelet volume (MPV) may indicate that a condition is affecting the production of platelets by the bone marrow. High mean platelet volume (MPV) indicates a high number of younger platelets in the blood; this may be due to the bone marrow producing and releasing platelets rapidly into circulation however, low platelet distribution width (PDW) indicates uniformity in size of platelets and high platelet distribution width (PDW) indicates increased variation in the size of the platelets, these facts are in support of what we obtained in the present study. In the present study, total white blood cell counts are within the normal range, although the mean value in post treatment is lower compared to pre treatment, this observation in the present study was due to effect of anti-malaria drug. However, there is a slight increase in white blood cells count in malaria infected patients compared with the control; this was due to immune response against malaria infection; the number of WBC may be decreased or increased depending on a disease condition or a reaction occurring in the body, such reactions could be normal or abnormal. Contrary to this present study, McKenzie, [24]; Taha *et al.,* [25] reported that increase in WBC count observed in the treated malaria group support the finding that malaria infection (*P. falciparum*) contributes to the localization of leukocytes away from the peripheral circulation and to the spleen and other marginal pools, rather than actual depletion or stasis.

However, differential leukocyte count in the present study shows a slight neutrophilia and monocytosis in pre treatment and lymphocytosis in post treatment, eosinophil count is normal, although the mean values of differential leukocyte counts are in normal range. Inconsistent with Sumbele *et al.,* [21] reported that, total and differential white blood cell counts were assessed at the onset and compared to the treated and untreated malaria groups at the end of the study, neutrophil counts increased over time in the untreated group while a drop was observed for those treated. Conversely, monocyte count decreased in the treated groups while an increase was observed in the untreated group [21]. Although neutrophil count positively correlated with parasitaemia density following treatment. On the contrary, Ladhani *et al.,* [26] reported that neutrophil counts were not raised by hyperparasitaemia Molyneux *et al.*, [27] reported that, the positive association of neutrophil and parasitaemia may have been influenced by intercurrent bacterial infection which was not investigated. Monocytes are also important in developing immunity against *P. falciparum* malaria, monocytes have been reported to act against the malaria parasite through several mechanisms; the higher WBC, lymphocyte and granulocyte counts during the progress of malaria could be associated with severe or acute malaria. Similarly, Facer, [22] reported that; leukocytosis is typically in a fraction of cases and may be associated with concurrent infections and/or poor prognosis. He reported that, total WBC count findings showed the vast majority to be in the normal range unlike some studies which showed that leukopenia appears to be a common finding in both non-immune patients with falciparum malaria and semi-immune children living in malaria-endemic regions, where WBC may be as low as $1\text{-}2\text{x}10^9$/L. Differential leukocyte count showed neutrophil counts are in the normal range, which differs from other studies that reported either neutropenia or neutrophilia among malaria infections [6]. About half the patients had low lymphocyte counts (lymphopenia), while others had lymphocyte counts in the normal range. Monocytes, eosinophils and basophils were in the normal range in the majority of the cases which is in conformity with this present study. Although monocytosis has been reported to occur [5,6]. Bashawri reported that the majority of malaria patients had a normal monocyte count. There was also no increase in eosinophils, which agrees with previous reports [22]. However, eosinophilia has been reported to occur after initiation of anti-malaria treatment. Facer, [22] is contrary to this present study. Phagocytosis of malaria pigment by monocytes/ macrophages, and less frequently by neutrophils, has been observed in peripheral blood cells and bone marrow of patients with malaria [6,22,28]. Erythrophagocytosis of infected and uninfected red cells by monocytes/macrophages has also been observed [6,26]. In consistent with this present report, anti-malaria drug may be associated with a decline in the total white cell and neutrophil counts; Neutropenia is related to increased splenic sequestration. Leukocytosis is associated with more severe disease and is a poor prognostic marker. In a study conducted by Penali in Côte d'Ivoire where WBC and neutrophil counts were assessed on Day 0 (pre-treatment) and Day 7 (post treatment). The values at each data-point were compared for changes after treatment with anti malaria drugs. He reported that, there was a general

trend of a slight decrease in both total WBCs and neutrophil counts after treatment. In a similar study, WBC and neutrophil counts were assessed at pre-treatment and Day 14 after start of treatment. The values at each data-point were compared across treatments for changes after treatment with anti malaria drugs. There were minimal changes in WBC counts after treatment and a slight decrease in neutrophil counts in all groups [29]; their findings were similar to this present study. However, the prevalence of malaria parasite infection in male and female in this present study was supported by Akanbi *et al.*, [30] reported the prevalence of *Plasmodium* infection was reportedly higher in male than in female malaria infected patients, it was concluded that the cause could be due to the fact that males expose their bodies more than females when the weather is hot and thus increases their chances of being bitten by the mosquito. Also, females are usually not naked and tend to stay indoors, helping out with household chores. This reduces their contact with the mosquito vector. Also, studies have shown that females have better immunity to parasitic diseases and this was attributed to genetic and hormonal factors [31].

6. Conclusion

The study demonstrated that *p. falciparum* malaria is an important health problem in West African countries. High parasite density was associated with severe clinical illness and complications. Parasite density was significantly reduced after taking anti-malaria drug. However, there is an indication of drug resistance in some patients manifested by increase in malaria parasite count during treatment; this was due to high parasiteamia, low immune response to malaria infection and incompliance to directive in taking anti-malaria drugs. Thrombocytopaenia is one of the haematological abnormalities observed in patients with malaria parasite infection which usually disappears with the treatment of malaria infection and requires no treatment for it. However, changes in the white blood cells were less dramatic in this study.

References

[1] UNICEF. Rolling back malaria goals. A United Nation Children's Fund document. 2000; 16 pp.

[2] Alaribe AAA, Ejekie GC, Ezedinachi ENU. The ecology of Bain BJ (1996). Ethnic and sex differences in the total and differential white cell count and platelet count. *J Clin Pathol*. (2006) 49: 664-666.

[3] Maina R.N, Douglas Walsh, Charla Gaddy, Gordon Hongo, John Waituumbi, Lucas Otieno, Danel Jones and Bernhard R Ogutu. Impact of plasmodium falciparum infection in haematological parameters in children living in western Kenya. *Malaria Journal*; (2010) 9 (3): 54.

[4] Ovuakporaye S.I. Effect of malaria parasite on some haematological parameters: red blood cell count, packed cell volume and haemoglobin concentration. *Journal of Medical and Applied Biosciences*; (2011) 3: 45-51.

[5] Jandl JH. Hemolytic anemias caused by infection of red cells. In: Blood. 2nd edition. New York: Little Brown and Company; (1996) :473-501.

[6] Abdalla SH. Peripheral blood and bone marrow leucocytes in Gambian children with malaria: Numerical changes and evaluation of phagocytosis. *Ann Trop Paediatr* (1988) 8: 250-258.

[7] Aduragbenro D. Adedapo et al. Age as a risk factor for thrombocytopenia and anaemia in children treated for acute uncomplicated falciparum malaria. *J Vector Borne Dis* (2007) 44, pp. 266-271.

[8] Saleem Ahmed Khan, Waqar Ali et al. Platelet count in malaria. *Pak J Pathol* (2008) 86; 19 (3): 86-88.

[9] Gérardin P, Rogier C et al. Prognostic value of thrombocytopenia in African children with falciparum malaria. *Am J Trop Med Hyg* (2002). 66 (6):686-691.

[10] Lathia TB, Joshi R. Can hematological parameters discriminate malaria from nonmalarious acute febrile illness in the tropics? *Indian J Med Sci*.; (2004) 58 (6): 239-244.

[11] Abdalla S, Pasvol G. Platelets and blood coagulation in human malaria. In: Newton PN, Essien E, White NJ, editors. The Haematology of Malaria. London, UK: Imperial College Press; (2004) 249-276.

[12] Tan SO, McGready R, Zwang J, et al). Thrombocytopenia in pregnant women with malaria on the Thai-Burmese border. *Malar J*; (2008) 7: 209.

[13] Rogerson SJ, Hvid L, Duffy PE, Leke RFG, Taylor DW. Malaria in pregnancy: pathogenesis and immunity. *Lancet Infect Dis*. (2007); 7: 105-117.

[14] Makkar, RPS, Mukhopadhyay S, Monga A, Gupta AK. Plasmodium Vivax Malaria Presenting With Severe Thrombocytopenia. *The Brazilian Journal of Infectious Diseases*; (2002); 6 (5): 263-265.

[15] Jadhav UM, VS Patkar, NN Kadam. Thrombocytopenia in Malaria-Correlation with Type and Severity of malaria. *JAPI* (2004) VOL. 52; 554.

[16] Kumar A, Shashirekha. Thromocytopenia-an indicator of acute vivax malaria *Indian journal of pathology and microbiology*; (2006) 49 (4): 505-508.

[17] McElroy PD, Beier JC, Oster CN, Beadle C, Sherwood JA, Oloo AJ, *et al.* Predicting outcome in malaria: correlation between rate of exposure to infected mosquitoes and level of *Plasmodium falciparum* parasitemia. *Am J Trop Med Hyg*; (1994) 51: 523-32.

[18] Murthy GL, Sahay RK, Srinivasan VR, Upadhaya AC, Shantaram V, Gayatri K. Clinical profile of *P. falciparum* malaria in a tertiary care hospital. *J Indian Med Assoc*; (2000) 98: 160-2, 169.

[19] Dhanashri S Kelkar, Mrinal M Patnaik, Shashank R Joshi. Malarial Hamatopathy. *JAPI*; (2004) 52: 611-612.

[20] Bhushan Katira & Ira Shah. Thrombocytopenia in *Plasmodium vivax* infected children. *J Vect Borne Dis* (2006) 43, pp. 147-149.

[21] Sumbele Irene Ule Ngole, Nkuo-Akenji Theresa, Samje Moses, Ndzeize Thomas Ngwa Elsy Manka and Titanji V. P. K. Haematological changes and recovery associated with treated and untreated *Plasmodium falciparum* infection in children in the Mount Cameroon *Region Journal of Clinical Medicine and Research.* (2010) 2 (9), 143-151.

[22] Facer CA. Hematological aspects of malaria.. Infection and Hematology. *Oxford: Butterworth Heinmann Ltd*., (1994): 259-294.

[23] Jamal A, Memon IA, Latif F. The association of plasmodium vivax malaria with thrombocytopenia in febrile children. *Pak Paed J*; (2007); 31 (2): 85-89.

[24] McKenzie FE, Prudhomme WA, Magill AJ, Forney JR, Permpanich B, Lucas C, Gasser Jr RA and Wongsrichanalai C. White blood cell counts and malaria. *J. Infect. Dis.,* (2005) 192: 323-330.

[25] Taha K, El-Dein Z, Idrees M, Makboul G, Ghassan B. Hematological changes in malaria: relation to *plasmodium* species. *Kuwait Med J.,* (2007); 39 (3): 262-267.

[26] Ladhani S, Lowe B, Cole AO, Kowuondo K, Newton CRJC. Changes in white blood cells and platelets in children with falciparum malaria: relationship to disease outcome. *Br. J. Haematol.,* (2002); 119: 839-847.

[27] Molyneux, M. E., Hien, T. T. and White, N. Clinical Features and Prognostic Indicators in Paediatic Cerebral Malaria: A Study of 131 Comatose Malawian Children. *Q. J. Medicine* (1989); 78: 441.

[28] Amodu OK, Adeyemo AA, Olumese PE, Gbadegesin RA. Intraleucocytic malaria pigment and clinical severity of malaria in children. *Trans R Soc Trop Med Hyg*; (1998); 92: 54-56.

[29] Adjuik M, Agnamey P, Babiker A, Borrmann S, Brasseur P, Cisse M, Cobelens F, Diallo S, Faucher JF, Garner P, Gikunda S, Kremsner PG, Krishna S, Lell B, Loolpapit M, Matsiegui PB, Missinou MA, Mwanza J, Ntoumi F, Olliaro P, Osimbo P, Rezbach P, Some E, Taylor WR. Amodiaquine-artesunate versus amodiaquine for uncomplicated Plasmodium falciparum malaria in African children: a randomised, multicentre trial. *Lancet*; (2002); 359: 1365-72.

[30] Akanbi, O.M., J.A. Badaki, O.Y. Adeniran and O.O. Olotu,. Effect of blood group and demographic characteristics on malaria infection, oxidative stress and haemoglobin levels in South Western Nigeria. *Afr. J. Microbiol. Res.,* (2010); 4: 877-880.

[31] Zuk M, McKean KA. Sex differences in parasite infections: patterns and processes. *Inter J Parasitol;* (1996); 26: 1009-1023.