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Effects of Uncomplicated Malaria Parasitaemia on Selected Haematological Parameters and Phagocytes of Children Living in Port Harcourt, Southern Nigeria

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Abstract

This cross-sectional and case control study evaluated the effects of malaria parasites on selected haematological parameters of children living in Port Harcourt, Nigeria. A total of 352 participants were randomly recruited and their blood samples collected. Malaria diagnosis and estimation of haematological parameters were determined using standard parasitological and haematological methods respectively. Sociodemographics of participants showed that 109 (31%) of female children and 106 (30%) of male children were infected with malaria parasites. Overall prevalence of *Plasmodium falciparum* found was 215(61%). The study found a statistically significant difference in the mean values of packed cell volume (PCV), haemoglobin concentration (Hb), and white blood cell count (WBC) of *Plasmodium* parasitized children compared with their matched controls: PCV(34.83±2.76% versus 36.06±1.41%; P=0.001); Hb(11.58±0.92g/dL versus 11.98±0.46g/dL; P=0.001); WBC (8.96±4.56($x10^9$/L) versus 7.33±1.39($x10^9$/L); P=0.001).While the mean values of lymphocyte counts were relatively reduced in malaria infected children than their control participants (41.66±13.57($x10^9$/L) versus 42.95±8.36($x10^9$/L); P=0.27). A weak relationship was found to exist between density of parasitaemia and ages of children infected with malaria parasites (R^2=0.0093; P=0.1584). Though more children had low parasitaemia (1-999 parasites/µL), followed with high parasitaemia (>10,000 parasites/µL), while few had moderate parasitaemia (1000-9999 parasites/µL). There was no case of complication with respect to WHO standard which described complicated or severe anaemia in malaria as haemoglobin (Hb) of < 5g/dl or packed cell volume (PCV) of < 15% with parasitemia of > 250,000 parasites/µL. Malaria parasites affect outcomes of some haematological parameters. We recommend that all febrile children in our study area should be tested for malaria parasites in conjunction with estimation of their full blood count for effective malaria diagnosis and treatment particularly in sub patent cases.

Keywords: children, haematological parameters, Nigeria, malaria parasitaemia

1. INTRODUCTION

Malaria is a major public health problem in Nigeria, and many parts of Africa. Malaria is caused by unicellular protozoan parasites, *Plasmodium* species, which belong to the phylum, Apicomplexa. The different species of malaria parasites that can cause infection in humans include *Plasmodium falciparum, Plasmodium ovale*, *Plasmodium malariae, Plasmodium vivax,* and *Plasmodium knowlesi*. Malaria mostly spreads to people through the bites of some infected female *Anopheles* mosquitoes.The f irst symptoms may be mild, similar to many febrile illnesses, and difficulty to recognize as malaria. Left untreated, *P. falciparum* malaria can progress to severe illness and death within 24 hours (WHO, 2023)

Malaria infection largely affect children, especially children aged 6 months to 5 years and pregnant women (Marotta et al., 2018; Mehta, 2020). In 2019, about 409,000 people died of malaria, majority of which were 274,000 young children, and 94% of such infections and deaths occurred in Africa (CDC, 2019; WHO, 2020). In 2020 to 2021, a total of 492 million cases of malaria were reported globally with 1,244,000 associated malaria deaths (WHO, 2023). Nigeria leads with 31.3% among the four African countries with the highest global malaria cases and deaths (WHO, 2023). It has been hypothesized that malaria may cause as many as 10% of all deaths amongst children living in malaria endemic settings (Mehta, 2020). Children of all ages living in non malarious areas are equally susceptible to malaria.

Children who are diagnosed of uncomplicated malaria caused by *P. malariae, P. ovale, P. vivax,* could recover fully without any sequelae. However, malaria caused by *P. falciparum*, the dominant malaria parasite in Nigeria is highly virulent; if not detected, treated quickly and completely can progress to complicated severe malaria, which has grave prognosis (Mehta, 2020).

Generalized bleeding due to disseminated intravascular coagulation has been reported in non immune children with heavy malaria parasitaemia. Some degree of haemolysis is part of malaria, but some children have excessive haemolysis, putting them at risk for renal failure. This haemolysis may be related to glucose-6-phosphate dehydrogenase (G-6-PD) deficiency or an antibody-mediated destruction of erythrocytes. Anaemia is so common in malaria that it is considered as part of the disease. Some children have anaemia far exceeding that attributable to erythrocyte destruction by malaria parasite. Malarial anaemia can be quite severe, sometimes causing death (Mehta, 2020).

The malaria parasites consume glucose voraciously, thus heavy parasitaemia can result in hypoglycemia which is difficult to differentiate from cerebral malaria (Mehta, 2020). Therefore, notable features of severe malaria commonly expressed in children than adults include anaemia, cerebral malaria and hypoglycaemia (WHO, 2019).

Microscopic detection and identification of *Plasmodium* species in Giemsa stained thick blood films, for screening, and thin blood films, for species confirmation is accepted worldwide as the "gold standard" used for the routine diagnosis of malaria (Jain et al., 2012; WHO, 2011). However, the proficiency of the microscopist, quality of equipment, and reagent would determine the effectiveness of malaria microscopy. Other requirements are clean water supply, power supply and good quality management system (WHO, 2011). Therefore, during the past decades, various efforts to replace the traditional blood film for the diagnosis of malaria have revived interests in the possibility of using routine haematological blood parameters to aid the presumptive diagnosis of malaria infection (Jain et al., 2012). Alterations in the haematological parameters are also thought to have the capacity to act as an adjuvant tool in strengthening the suspicion of malaria, thereby prompting a more meticulous search for malaria parasites (George & Ewelike-Ezeani, 2011).

Changes in haematological parameters due to malaria parasitaemia could be as a result of biochemical changes that occurred during the asexual life cycle stage of the parasite. Malaria

infection causes destruction of erythrocytes and brings about changes in haematological parameters. Reports from studies have shown that episodes of malaria brings a lot of physiological disturbances in the haematological system of the host such as alteration in erythrocytes, leucocytes and thrombocytes subpopulations in the blood (WHO, 2009). Haematological parameter changes could be influenced by any pathological condition including malaria, that affects formation, development and differentiation of whole blood. Infection with malaria in human is associated with decrease haemoglobin concetration that brings about severe anaemia with high rate of mortality (Hussain et al., 2013).

Patients with malaria infection are liable to present significantly lower platelets, white blood cell counts, lymphocytes and eosinophils, red blood cells and haemoglobin level but have considerably higher monocyte and neutrophil count when compared with non-infected malaria patient (Bakhubaira, 2013). Some endemic regions lack these basic needs to accomplish microscopic examination to effectively diagnose malaria, therefore efforts have been made to replace malaria microscopy with other methods such as rapid diagnostic tests (RDTs) and automated machines including and using changes in haematological parameters to support malaria diagnosis (Jain et al., 2012). This study, therefore, determined changes in haematological parameters of children infected with malaria parasites in Port Harcourt, Rivers State, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Area

This cross-sectional and case control study was carried out in three health care facilities; Rivers State University Teaching Hospital (formerly known as BraithWaite Memorial Specialist Hospital (BMSH), New Mile One Hospital (formerly known as Mile One Clinic) and Rivers State College of Health Science and Management Technology Health Centre, all located in Port Harcourt, Rivers State, South-South geopolitical zone of Nigeria. The study was conducted between the months of February to July, 2022. Port Harcourt is a metropolitan city in Niger Delta region, located at 4^{o} 45^{1}N 6^{o} 50^{1}E/ 4.750^{o}N 6.833^{o}E of Nigeria, proximate to the Atlantic Ocean. The climate in Port Harcourt is marked by two distinct seasons, rainy season which starts in May and ends in October, and the dry season which begins in November and ends in March. The main occupations of residents include trading, fishing, civil service, and oil and gas company workers.

2.2 Ethical Statement

Prior to the study, approval was obtained from committee on ethics, Rivers State Hospitals Management Board, Port Harcourt. Also, informed consent was obtained from the participants' parents or guardians before their blood samples were collected for malaria microscopic examination, and evaluation of haematological variables.

2.3 Determination of Sample Size

The sample size was ascertained using a prevalence rate of 35.5% of malaria parasites amongst children residents in Port Harcourt as reported by Abah et al. (2017) at a confidence interval (CI) of 95% and a precision of 5% following the formula, $N=Z^2P\ (1-P)/d^2=(1.96)^2x\ 0.355x(1-0.355)/(0.05)^2$ for calculating sample size (Naing et al., 2006) which gave rise to a total of 352 participants.

2.4 Eligibility Criteria

Children whose age falls between 2-12 years that were infected with malaria parasite, children whose age falls between 2-12 years that were not infected with malaria parasites (control group) and children whose age falls between 2-12 years that have not been treated of malaria for at least four weeks before the sample collection day. Children whose age falls below the age of 2 years and those whose age is above the age of 12, children that have been treated of malaria within the space of 2-3 weeks before the day of sample collection were excluded.

2.5 Sample Collection and Laboratory Analysis

Five milliliters (5mls) of whole blood were randomly collected into ethylene diamine tetra-acetate acid (EDTA) tubes through venipuncture technique from a total of 352 children, aged 2-12 years, who were visiting the aforementioned Health facilities. A structured questionnaire was used to obtain socio-demographic data and history of malaria treatment with antimalarial drugs from participants. Thick blood films were made on glass slide, dried and stained with 3% solution of Giemsa stain and examined under the microscope using 100X objective for the presence of malaria parasite. Haematological parameters such as haemoglobin concentration, white blood cells count, packed cell volume, lymphocyte count, and neutrophil count were determined using Sysmex XP-300 haematology auto-analyzer according to the manufacturer's instruction.

2.6 Estimation of Parasite Density

The absolute density of parasitaemia in each malaria infected participant was estimated as the product of malaria parasite counted and absolute values of each participant's white blood counts as against a predetermined set range of white blood cells as described by Agomo et al. (2009). And the level of parasitaemia in each infected participant was graded as low, moderate, and high as Adesina et al. (2009) and Azuonwu et al. (2019).

2.7 Statistical Analysis

The raw data collated from this study were analyzed using Graph Pad prism version 5.0.3. Means and standard deviations were calculated for appropriate variables, while student's t test was used to evaluate the difference between means of two groups. Pearson product moment correlation coefficient was used to test the difference between variables. Results were represented in table and graph.The level of statistical significance was set at p-value of ≤ 0.05.

3. RESULTS

The findings from this study were presented below in Tables 1-3, and Figures 1-3. This study recorded an overall prevalence of 215 (61%) of *Plasmodium falciparum* malaria parasite among the participants. A total of 215 laboratory confirmed infected participants were used as the test group, while 137 non-infected participants of similar age group and gender were recruited as healthy-matched control groups.

3.1 Effect of Malaria Parasites on Haematological Values of Study Participants

Table 1 shows the difference in haematological values of malaria infected and non-infected children. Malaria infected children had a relatively low mean PCV values of 34.83±2.76%, compared with that of non-infected children of 36.06±1.41%. The difference between them was statistically significant (P=0.001). Children who were positive for malaria parasites had a relatively low mean Hb concentration of 11.58±0.92 g/dl, compared with that of malaria negative children of 11.98±0.46 g/dl. The difference between them was statistically significant (P=0.001). The total WBC counts of those infected with malaria parasites were

higher, 8.96±4.56 ($x10^9$/L), compared with those of non-infected control participants, 7.33±1.39($x10^9$/L). The difference between them was statistically significant (*P*=0.001). The mean Neutrophil count values of malaria parasite infected children were slightly higher 57.25±14.00 ($x10^9$/L), compared with that of the non-infected children, 56.54±8.36($x10^9$/L). But the difference between them was not statistically significant (*P*=0.549). The total mean count value for Lymphocyte was relatively low, 41.66±13.57($x10^9$/L), compared with that of non-infected children, 42.95±8.36($x10^9$/L). The difference between the two groups was not statistically significant (*P*=0.27).

Table 2 shows changes in haematological values of female children infected with malaria parasites. The mean percentage of PCV of infected female children was relatively low, 34.68±3.27%, compared with their non-infected counterparts, 36.06±1.41%. The difference between them was not statistically significant (*P*=0.001). The mean Hb values of malaria parasite infected female children was significantly different from those of non-infected female (11.52±1.09g/dl versus 11.92±0.46g/dl; *P*=0.001). The mean total WBC count of infected female children was relatively high, 9.86±5.77($x10^9$/L), compared with that of non-infected female, 7.33±1.39($x10^9$/L). And the difference between them was statistically significant (*P*=0.001). The mean counts for Neutrophils (58.45±11.32$x10^9$/L, versus 56.54±8.36 $x10^9$/L) and Lymphocyte (40.69±11.31$x10^9$/L, versus 42.95±8.36 $x10^9$/L) among infected female children and their non-infected counterparts were not statistically significant (*P*=0.141; 0.8).

Table 1. Comparison of haematological variables of malaria-infected children and control

Parameter	**PCV**	**Hb**	**WBC**	**NEUT.**	**LYMP.**
Test n= 215	34.83± 2.76	11.58±0.92	8.96 ± 4.56	57.25±14.00	41.66 ± 13.57
Control					
n= 137	36.06± 1.41	11.98±0.46	7.33 ± 1.39	56.54 ± 8.36	42.95 ± 8.36
p-values	0.001	0.001	0.001	0.549	0.27
t Stat	5.511	5.506	4.904	0.598	1.1

PCV=Packed Cell Volume; Hb=Haemoglobin; WBC=White Blood Cell; NEUT.=Neutrophil; LYMP.=Lymphocyte

Table 2. Changes in haematological variables of malaria parasite infected female children and non-infected subjects control

Parameter	**PCV**		**Hb**		**WBC**		**NEUT.**		**LYMP.**	
Female n=109	34.68	±3.27	11.52	±1.09	9.86	±5.77	58.45	±11.32	40.69	±11.31
Control n= 69	36.06	±1.41	11.98	±0.46	7.33	±1.39	56.54	± 8.36	42.95	± 8.36
p-values	0.001		0.001		0.001		0.141		0.8	
t Stat	4.098		5.72		16		1.476		1.74	

PCV=Packed Cell Volume; Hb=Haemoglobin; WBC=White Blood Cell; NEUT.=Neutrophil; LYMP.=Lymphocyte

Table 3 shows changes in haematological values of male children infected with malaria parasites. The mean percentage of PCV of infected male children was relatively low, 34.98±2.12%, compared with their non-infected counterparts, 36.06±1.41%. The difference between them was statistically significant (*P*=0.001). The mean Hb values of malaria parasite infected male children was significantly different from those of non-infected male (11.62±0.71g/dl versus 11.98±0.46g/dl; *P*=0.001). The mean total WBC count of infected male children was relatively high, 8.04±2.52(x10^9/L), compared with that of non-infected male, 7.33±1.39(x10^9/L). And the difference between them was statistically significant (*P*=0.009). The mean counts for Neutrophil (56.02±16.27x10^9/L, versus 56.54±8.36 x10^9/L) and Lymphocyte (42.66±15.55x10^9/L, versus 42.95±8.36 x10^9/L) among infected male children and their non-infected counterparts were not statistically significant (*P*=0.764; 0.859).

Table 3. Changes in haematological values of male children infected with malaria parasites and their matched control

Parameter	**PCV**		**Hb**		**WBC**		**NEUT.**		**LYMP.**	
Male n=106	34.98	±2.12	11.62	±0.71	8.04	±2.52	56.02	±16.27	42.66	±15.55
Control n= 68	36.06	±1.41	11.98	±0.46	7.33	±1.39	56.54	± 8.36	42.95	± 8.36
p-values	0.001		0.001		0.009		0.764		0.859	
t Stat	4.55		4.56		2.61		0.301		0.178	

PCV=Packed Cell Volume; Hb=Haemoglobin; WBC=White Blood Cell; NEUT.=Neutrophil; LYMP.=Lymphocyte

3.2 Relationship between Malaria Parasite Density and Age of Participants

Figure 1 shows correlation between malaria parasite densities and different ages of participants infected with malaria parasites. There was a weak relationship between malaria parasite density and the age of children infected with malaria parasites (R^2=0.0093; *P*=0.1584). The graphic representation of the relationship between malaria parasites density and age of infected children shows that more of the infected children had low parasitaemia (1-999 parasites/µL), followed by high parasitaemia (>10,000 parasites/µL), while infected children with moderate parasitaemia (1000-9999 parasites/µL) was significantly low.

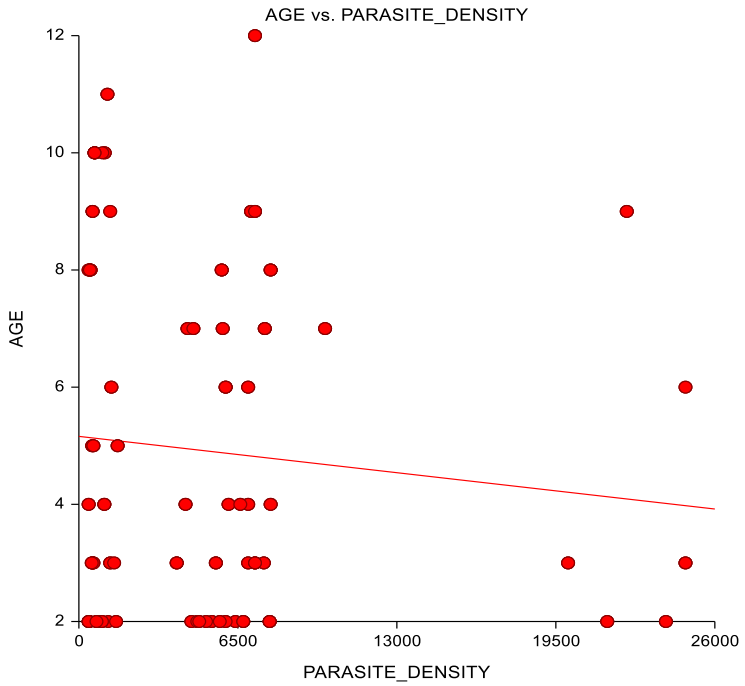

Figure 1. Correlation between age and parasite density of malaria infected children

3.3 Relationship between Packed Cell Volume (PCV) and Age of Infected Participants

Figure 2 shows correlation between different ages of participants infected with malaria parasites and their packed cell volume, PCV, values. There was a weak relationship between age of children infected with malaria parasites and their PCV values (R^2=0.0104; *P*=0.1356). The graphic representation of the relationship between the age of infected children and PCV values shows that more of the infected children had PCV values ranging from 30% to < 40%. Infected children within the age range of 2 to 4 years had a seemingly steady PCV values as represented graphically.

3.4 Relationship between White Blood Cells (WBC) and Age of Infected Participants

Figure 3 shows a relationship between age and white blood cell (WBC) in children infected with malaria parasites (R^2=0.054; *P*=0.006). Although no obvious linear relationship exist between the age and WBC of infected children but more of the WBC values are >5x10^9/L and <15 x10^9/L.

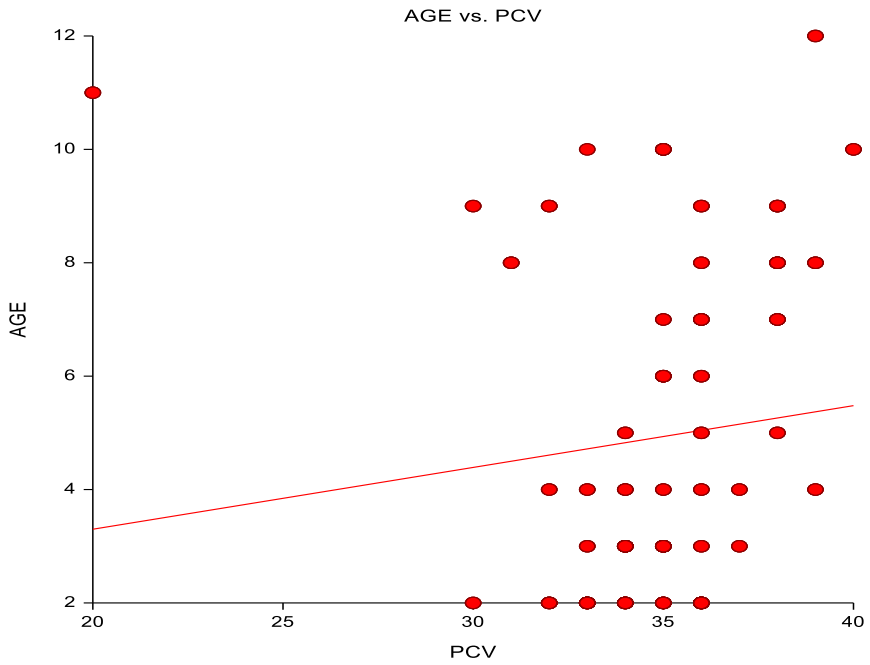

Figure 2. Correlation between age and PCV in malaria infected children

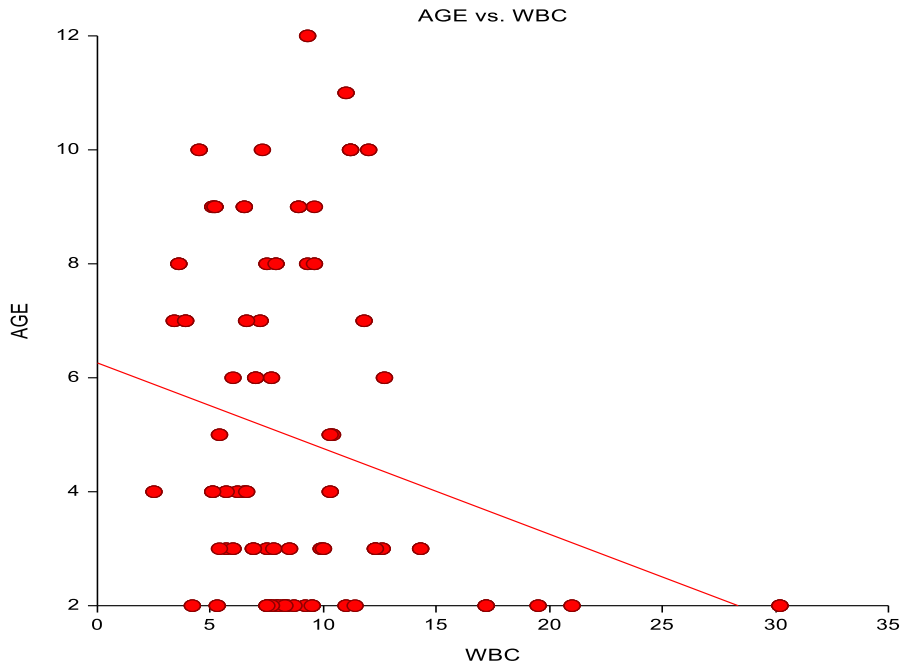

Figure 3. Correlation between age and WBC of malaria infected children

4. DISCUSSION

The deleterious impact of malaria is huge particularly on children living in endemic settings such as Nigeria. This study evaluated the effect of malaria parasite, *Plasmodium falciparum*, on some haematological parameters of children infected with the asexual stages of malaria parasites. Children are one of the high risk groups of individuals to malaria mostly due to undeveloped or partially developed immunity. This study found out an overall prevalence of 61% of malaria parasite infection among children. This finding is consistent with a prevalence of 62.5% reported by Nmadu et al.(2015) in a similar study conducted amongst children between the ages 2 to 15 years who visited Gwarinpa General Hospital Life-camp, Abuja, Nigeria. Although a relatively high prevalence of 87% of *Plasmodium falciparum* malaria parasite was earlier reported by Ayanful-Torgby et al. (2018). However, Azuonwu et al. (2019) published a comparatively low prevalence of 50% of *Plasmodium falciparum* malaria parasites among children living in Port Harcourt, Niger Delta. The high prevalence found in this study might be attributed to the rainy season of peak transmission of the parasite by female *Anopheles* mosquitoes which the study was conducted.

Findings in this study confirm that changes in haematological parameters are frequent in malaria parasite infection, even in uncomplicated malaria. This study demonstrated that the mean values of packed cell volume (PCV), and haemoglobin concentration (Hb), were significantly reduced, while that of total white blood cell counts were significantly increased among children infected with malaria parasites compared with their matched controls (P=0.001). This finding corroborates previous reports by Menendez et al. (2000), and Bashawri et al. (2002) which reported mild differences in white blood cell counts of *Plasmodium* parasitized individuals and their matched controls. However, earlier research works conducted by Erhart et al. (2004), Lathia et al. (2004) and Beale et al. (1972) observed leucocytopenia which is not consistent with some of our findings.

The reduced mean levels of PCV and Hb as observed in this study may suggest that *Plasmodium* induced anaemia which is primarily likely caused by mechanical destruction of infected children's red blood cells by malaria parasites. Other associated causes of possible anaemia could be nutritional status of *Plasmodium* parasitized children, and clearance of defected and infected red blood cells from the system.

The researchers found in this study a significant increase in the mean counts variations of WBC in both *Plasmodia* parasitized and non-parasitized children, however, the increase was not clinically significant, as the mean values of both infected and non-infected children were within the limits of normal reference range. In a similar study carried out by Gansane et al. (2013), showed that the differences in the mean values of total white blood cells and neutrophil counts of malaria parasite infected children and non-infected children were not statistically significant (P>0.05). The variation in differences of mean values of haematological parameters with that of this study could be due to different study settings and confounding factors. The increased levels of mean total white blood cell count observed among infected children in this study further affirms the basic immunological role of leucocytes in immunomodulation and defense against infectious agents such as *Plasmodium falciparum*.

This study also showed an increase in mean values of absolute neutrophil and a decrease in mean values of absolute lymphocyte counts in parasitized children against their control counterparts (P>0.005). This agrees with the report of Olliaro et al. (2011) on neutrophil count which was associated with higher *Plasmodium* parasitaemia. The reduced lymphocyte count observed in this study is consistent with report of earlier study conducted by Gansane *et al*. (2013). Lymphopenia according to findings of some researchers is sometimes profound but transient or temporary common in malaria vulnerable groups, such

as *Plasmodium* parasitized children living in malaria endemic areas and non-immune adults (Osaro et al., 2019; Maina et al., 2010).

This study has demonstrated the fact that the effect of malaria parasites on the haematological parameters of children is not gender specific as it affects both male and female children when compared to their various matched control groups.This study has pointed out that age is a factor in immunity against malaria parasites in children. As the age increases, the level of parasitemia decreases. This could be due to the immunity of the children becoming more matured and protective. This agrees with a study by Rodriguez-Barraquer et al. (2016) on blood parasite reduction and the ability to withstand a particular level of parasite without complication and observed that older children had less parasites as compared to the younger children, though with a p-value=0.1584 and R^2=0.0093 that makes it insignificant. Another related study done by Males et al. (2008) had same observation that parasite density is more in younger children. It was also found out in this study that older children have higher percentages of packed cell volume (PCV), which means a positive relationship exist between age of infected children and their PCV values (p=0.1356; R^2=0.0546).

5. CONCLUSION

Children infected with malaria parasites had significant changes in most of their haematological parameters. Findings of this study have shown significant decrease in PCV, Hb, and lymphocyte values of *Plasmodium falciparum*-parasitized children in our study area. These parameters could serve as malaria predictor markers in our study area. We recommend that all febrile children in our study area should be tested for malaria parasites in conjunction with estimation of their full blood count for effective malaria diagnosis and treatment particularly in sub patent cases.

References

Abah, A., Awi-Waadu, G., Nduka, F. & Richard, A. (2017). Malaria infection and socioeconomic status of some residents of Port Harcourt metropolis Rivers State. *Journal of Applied Science and Environmental Management*, 21(2), 299-304.

Adesina, K. T., Balogun, R. O., Babatunde, A.S., Sanni, M. A., Fadeyi, A.,& Aderibigbe, S. (2009). Impact of malaria parasitaemia on haematologic parameters in pregnant women at booking in Ilorin, Nigeria. *Trends in Medical Research*, *4*(4), 84-90.

Agomo, C. O., Oyibo, W. A., Anorlu, R. I. & Agomo, P. U. (2009). Prevalence of malaria in pregnant women in Lagos, South-West, Nigeria. *The Korean Journal of Parasitology, 47*(2), 179-183.

Ayanful-Torgby, R., Quashie, N. B., Boampong, J. N., Williamson, K. C. & Amoah, L. E. (2018). Seasonal variations in *Plasmodium falciparum* assessed by varying diagnostic tests in asymptomatic children in southern Ghana. *Public Library of Science One*, 13(6), 199-202.

Azuonwu, O., Wokem, G. N. & Dimkpa, F. B. (2019). Differential molecular investigation assay of tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-10(IL-10) among children potentially diagnosed of *falciparum* malaria of Niger Delta extract. *Lupine Online Journal of Medical Sciences, 4* (2), 358-363.

Bakhubaira, S. (2013). Haematological parameters in severe complicated *Plasmodium falciparum* malaria among adults in Aden.*Turkish Journal of Haematology*, *30*,394-399.

Bashawri, L. A., Mandil, A. A., Bahnassy, A. A. & Ahmed, M. A. (2002). Malaria: Haematological aspects. *Annals Saudi Medicine, 22*, 372-376.

Beale, P. J., Cormack, J. D. & Oldrey, T. B. (1972). Thrombocytopenia in malaria with immunoglobulin (IgM) changes. *British Medical Journal, 1* (5796), 345-349.

Centre for Disease Control and Prevention. (2019). *Impact of malaria*. https://www.cdc.gov/-malaria/hc/malaria/malaria_worldwide/impact.html

Erhart, L. M., Yingyuen, K., Chuanak, N., Buathong, N., Laoboonchai, A., Miller, R.S., Meshnick, S.R., Gasser, R.A. & Wongsrichanalai, C. (2004). Haematological and clinical indices of malaria in a semi-immune population of Western Thailand. *American Journal of Tropical Medicine and Hygiene*, *70*, 8-14.

Gansane, A., Quedraogo, I. N., Henry, N. B., Soulama, I., Quedraogo, E., Yaro, J., Diarra, A., Benjamin, S., Konate, A. T., Tiono, A. & Sirima, S. B. (2013). Variations in haematological parameters in children less than five years of age with asymptomatic *Plasmodium* infection: Implication for malaria field studies. *Memorias Do Instituto Oswaldo Cruz,108* (5), 533-670.

George, I. O. & Ewelike-Ezeani, C. S. (2011). Haematological changes in kids with jungle fever contamination in Nigeria. *Journal of Medicine and Medical Sciences*, *2*(4),768-771.

Hussain, M. M., Sohail, M., Abhishek, K. & Raziuddin, M. (2013). Investigation on *Plasmodium falciparum* and *Plasmodium vivax* infection influencing host haematological factors in tribal dominant and malaria endemic population of Jharkhand. *Saudi Journal of Biological Sciences*, *20*(2), 195–203.

Jain, M., Gupta, S., Jain, J., & Grover, R.K. (2012). Usefulness of automated cell counter in detection of malaria in a cancer set up-our experience. *Indian Journal of Pathology and Microbiology*, 55(4), 467–473.

Lathia, T. B. & Joshi, R. (2004). Can hematological parameters discriminate malaria from non malarious acute febrile illness in the tropics? *Indian Journal of Medical Sciences*, *58*, 239-244.

Maina, R. N., Walsh, D., Gaddy, C., Hongo, G., Waitumbi, J., Otieno, L., Jones, D., & Ogutu, B. R. (2010). Impact of *Plasmodium falciparum* infection on haematological parameters in children living in Western Kenya. *Malaria Journal, 9* (3). https://doi.org/10.1186/147 -2875-9-S3-S4

Males, S., Gaye, O., & Garcia, A.(2008). Long-term asymptomatic carriage of *Plasmodium falciparum* protects from malaria attacks: A prospective study among Senegalese children. *Clinical Infectious Disease*, *46*, 516-522.

Marotta, C., Di Gennaro, F., & Pizzol, D. (2018). The at-risk child Clinic (ARCC): 3years of health activities in support of the most vulnerable children in Beira, Mozambique. *International Journal of Environmental Research and Public Health*, *15*(7), 1350.

Mehta, P.N.(2020). Pediatric malaria. *Medscape*. https://www.emedicine.medscape.com

Menendez, C., Fleming, A.F., & Alonso, P.L. (2000). Malaria-related anaemia. *Parasitology Today*, 16, 469-476.

Naing, L., Winn, T., & Rusli, B.N. (2006). Practical issues in calculating the sample size for prevalence studies. *Archives of Orofacial Sciences*, *1*, 9-14.

Nmadu, P. M., Peter, E., Alexander, P., Koggie, A. Z. & Maikenti, J.I. (2015). The prevalence of malaria in children between the ages of 2-15 visiting Gwarinpa general hospital Life camp, Abuja, Nigeria. *Journal of Health Science*, 5(3), 47-51.

Olliaro, P., Djimde, A., Dorsey. G., Karema, C., Martensson, A., Ndiaye, J.L., Sirima, S.B., Vaillant, M., & Zwang, J. (2011). Hematologic parameters in pediatric uncomplicated *Plasmodium falciparum* malaria in sub-Saharan Africa. *American Journal of Tropical Medicine and Hygiene, 85*, 619–625.

Osaro, E., Abdulrahaman, A., & Erhabor, T. (2019). Effects of malaria parasitaemia on some haematological parameters of pregnant women of African descent in specialist hospital Sokoto, North Western Nigeria. *JOJ Nurse Health Care*, 10(4), 555795. https://junip-erpublishers.com/jojnhc/JOJNHC.MS.ID.555795.php

Rodriguez-Barraqer, I., Arinaitwe, E., Jagannathan, P., Boyle, M.J., Tappero, J., Muhindo, M., Kamya, M.R., Dorsey, G., Drakeley, C.,Ssewanyana, I., Smith, D.L., & Greenhouse, B. (2016). Quantifying heterogenous malaria exposure and clinical protection in a cohort of Uganda children. *Journal of Infectious Diseases*, 214(7), 1072-1080.

World Health Organization. (2011). *Universal access to malaria diagnostic testing: An operational manual.* World Health Organization. https://apps.who.int/iris/handle/10665-/44657

World Health Organization (2019). *Malaria in children under five*. World Health Organization. https://www.who.int/malaria/areas/highriskgroups/children/en/

World Health Organization (2020). *Fact sheet malaria*. World Health Organization. https//www.who.int/news-room/fact-sheet/detail/malaria

World Health Organization (2023). *Fact sheet malaria*. World Health Organization. https://www.who.int/news-room/fact-sheet/detail/malaria