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Effect of plasmodium Parasitaemia on some haematological parameters in children living in Sokoto, North Western, Nigeria

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Abstract
Objectives: Malaria infection is a major public health problem and cause of morbidity and mortality particularly among children in tropical and subtropical regions of the world. The aim of this present study was to determine the effect of plasmodium parasitaemia on some haematological parameters of children visiting the children emergency unit of Sokoto State Specialist Hospital in Sokoto, North Western, Nigeria. Method: This study was conducted among 126 children aged 2-11 years with mean age 5.36 ± 2.50 years presenting to the children emergency unit of Sokoto Specialist Hospital with history of febrile illness. Out of the children studied, 66 (52.4%) were positive for malaria while 60 (47.6%) were negative. Haematological parameters were analyzed using Mythic 22 CT 5- part differential Haematology analyzer (Orphée, Switzerland). Testing for malaria was carried out using the Onset Malaria Plasmodium falciparum (Pf) antibody (Ab) rapid test (CTK Biotech, Inc. USA) and speciation and number of parasites per high field was carried out on the Giemsa stained thing blood film. Results: The mean PCV, haemoglobin and platelet count of plasmodium-parasitized children was significantly lower compared to un-infected controls (29.48, 10.36 and 188.68) versus (32.76, 11.34 and 327.50) respectively (p=0.01). The prevalence of anaemia and thrombocytopenia was significantly higher among Plasmodium parasitized subjects compared to non-parasitized controls. Plasmodium falciparum was the predominant specie among the parasitized subjects. A negative and significant correlation was observed between the high number of parasite per high field and platelet count as index of thrombocytopenia and haemoglobin as index of anaemia (r=0.62 and p=0.75) respectively (p= 0.01) among parasitized subjects. Plasmodium parasitaemia was more prevalent among children in the 2-5 years age group (52.4%) compared to children in the 6-11 years age group (47.6%). Male children were more predisposed to malaria (53.0%) compared to female children (47.0%). Conclusion: Plasmodium parasitaemia has a significant impact on the haemoglobin, packed cell volume and platelet count of malaria parasitized children in Sokoto, Nigeria. Preventative strategies including regular chemoprophylaxis, intermittent preventative treatment with antimalarials, provision of iron supplementation and insecticide-treated bed nets should be implemented urgently to prevent the negative impact of malaria

parasitaemia on the haematological parameters of children in the area. There is need for community and peer-based awareness and education initiatives to strengthen the malaria prevention programme by educating parents on the benefits of effective environmental sanitation to destroy the breeding sites of Anopheles mosquito –the vector of malaria.

1. Introduction

Malaria remains a major health concern worldwide, causing 216 million infections and approximately 655,000 deaths in the year 2010 (1). About 91 percent of malaria–related deaths are in Africa with 86 percent of victims being children aged under five (2). Malaria is responsible for a significant number of deaths in endemic countries particularly in sub Saharan Africa (3, 4). Malaria is one of the three killers among communicable diseases in Africa (5). In southern Nigeria, at least 35,000 children die annually from direct effects of malaria alone (6). Despite frantic effort at eradicating malaria, about 40% of the world population in 91 countries continue to be plagued by this disease (7, 8).

The Roll back malaria (RBM) partnership goal to half the number of malaria infection by 2010 suggests the need for integrated approaches to combat malaria and reduce its consequences. Despite the advocacy for reduction of malaria by 2010, malaria still remains the major cause of outpatient visits and admission particularly among children under the age of 5 years. In Nigeria, a significant amount of budgetary allocation for health goes into the control and management of malaria (9). Over 45% of outpatients visits to primary, secondary and tertiary health facilities are attributable to malaria (1). Approximately 0.25 million Nigerian children under the age of 5 die from malaria – related complications annually (10).

Haematological changes are some of the most common complications in malaria and they play a major role in malaria pathology (11-12). These changes involve the major cell lines (red blood cells, leucocytes and thrombocytes) (13, 15). Anaemia is defined as a decrease in number of red blood cells (RBCs) or less than the normal quantity of haemoglobin for an individual age and gender. Although normal values can vary between laboratories, typical values would be less than 13.5 g/dL in adult males and less than 12.0 g/dL in adult non-pregnant females and less than 11 g/dL among adult pregnant females (16). From the age of 2 years to puberty, haemoglobin of less than 11.0 g/dL indicates anaemia. Malaria is thought to be the primary cause of severe anaemia in at least 50% of people living in malaria endemic area (17).

There appear to be a paucity of data on the effect of Plasmodium parasitaemia on the haematological parameters of malaria -infected children in Sokoto, North Western geopolitical zone of Nigeria. The aim of this study was to determine the impact of Plasmodium parasitaemia on some haematological parameters of children 2-11 years in Sokoto, Nigeria and to compare the haematological parameters of plasmodium parasitized children with non-parasitized controls.

2. Methods

The full blood count was carried out using Mythic 22 CT fully automated 5 part-differential haematology analyser. The analyser is based on impedance principle on the basis that red or white cells are poor conductor of electricity compared to the diluents such as saline. Malaria diagnosis was carried out using the Onset Malaria Plasmodium falciparum (Pf) antibody (Ab) rapid test (CTK Biotech, Inc. USA). Blood film was prepared by the push wedged method, air dried, fixed in methanol and stained with Giemsa stain.

2.1. Subjects

This study was conducted among 126 children aged 2-11 years with mean age 5.36 ± 2.50 years presenting to the children emergency unit of Sokoto Specialist Hospital with history of febrile illness. Out of the children studied, 66 (52.4%) were positive for malaria while 60 (47.6%) were negative. Verbal informed consent was obtained from the parents/guardians of the subjects. Children who presented with clinical signs of malaria infection; elevation of temperature (aural < 37.5°C), history of fever or any of the following symptoms: headache, dizziness, joint pain, anorexia, nausea, spontaneous bleeding who were 2-11 years who showed laboratory evidence of malaria were enlisted as subjects into the study. Ethical clearance was obtained from the ethical committee in Sokoto Specialist Hospital (SHS/SUB/133/VOL. 1) Sokoto, Nigeria.

2.2. Inclusion Criteria

All children of consenting parents aged between 2-11 years attending children emergency unit of SHS with history of febrile illness were eligible to participate in the study.

2.3. Exclusion Criteria

All non-febrile children < 2 and > 11years and children whose parent have not given informed consent were excluded from participating as subjects in this study.

2.4. Study Area

This present research work was carried out at the Pathology Department of Sokoto Specialist Hospital and the service laboratory at the Faculty of Medical Laboratory Science of Usmanu Danfodiyo University in Sokoto in the North West geo-political zone of Nigeria. The hospital is a secondary health facility and a center of excellence in the rendering of good standard of care to residents in Sokoto emirate and its environs. Sokoto State is located in the extreme North Western part of Nigeria near to the

confluence of the Sokoto River and the Rima River. With an annual average temperature of 28.3 °C (82.9 °F), Sokoto is, on the whole, a very hot area. However, maximum daytime temperatures are for most of the year generally under 40 °C (104.0 °F). The warmest months are February to April when daytime temperatures can exceed 45 °C (113.0 °F). The rainy season is from June to October during which showers are a daily occurrence. There are two major seasons, wet and dry which are distinct and are characterized by high and low malarial transmission respectively. Report from the 2007 National Population Commission indicated that the state had a population of 3.6 million (18).

2.5. Data Analysis

Statistical analyses were conducted using SPSS (Version 17, Chicago Illinois) software. Comparisons were assessed using mean and chi-square test. A p-value of ≤ 0.05 was considered statistically significant in all statistical comparison. Correlation was compared using a version of linear regression analysis.

2.6. Methods

2.6.1. Full Blood Count (Principle and Procedure)

The full blood count was carried out using Mythic 22 CT Haematology analyser (Orphée, Switzerland). The analyzer is 5-part differential fully automated haematology analyser. The analyser is based on impedance principle on the basis that red or white cells are poor conductor of electricity compared to the diluents such as saline. The cell suspension is drawn through the aperture with help of vacuum pump into a system of tubing. When a cell passes through the aperture, it displaces an equal volume of the conducting solution and increases the electrical resistance, creating a voltage pulse. The height of the pulse (impedance) is proportional to the volume of the cell.

2.6.2. Malaria Antibody Rapid Test (Principle and Procedure)

The *Onset* Malaria Plasmodium falciparum (Pf) antibody (Ab) Rapid test (CTK Biotech, Inc. USA) is a double antigen based lateral flow immunochromatographic assay. The strip consists of a burgundy coloured conjugate pad containing recombinant Pf – MSP conjugated with colloid gold (Pf conjugates) and Rabbit IgG – gold conjugates and a nitrocellulose membrane strip containing one test band (T band) and a control band (C band). The T band is pre-coated with recombinant Pf – MSP for the detection of antibodies to Pf only and the C band is pre-coated with goat anti rabbit IgG.

2.7. Thin Blood Film for Malaria Parasite

A small drop of EDTA anticoagulated blood, about 2mm in diameter was placed, about 1cm from one end of the slide and used for the preparation of a blood film using the push wedged method. The slide was placed on a flat surface. Held down firmly at the opposite end with thumb and forefinger. Quickly, the spreader was placed just in front of the drop of blood at 45^0 angle. If the patient is anaemic, the spreader was held more erect (at 60^0), and blood spread more quickly to obtain a thicker smear. The thin film was air-dried. The slide was flooded with Giemsa stain and allowed to act for 15 minutes. Excess stain was washed off under running tap water. Slide was drained, air dried and examine microscopically.

3. Results

3.1. Age and Malaria

A total of 126 consecutively recruited children visiting the children visiting the children emergency unit of Specialist Hospital Sokoto with history of febrile illness were tested for malaria. Of this number 66 (52.4%) were positive for malaria while 60 (47.6%) negative were processed. Malaria positivity was significantly higher among subjects in the 6-11years age group 41 (32.5%) compared to children in the 2-5 years age groups 25 (19.8%). Table 1 show the age –related distribution of Plasmodium falciparum among subjects.

Table 1. *Age –related distribution of Plasmodium falciparum among subjects*

Age (Years)	Number (%) Tested	Number (%) Malaria positive	Number (%) Malaria Negative
2-5	56 (44.4%)	25 (52.4%)	31 (51.7%)
6-11	70 (55.6%)	41 (47.6%)	29 (48.3%)
Total	126 (100%)	66 (100%)	60 (100%)

3.2. Gender-Related Distribution and Malaria Parasitaemia among Subjects

The distribution of malaria parasitaemia was compared among subjects based on gender. Of the 126 blood samples were processed, 66(%) were positive for malaria while 60 (%) were negative. Out of the 66 malaria parasitized subjects 35 (53.0%) were males while 31(47%) were females.

3.2.1. Effect of Malaria Parasitaemia on Haematological Parameters

Haematological parameters was compared between parasitized and non-parasitized children. The mean PCV, haemoglobin and platelet count of plasmodium parasitized and non-parasitized children was significantly lower among malaria-infected children compared to un-infected controls (29.48, 10.36 and 188.68) and (-32.76, 11.34 and 327.50) respectively (p=0.01). The prevalence of anaemia (HB<11g/dl) and thrombocytopenia (< 140 $x10^9$/L) was significantly higher among Plasmodium parasitized subjects 37(56.1%) and 35(53%) compared to non-parasitized controls 20(33.3%) and 13(21.7%) respectively

(p=0.01). A negative and significant correlation was observed between high numbers of parasite per high field on the blood film and platelets as an index of thrombocytopenia and haemoglobin as index of anaemia (r= 0.62 and respectively, p=0.75; p= 0.01) among parasitized subjects. The distribution of anaemia and thrombocytopenia among malaria parasitized and non-parasitized children is shown in table 3. Plasmodium parasitaemia was more prevalent among children in the 2-5 years age group (52.4%) compared to children in the 6-11 years age group (47.6%). Male children were more predisposed to malaria (53.0%) compared to female children (47.0%). Table 4 show the distribution of malaria parasitaemia among subjects based on gender.

Table 2. *Some haematological parameters in malaria parasitized subjects*

Haematology parameter	Mean value of Parasitized subjects	Mean Value of Non-parasitized Control	t-value	p-value
Hb (g/dl)	10.38	11.34	2.86	0.01
PCV (%)	29.48	32.76	2.63	0.01
MCV (fl)	78.41	77.87	-0.37	0.71
MCH (pg)	27.54	27.62	0.17	0.87
MCHC (g/l)	35.15	35.50	1.16	0.25
RDW (%)	16.50	15.90	-0.11	0.27
Platelet count ($x10^9$/L)	188.68	327.50	2.32	0.01

Table 3. *Prevalence of anaemia and thrombocytopenia in malaria –infected and non-infected children*

Haematological abnormality	Number Malaria infected	% Malaria infected	Number Malaria non- infected	% Malaria non-infected	p-value
Anaemia (HB< 11g/dL)	37	56.1	20	33.3	0.01
Thrombocytopenia (Platelet count < 140 $x10^9$/L)	35	53.0	13	21.7	0.01

Table 4. *Malaria parasitaemia based on gender parasitized subjects*

Gender	Number (%) malaria positive	Number (%) malaria negative	Total (%)
Male	35 (53.0)	28 (46.7 %)	63 (50.0%)
Female	31 (47%)	32 (53.3%)	63 (50.0%)
Total	66(100%)	60(100%)	126 (100%)

3.2.2. Malaria Parasite Identification and Speciation

Blood smears (thin and thick films) were prepared for all malaria positive samples and stained using Giemsa stain (for confirmation, speciation and parasite load determination). T Plasmodium falciparum was the predominant specie among the parasitized subjects. A significant number of malaria-infected children 43 (65.2%) had mild parasitaemia (+) defined as average of 1 parasite per high field while 7(10.6%) had moderate parasitaemia (2+) defines as minimum of average of 2 parasites per high field while 2(3.03%) had marked parasitaemia (3+) defined as an average of 3 parasites per high field. We did not find any malaria parasites in the blood film of 14(21.2%) despite the rapid malaria antibody based test being positive and child presenting with febrile illness. Table 5 show the distribution of malaria parasitaemia per high field in stained blood film

Table 5. *Malaria parasite identification and numbers per high field on stained film*

Malaria result based on rapid antibody test Positive	Malaria parasites per high field				
	+	++	+++	No parasite seen	Total
Number (%)	43 (65.2)	7(10.6)	2(3.03)	14(21.2%)	66(100)

4. Discussion

Malaria alone accounts for up to 25% or more of all hospital attendance, with young children under 5 years in developing countries worst hit (9). Globally, malaria causes 3,000 deaths per day, an annual total that exceeds one million deaths worldwide (19).

In this present study to investigate the effect of malaria on some haematological parameters among children in Sokoto, we observed that 52.3% of children presenting with history of febrile illness to the children emergency unit were found to be positive for malaria. Our finding is consistent with previous report which indicated that 52.3% of children presenting with history of febrile illness to the children emergency unit were found to be positive for malaria. Our finding is also consistent with previous report by Ejezie and colleagues (20) who reported that malaria was responsible for over 45% of outpatient's admission in rural Nigeria. Our finding is also consistent with findings from previous reports from various parts of Nigeria; Mbanugo and Ejims (57.9%) (21) in Akwa Anambra State, Imam (66.3%) (22) in Kano, Northern Nigeria, Olasehinde

and colleagues (80.5%) (23) in Ota, Ogun state and Nwaorgu and Orajaka (52.4%) (24). The high prevalence (52.3%) obtained in this study in Specialist Hospital Sokoto (SHS) may be as a result of the fact that this present study was carried out during the raining season. During raining season there is ecological alterations favouring the breeding of the mosquito vector which facilitate the spread of malaria infection. Other incriminating factors include the rapid rate of urbanisation of Sokoto and its attendant sanitation and public health problems. These problems have arisen as a result of inadequate waste disposal facilities, poor drainage system and poor water supply among many others. Many farmers in the state, in a bid to meet the food demands of the rising population, have undertaken some water-related projects involving the impoundment of drains or streams to create reservoirs for the purposes of irrigating farms. Despite the economic significance of these projects, these reservoirs also become breeding grounds of mosquitoes.

In this study, we observed a significantly lower values of haematocrit and haemoglobin concentration among malaria-infected children compared to the controls. The incidence of anaemia (HB< <11g/dl) was significantly higher among malaria parasitized children (56.1%) compared to non- infected children (33.3%). Our findings is consistent with previous reports (12, 14-15, 25) which observed a higher incidence of anaemia among parasitized children compared to controls. Similarly our observed prevalence is also lower that that obtained by Fowowe (26) who reported a prevalence rate of 28% in State Specialist Hospital Ondo, Imam and Inbadawa (27) who obtained a prevalence rates of 69.4% respectively among children in Kano State. In Ibadan, South western Nigeria, Igbeneghu (28) obtained a prevalence of (66.3%) of anaemia among children infected with Malaria. Similarly studies in other African countries obtained prevalence of 83.6% (29) and (56.3%) (30).

Haematological changes are common complications encountered in severe malaria (31). Our finding is consistent with previous reports (12, 14, 32-34). The etiology of anaemia among parasitized children is thought to be multifactorial; haemolysis of parasitized red blood cells, accelerated removal of both parasitized and non-parasitized red blood cells, depressed and ineffective erythropoiesis due to tumour necrosis factor alpha, anaemia of chronic disease, and splenic phagocytosis or pooling (18–21, 35-38). Similarly, a previous report indicates that there is an abnormally high level of tumor necrosis factor (TNF), in malaria parasitized subjects and that it is associated with marrow suppression (36) and imbalance in RBC surface markers such as CR1(39). Potential causes of haemolysis include loss of infected cells by rupture or phagocytosis, removal of uninfected cells due to antibody sensitization or other physicochemical membrane changes, and increased reticuloendothelial activity, particularly in organs such as the spleen. Decreased production results from marrow hypoplasia seen in acute infections, reduced erythropoiesis and dyserythropoiesis, a morphological appearance, which in functional terms results in ineffective erythropoiesis, specific/nonspecific immune responses whereby red cell survival is shortened. The potential role of parvovirus B19 as a possible cause of bone marrow aplasia has been postulated (36, 40).

In this present study we observed that malaria parasite exerted a significant reduction in platelet count in parasitized subjects. An inverse relationship was observed between number of parasite per high field on blood film and platelet count. This finding is consistent with previous reports which found thrombocytopenia a common occurrence in children infected with *P. falciparum (10, 13, 41)*. Thrombocytopenia is a one of the significant haematological challenges associated with malaria infection in children (42). Thrombocytopenia appear a common finding associated with malaria infection among children. A previous report (43) advocated that thrombocytopenia should be included in severe malaria criterion described by WHO. The mechanisms leading to thrombocytopenia in malaria is thought to include immune mechanisms, oxidative stress, alterations in splenic functions and direct interaction between plasmodium and platelets (44). Similarly, P. vivax infection has been found to exert a negative effect on the platelet count (34, 41). Thrombocytopenia is one of the most common complications of both Plasmodium vivax and Plasmodium falciparum malaria (45-47).

The aetiology of malaria-related thrombocytopenia is thought to include immune mechanisms, coagulation disturbances, splenomegaly, bone marrow alterations, oxidative stress, alterations in splenic functions, a direct interaction between plasmodium and platelets, sequestration and pooling of the platelets in the spleen, immune-mediated destruction of circulating platelets, and platelets -mediated clumping of P. falciparum-infected erythrocytes resulting in pseudo-thrombocytopenia (12,34,41,48). There is increasing advocacy to include thrombocytopenia as one of the WHO criterion for severe malaria (49).

Human malaria is commonly caused by predominantly 4 species of Plasmodium; P. falciparum, P. vivax, P. ovale and P. malariae (50). In this study, the predominant

Specie of Plasmodium responsible for all malaria infection among the children studied was Plasmodium falciparum. Our finding is consistent with previous report which found P. falciparum the predominant specie responsible for malaria infection in Nigeria (34, 50-52). Plasmodium falciparum is much more prevalent in sub-Saharan Africa than in many other regions of the world. In most African countries, over 75% of cases were due to P. falciparum, whereas in most other countries with malaria transmission, other, less virulent plasmodial species predominate.

The mainstay of malaria diagnosis has been the microscopic examination of blood, utilizing stained blood films (53). The most economic, preferred, and reliable

diagnosis of malaria is microscopic examination of blood film because each of the four major parasite species has distinguishing characteristics. Two sorts of blood film are traditionally used. Thin films are similar to usual blood films and allow species identification because the parasite's appearance is best preserved in this preparation. Thick films allow the microscopist to screen a larger volume of blood and are about eleven times more sensitive than the thin film, so picking up low levels of parasitaemia is easier on the thick film, but the appearance of the parasite is much more distorted and therefore distinguishing between the different species can be much more difficult.

In this study, we did not see any parasite in the blood film of 14(21.2%) of children who presented with febrile illness and tested positive using the *Onsite* Malaria Plasmodium falciparum (Pf). The OnSite Pf/Pv test is capable of detecting Plasmodium falciparum-specific histidine rich protein-2 (Pf HRP2) and P. vivax-specific parasitic lactate dehydrogenase (pLDH) antigens. There may be several reasons for this observation; it is possible that the degree of parasitaemia may be significantly low. It may also be as a result of prior suboptimal management with self-prescribed antimalarial therapy. PLDH does not persist in the blood but clears about the same time as the parasites following successful treatment. The lack of antigen persistence after treatment makes the pLDH test useful in predicting treatment failure.

5. Conclusion

In this present study, we have shown that malaria parasitaemia produces a significant effect on the incidence of anaemia and thrombocytopenia in malaria-infected children. We observed a significant negative correlation between platelet count and degree of parasitaemia. Preventative strategies including regular chemoprophylaxis, intermittent preventative treatment with antimalarials, provision of iron supplementation and insecticide-treated bed nets should be implemented urgently to prevent the negative impact of malaria parasitaemia on the haematological parameters children. There is need for community and peer-based awareness and education programmes to strengthen the malaria prevention programme by educating parents on the benefits of regular check-up particularly when their ward presents with symptoms of malaria. There is also the need to encourage parents to ensure that their plasmodium parasitized children adhere strictly to recommended malaria chemoprophylaxis to prevent the development if drug –resistant malaria strains. We reinforce the advocacy to include thrombocytopenia as one of the WHO criterion for severe malaria.

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Conflict of Interest

Authors declare that there are no conflicting interest with this article

Authors Contribution

O Erhabor designed the study, ACU Ezimah facilitated the recruitment and counselling of the pregnant subjects while Mohammad Horo Jamilu and Ahmed HM were responsible for obtaining informed consent, sampling and laboratory testing of samples. All authors read and approved the final report.

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