

Research Article

Anaemia and Thrombocytopenia among Malaria Parasitized Children in Sokoto, North Western Nigeria

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Submitted: 22 May 2014

Accepted: 25 June 2014

Published: 02 July 2014

ISSN: 2333-6684

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OPEN ACCESS**Keywords**

- Anaemia
- Thrombocytopenia
- Malaria
- Children
- Sokoto
- Nigeria

Abstract

Malaria infection is a major public health problem and cause of morbidity and mortality particularly among children and pregnant women in tropical and subtropical regions of the world. The aim of this present study was to determine the effect of plasmodium parasitaemia on the incidence of anaemia and thrombocytopenia among 126 children aged 2-11 years with mean age 5.36 ± 2.50 years who presented 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 thin blood film. The mean PCV, haemoglobin and platelet count of plasmodium- parasitized children was significantly lower compared to non-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 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 has a significant impact on the haemoglobin, packed cell volume and platelet count of malaria parasitized children. 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 malaria-related negative impact of anaemia and thrombocytopenia among malaria parasitized children in North Western Nigeria.

INTRODUCTION

Malaria is a global public health problem and the most widespread disease in the tropics with high morbidity and mortality [1-3]. Anaemia and thrombocytopenia are the most frequent malaria-associated haematological complications [4]. According to the World Health Organization Scientific Group¹, the levels of haemoglobin below which anaemia is likely to occur for a population living at sea level are: 11g/dl for children aged six months to six years, 12g/dl for children aged between 6 and

14 years, 13g/dl for adult males, 12g/dl for non-pregnant adult females and 11g/dl for adult pregnant females [5].

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. The main parasitic infections associated with anaemia include malaria and helminthic infections [6]. Malaria related anaemia is associated with many factors which involve increased destruction and reduced production of red blood cells [7].

Thrombocytopenia is a common feature of *Plasmodium falciparum* malaria and it is frequent in patients with acute malaria and is sometimes profound in cases of severe disease [8,9]. The presence of thrombocytopenia in acute febrile travellers returning from tropical areas has become a highly sensitive clinical marker for malaria diagnosis [10]. A previous report indicates 60% sensitivity and 88% specificity of thrombocytopenia for malaria diagnosis in acute febrile patients [11]. The sensitivity of thrombocytopenia together with the acute febrile syndrome was 100% for malaria diagnosis, with a specificity of 70%, a positive predictive value of 86% and a negative predictive value of 100% [12,13]. The mechanism of thrombocytopenia in malaria is probably the consequence of several factors including immune factors and the destruction or sequestration of platelets [14]. There is paucity of data on the prevalence of malaria parasitaemia among children in Sokoto, North Western Nigeria. It is not known what effect malaria infection has on the prevalence of anaemia and thrombocytopenia in the area. This present study was carried out to assess the prevalence of malaria parasitaemia among children and to determine the effect of malaria infection on the prevalence of anaemia and thrombocytopenia among children with febrile illness in the area.

METHOD

Study area

The selected area for this study is Usmanu Danfodiyo University Teaching Hospital (UDUTH) which is located in Wamakko Local Government within Sokoto Metropolitan city in Sokoto State. Sokoto State is located in the extreme Northwest of Nigeria, near the confluence of the Sokoto River and 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 day time 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 May 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 [15].

Study setting

The study was conducted in the Faculty of Medical Laboratory Science of Usmanu Danfodiyo University in collaboration with Haematology Department of Usmanu Danfodiyo University Teaching Hospital and Haematology Department of Specialist Hospital Sokoto.

Subjects

This study included One Hundred and twenty six (126) children aged 2-11 years and mean age 5.36 ± 2.50 years visiting the children emergency unit of Sokoto State Specialist Hospital (SHS) with history of febrile illness. The hospital is a secondary health care facility rendering quality specialist health care services to residents of Sokoto state.

Inclusion criteria

All consecutively recruited children aged between 2-11 years visiting the emergency unit of Specialist Hospital Sokoto with history of febrile illness and whose parents and guardians consented to their inclusion in this study were eligible to participate as subjects for this study.

Exclusion criteria

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

Sampling and methods

This study included 126 consecutively recruited children aged 2-11 years and mean age 5.36 ± 2.50 years visiting the children emergency unit of Specialist Hospital Sokoto with a history of febrile illness. About 3 millilitres of whole blood were collected using monovette vacutainer syringe into EDTA anticoagulated tube to be used for malarial rapid diagnostic test and full blood count. Thin blood film was prepared by the Push Wedged method and stained with Giemsa for malaria confirmation and specification. The *Onset Malaria Plasmodium Falciparum* (Pf) Antibody (Ab) Rapid test (CTK Biotech, Inc. USA) a double antigen based lateral flow immunochromatographic assay was used for malaria diagnosis. Full blood count was carried out using Mythic 22 CT fully automated haematology analyser (Orphée, Switzerland).

RESULTS AND DISCUSSION

Results

A total of 126 consecutively recruited 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.

Effect of malaria parasitaemia on haematological parameters

Haematological parameters were compared between parasitized and non-parasitized children. The mean PCV, haemoglobin and platelet count of plasmodium parasitized children was significantly lower among parasitized children compared to non-parasitized controls (29.48, 10.36 and 188.68) and (32.76, 11.34 and 327.50) respectively (p=0.01). There were no statistically significant differences between the mean MCV, MCH, MCHC and RDW among malaria -infected and non-infected children. The prevalence of anaemia (HB<11.0 g/dl) and thrombocytopenia (< 140 x10⁹/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 the numbers of parasite per high field on the blood film and platelets count 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%). Plasmodium falciparum was the predominant specie of malaria observed among parasitized children.

Anaemia and thrombocytopenia in malaria -infected

The prevalence of anaemia (HB<11.0 g/dL) and Thrombocytopenia (platelet count<140 x 10⁹/L) was compared between malaria- parasitized subjects and non-parasitized controls. The prevalence of anaemia and thrombocytopenia among malaria parasitized subjects was 56.1% and 53% respectively compared to 33.3% and 21.7% respectively among non-parasitized children. Table 2 show the prevalence of anaemia and thrombocytopenia among malaria parasitized and non-parasitized children.

Malaria parasite identification and speciation

Thin blood smears were prepared for all malaria positive samples and stained using Giemsa stain (for confirmation and speciation). 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.. Table 3

Table 1: 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

Abbreviations: HB: Haemoglobin; PCV: Packed Cell Volume; MCV: Mean Cell Volume; MCH: Mean Cell Haemoglobin; MCHC: Mean Cell Haemoglobin Concentration; RDW: Read Cell Distribution Width

Table 2: 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 (Haemoglobin < 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 3: Malaria parasite speciation and number of parasites per high field on stained film.

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

show the distribution of malaria parasitaemia per high field in stained blood film

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 [16]. Globally, malaria causes 3,000 deaths per day, an annual total that exceeds one million deaths worldwide. Malaria remains one of the world's greatest childhood killers and is a substantial obstacle to social and economic development in the tropics particularly among children aged less than 5 years [17].

In this present study to investigate the effect of malaria on the prevalence of anaemia and thrombocytopenia among children presenting to the emergency department of Sokoto Specialist Hospital, we observed that 52.3% of children presenting with history of febrile illness to the children emergency unit were positive for malaria. Our finding is consistent with previous report by Ejezie and colleagues [16] 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 by Mbanugo and Ejim [18], Imam and colleagues [19], Olasehinde and colleagues [20] and Nwaorgu and Orajaka [21] who obtained malaria prevalence of 57.9%, 66.3%, 80.5% and 52.4% respectively among children visiting the paediatric units in hospitals in Akwa, Anambra State, Kano, Northern Nigeria, Ota, Ogun state and Akwa North, Anambra state respectively. The high prevalence (52.3%) obtained in this study in the Specialist Hospital Sokoto may be due to the fact that this present study was carried out during the raining season. During raining season there are 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 meeting 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.

Anaemia is the commonest complication of malaria among children [22]. Studies in East Africa have shown that P. falciparum malaria and iron deficiency account for much of the anaemia seen in young children [23]. Some randomized studies concluded that anaemia in infancy could be prevented by antimalarial chemoprophylaxis [24]. In this study, we observed 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 report by Mustapha and Aliyu [25] who observed a higher incidence of anaemia among parasitized children compared to controls. Similarly our observed prevalence is consistent with report by Fowowe [26] who reported a prevalence rate of 28% in State Specialist Hospital Ondo and Imam and Inbadawa [27] who obtained prevalence rates of 69.4% respectively among children in Kano State. Similarly, studies in other African countries obtained prevalence of 83.6% 56.3% and 42% respectively in Gabon, Uganda and Southern Cameroon respectively [28-30].

Haematological changes including anaemia and thrombocytopenia are common complications encountered in severe malaria [31-34]. 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 [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 [35] and imbalance in RBC surface markers such as CR1 [38]. 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 [35,39]. Malaria -associated anaemia predisposes children particularly in malaria endemic countries in Africa to blood transfusion. One of the challenges in most African Countries is assessing adequate and safe blood. The World Health Organization (WHO) recommends that all blood donations should be screened for malaria. Although this policy can potentially have significant implications of the number of suitable units for transfusion, it has not been implemented by some transfusion services in sub-Saharan Africa [40]. Socioeconomic status may also affect the risk of anaemia by affecting nutritional status, family size, and birth interval, as well as intensifying problems of affordability and accessibility of preventive and curative measures [41].

Thrombocytopenia is a one of the significant haematological challenges associated with malaria infection in children [42]. Previous report advocates that thrombocytopenia be included in severe malaria criterion described by WHO [43]. In this present study we observed that malaria parasite exerted a significant reduction in platelet count of 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* [44-45].

Thrombocytopenia is a one of the significant haematological challenges associated with malaria infection in children [43,46]. Thrombocytopenia appears a common finding associated with malaria infection among children. There is increasing advocacy [47] to include thrombocytopenia 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 [48]. Similarly, *P. vivax* infection has been found to exert a negative effect on the platelet count [31,44]. Thrombocytopenia is one of the most common complications of both *Plasmodium vivax* and *Plasmodium falciparum* malaria [43,49-50]. The aetiology of malaria-related thrombocytopenia is thought to also include coagulation disturbances, splenomegaly, bone marrow alterations, 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 [44,48].

In this study we observed a negative correlation between malaria parasitaemia and thrombocytopenia. Our finding is consistent with previous reports which indicated an inverse correlation between platelet count and malaria infection [51-53]. Similarly previous report showed an association between thrombocytopenia and either severity or prognosis in childhood *falciparum* malaria [54-56].

CONCLUSION

The study clearly shows that malaria still poses a significant problem particularly among children visiting the children emergency unit of Specialist Hospital Sokoto, North western Nigeria. There is a high prevalence of anaemia and thrombocytopenia among plasmodium parasitized children.

RECOMMENDATION

Awareness campaign on malaria-induced anaemia and thrombocytopenia in the community should be conducted highlighting signs of its onset, quick referral and early intervention. Clinicians should be alerted by the diagnosis of anaemia and thrombocytopenia among children presenting to the children with history of febrile illness. We advocate that thrombocytopenia and anaemia should be included in severe malaria criterion described by WHO. Roll back malarial campaign should be accessible, and affordable to the entire populace. Iron supplementation policy for malaria infected children should be implemented.

ACKNOWLEDGEMENT

Authors are grateful to the parents and children that constituted the subjects in this study. Our sincere gratitude also to the Assistant Chief Medical Laboratory Scientist and staff of the Department of Haematology in Usmanu Danfodiyo University, Sokoto, Nigeria for their assistance with testing of the samples.

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Cite this article

Erhabor O, Mohammad HJ, Onuigbo FU, Abdulrahman Y, Ezimah AC (2014) Anaemia and Thrombocytopenia among Malaria Parasitized Children in Sokoto, North Western Nigeria. *J Hematol Transfus* 2(2): 1020.