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Research Article

Severe Malarial Anaemia in Children in Sokoto, Nigeria

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Abstract

Background: Severe malarial anaemia is responsible for approximately a third of the deaths associated with severe malaria. In Sokoto, North Western Nigeria where there is increased seasonal transmission of malaria the prevalence of anaemia due to severe malaria in children is yet to be studied.

Objective: To determine the prevalence and clinical characteristics of children with severe malarial anaemia admitted into the Department of Paediatrics of Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto, Nigeria.

Methods: This was a 3-year prospective and descriptive observational study from January 2013 to December 2015. Cases were children aged 6 months to 15 years admitted with severe malaria and severe anaemia based on WHO criteria. Relevant information from study proforma data sheets were extracted and analyzed using SPSS version 22.

Results: Of the 3753 children admitted during the study period, 1205 (32.1%) had severe malaria. Whereas 66(1.8%) children with severe malaria had blood transfusion for anaemia, only 38 of them accounting for 1% of the total admissions had severe malaria anaemia (PCV < 15%). The mean age was 3.3 ± 2.9 yrs. Majority (78.9%) were aged 1 to 5 years, and females accounted for 71.1%. All were transfused packed cell blood; median time of transfusion was within 12 hours of admission. Five patients (13.2%) died and mortality was higher in those who had complications of respiratory distress (p = 0.13), hyperparasitemia (p = 0.16), and cerebral malaria (p = 0.004).

Conclusion: Severe malarial anaemia is an important cause of childhood mortality in the study area. Prompt evaluation and early transfusion may reduce mortality.

Keywords: Severe Malaria; Anaemia; Children; Prospective; Study

Introduction

Malaria is a major public health burden. About 3.3 billion persons are at risk of the infection worldwide and it affects almost 300 million yearly leading to about 1 million deaths. Majority of the infections (90%) and the mortality occurs in Sub Saharan Africa amongst children under the age of five years [1,2]. Severe malarial anemia (SMA) caused by *P. falciparum* is responsible for approximately a third of the deaths associated with severe malaria [3]. As many as 5 million cases of severe malarial anemia occur in African children every year, and 13% of these cases are fatal [3].

The World Health Organization (WHO) defines SMA as hemoglobin concentration of <5.0 g/dl (or a hematocrit <15.0%) in the presence of any density of malaria parasitaemia [4]. Severe anaemia may occur alone or in combination with other complications of severe malaria particularly cerebral malaria and respiratory distress in which it portends worse prognosis [4-6]. More than half of young children in African countries where malaria is endemic are anemic. Nutritional deficiencies and various infections account for some of this disease burden, but malaria is one of the most important factors contributing to anemia as shown by studies on se-

vere anemia in Nigeria and Malawi [7-9]. Some studies carried out in holo-endemic regions in South West Nigeria and Zambia have shown severe anaemia as the predominant presentation of severe malaria [10-13].

Malarial anemia causation is multi-factorial [3,5]. It involves increased removal of infected circulating erythrocytes as well as decreased production of erythrocytes in the bone marrow. Although most children in sub-Saharan Africa are repeatedly infected with *Plasmodium falciparum,* life-threatening anemia develops only in some of the children. It is unclear which factors predispose these children to become markedly more anemic than others. This huge burden of SMA may even be underestimated as a result of large numbers of children who die in the community, under diagnosis and poor record keeping in the limited health facilities [10].

Treatment of severe anaemia requires blood transfusion which is also fraught with the danger of transmission of infections particularly retroviral infection in areas where properly screened blood is scarce [10].

Sokoto in North Western Nigeria is a region with where malaria is partly mesoendemic and hyperendemic with increase in seasonal transmission during the wet rainy season [14]. The prevalence and pattern of SMA is yet to be studied in the region. It is essential to therefore know the burden in this environment for better approach to risk management and reduction of attendant mortality.

Subjects, Materials and Methods

- **Study area:** The study was carried out at the Emergency Paediatrics Unit (EPU) of Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto, Nigeria. This is a tertiary health facility located in Sokoto, the Sokoto State capital. The hospital serves as a referral centre for more than 10 million people of the States of Sokoto, Zamfara and Kebbi; and the neighbouring Niger and Benin Republics in the West African sub-region [15]. Sokoto State is located in the dry Sudan Savannah. Sokoto town lies between latitude 10º and 14ºN, and longitude 3º3^{1} and 7º7^{1} east of the Equator [15]. It has an annual average temperature of 28.3ºC, with the highest temperatures reaching up to 45° C during the hot dry months. The rainy season is short and begins late in May till September with a mean annual rainfall of 550 mm. The dry season comprises the hot dry season before the rains from March to April and the cold dry season from November to February [16]. There is intense malaria transmission throughout the year with peaks during the rainy season [14,17]. Even though the rainy season is short, poor drainage systems also contribute to mosquito breeding sites throughout the year.

- **Study design:** This was a 3-year prospective and descriptive observational study conducted from 1st January 2013 to 31st December 2015.

- **Study subjects:** Comprised children aged 6 months to 15 years admitted into the EPU with acute febrile illness and associated pallor eventually diagnosed as severe malarial anaemia were enrolled. Their diagnosis was based on WHO criteria of packed cell volume (PCV) of less or equal to 15% in the presence of malaria parasitaemia. Additionally, subjects with severe malaria whose PCV was not less than 15% but less than 20% who were transfused on account of cardiovascular decompensation were also included but analyzed separately. Excluded were cases of severe malaria without anaemia, those who had haemoglobinopathies like sickle cell disease, lymphoproliferative disorders and those who had any other diagnostic cause of their anaemia apart from severe malaria. Approval for the study was obtained from the Health Research and Ethics Committee of the UDUTH, Sokoto, Nigeria.

Procedure of patient management

Children with severe malarial anaemia were admitted into the emergency paediatric unit under close monitoring, some were placed on oxygen therapy immediately while awaiting blood transfusion. After resuscitation, urgent sample collection including malaria parasite test and packed cell volume was done. Thick film for malaria parasite was done. This film was stained with a 3% Giemsa solution for 45 min and observed for the number of asexual parasites per 200 white blood cells (WBCs). Blood sample via Venepuncture into a sample bottle or vacutainer with anticoagulant EDTA was drawn via aseptic technique. A plain bottle was used for taking samples for urgent grouping and cross-matching. Blood samples were analyzed in the Side Laboratory of the Paediatrics Department and the Hematology Department of the hospital.

History and physical findings were documented. Their anthropometric measurements (weight and height/length) were also taken. Socioeconomic index scores were awarded to each child based on the occupation and educational attainment of the parents or their substitutes according to the method proposed by Oyedeji [18].

On admission, the patients were placed on the first line anti-malarial agent for severe malaria recommended by WHO which is intravenous artesunate. Intravenous quinine infusion was used if there was persistence of symptoms after 72 hours. After 48 hours of intravenous anti- malarial medication, the patients were them placed on oral anti- malarial, Artemisinin Combination Therapy (ACT). They were given Artemeter - Lumefantrine (AL) with adequate clinical and parasitological response. They were all transfused on admission with fully screened packed red cell blood against Human Immunodeficiency Virus, Hepatitis B and C viruses. Other necessary supportive care was provided as required.

Data entry and analysis

The demographic, clinical characteristics including age, gender, presenting symptoms, physical findings, and level of consciousness were documented. The criteria used for the diagnosis of severe malaria in addition to anaemia were recorded. Also, the results of malaria parasite test, pre-transfusion and post-transfusion packed cell volume, ABO blood group and haemoglobin electrophoresis were also recorded. The duration of admission before blood transfusion and length of hospital stay were noted. All relevant data were entered into a proforma sheet then analyzed using SPSS statistical software version 22. Those who had PCV above 15% and were transfused were entered separately and analyzed for comparison. Quantitative data were expressed as means and standard deviation while categorical variables were expressed as proportions. Chi-square or where necessary, Fisher's Exact test, was used to test for statistical significance. A p-value of <0.05 was considered statistically significant.

Results

Socio-demographic characteristics of patients:

There were 3753 children admitted into the EPU of the hospital during the study period from January 1st 2013 to 31st December 2015. Out of this number, 1205 (32.1%) had severe malaria with various complications. Thirty-eight children (3.2%) of those with severe malaria had severe malarial anaemia (PCV <15%). This accounted for 1% of the total admissions for the study period. The mean age was 3.3 ± 2.9 years with a range of 10 months to 12 years. Majority (78.9%) were aged 1 to 5 years. The male to female ratio was 1: 2.5 with females accounting for 71.1%. They were mainly from the lower socio-economic class (92.1%). This is shown in table 1.

Table 1: Age and gender distribution of the children with severe malarial anaemia (n = 38).

Age (Years)	Male n (%)	Female n (%)	Total n (%)
< 1	0 (0.0)	2 (5.3)	2 (5.3)
1.0 - 5.0	10 (26.3)	20 (52.6)	30 (78.9)
5.1 and above	1 (2.6)	5 (13.2)	6 (15.8)
Total	11 (28.9)	27 (71.1)	38 (100.0)

$x^2 = 1.54$, df = 2, p = 0.46.

Another subset of patients with severe malaria had moderate anaemia because their PCV did not reach the threshold of SMA of< 15% according to the WHO criteria. Their PCV ranged from 16% to 20%. However, they had blood transfusion on account of their worsening clinical condition and signs of cardiovascular decompensation. They were 28 in number accounting for 2.3% of the patients with severe malaria and 0.75% of the total admissions during the study period. These groups of patients were mainly above the age of 5 years (57.1%). Their mean age was 5.4 ± 3.4 years with a range of 6 months to 13 years. Male to female ratio was 1:1 and twenty-three (82.2%) belonged to the lower socio-economic class. This is shown in table 2 below.

Table 2: Age and gender distribution of the children with severe malarial and moderate anaemia (n = 28).

Age (Years)	Male n (%)	Female n (%)	Total n (%)
< 1	4 (14.3)	0 (0)	4 (14.3)
1. 0 - 5.0	0 (0.0)	8 (28.6)	8 (28.6)
5.1 and above	10 (35.7)	6 (21.4)	16 (57.1)
Total	14 (50.0)	14 (50.0)	28 (100.0)

$x^2 = 13$, df = 2, p = 0.002.

Yearly and monthly prevalence

During the 3-year period of the study, the highest number of cases was seen in the year 2013 accounting for 48.4% of all cases and cumulatively, most cases were in the month of September accounting for 40.9%. This coincided with the rainy season peak from August to October.

Presenting symptoms and signs of patients with SMA

The symptoms patients had at presentation included fever (92.1%), persistent vomiting (47.4%), prostration (39.5%), convulsions (28.9%), and altered consciousness (26.3%). These and other complications they presented with are shown in table 3.

Table 3: Presenting features of children with Severe Malaria and Moderate Anaemia.

*Presenting feature	Number	%
Symptoms		
Fever	35	92.1%
Underweight	19	50%
Vomiting	18	47.4%
Prostration	15	39.5%
Convulsions	11	28.9%
Altered consciousness	10	26.3%
Complications		
Respiratory distress	26	68.4%
Heart failure	25	65.8%
Hyperpyrexia	19	50%
Cerebral malaria	8	21.1%
Hyperparasitemia	6	15.8%
Haemoglobinuria	1	2.6%

*A patient may have more than one symptom or complication

The pattern of presentation of those with moderate anaemia is also shown in table 4. Though, not significant, a higher proportion of the complications occurred in those who were below 3 years of age.

Table 4: Presenting features of children with severe malarial and moderate anaemia (n = 28).

*A patient may have more than one symptom or complication

Presenting feature	Number	%
Symptoms		
Fever	26	92.9%
Prostration	15	39.5%
Vomiting	14	50%
Convulsions	14	50%
Underweight	10	35.7%
Altered consciousness	4	14.3%
Complications		
Hyperpyrexia	19	67.9%
Heart failure	15	53.6%
Respiratory distress	10	35.7%
Cerebral malaria	3	10.7%
Hyperparasitemia	0	0%
Haemoglobinuria	0	0%

Results of Investigations

The mean PCV of those with SMA was 12.6 ± 1.8% (range of 7 to 15%). Two patients had PCV less than 10%. The haemoglobin electrophoretic pattern was mainly AA in 70.2% while blood group was mainly Group O in 42.9% of them. Similar findings of electrophoretic pattern and blood group were seen in the group with moderate anaemia. However, their mean PCV was 17.6% (range of 16 to 20%).

Treatment

All of the patients were transfused with fully screened packed red cell blood. About half (52.8%) were transfused within 24 hours of admission in the group with SMA compared to 32.1% transfused within 24 hours in the group with moderate anaemia. The mean transfusion time was within 12 hours of admission for those with severe anaemia. Most (85%) were treated with intra-venous artesunate, then artemisinin combination therapy (ACT) as stated earlier on, while 15% received quinine infusion as a 2nd line antimalarial agent followed by ACT or oral quinine.

Outcome

There were 6 mortalities in all. Five patients (13.2%) died among the 38 patients with SMA while 1 patient (3.5%) died amongst the 28 patients with moderate anaemia. The outcome was not related to age, gender, social class, complications of respiratory distress nor hyperparasitemia but it was related significantly to the presence of cerebral malaria as a complication. This is shown in table 5. It was note-worthy that none of the patients with severe anaemia and cerebral malaria were underweight (p = 0.002).

Table 5: Factors related to outcome of children with severe malarial anaemia (n = 38).

Complication	Number died	p-value
Cerebral malaria	4	0.004
Respiratory distress	5	0.13
Hyperparasitemia	2	0.17
Underweight	1	0.17
Low socioeconomic class	4	0.27

Discussion

During the study period, severe malarial anaemia (SMA) accounted for 1% of the total admissions into EPU and 3.2% of the cases of severe malaria. This 3.2% is lower than figures of 7.8% to 45.9% that were reported from Ilorin, Ibadan and Zambia which are all holoendemic regions [10-12]. Malaria in Sokoto is partly mesoendemic and hyperendemic as reported recently by Jiya., *et al.* [14]. Several studies of syndromes and pattern of presentation of severe malaria across Africa have shown that SMA is a predomi-

nant presentation in areas with marked transmission throughout the year (holoendemic areas) while cerebral malaria is more prevalent in areas with seasonal transmission like the present study area [3,19,20]. Therefore the apparently low prevalence compared to the other above quoted studies is not surprising. However, it is note-worthy that being a hospital based study, this figure may be an under-estimation as a proportion of the affected may not present to the hospital and die at home depending on the health seeking behaviour of care-givers [21].

In another earlier report from the study area, Jiya., *et al.* [22] found a high prevalence of 8% of cerebral malaria even though the study period then was shorter, this may also lend credence to the previous findings of lower findings of SMA in areas of moderately high transmission of malaria. In consonance with this, a previous study from the area also showed a low prevalence of anaemia and no severe anaemia in children in an outpatient clinic where febrile children were presented early for treatment [23]. However, this present study was on children admitted with severe forms of malaria who were more likely to be complicated with longer duration of illness. Malaria is transmitted throughout the year with the peak period in the rainy season of September. This is similar to findings from other studies which are from the holoendemic areas of the country [10].

The age distribution showed that most of the patients (74%) were between the ages of 6 months to three years which is similar to the findings from other report that SMA predominates in the younger age groups who have a lower red cell mass, higher parasite densities and are more predisposed to nutritional deficiencies [4]. Some have quoted age below 2 years as a risk factor for SMA [24]. However, for the group with moderate anaemia, most were above the age of 5 years. This also supports the fact that SMA is more of a problem in younger children. There was also a higher rate of complications especially those associated with higher mortality like respiratory distress, cerebral malaria and hyperparasitemia among the children with SMA than those with moderate anaemia.

Though, the study did not aim to study those with moderate anaemia, the fact that they were transfused expanded the scope of the study to also include them. Other studies that have compared SMA with other children with severe malaria (a case control study) in Ilorin [10], did not highlight whether there was any such group while recruiting their controls. In a study in Gambia, where children with SMA were transfused when PCV was less than 12%, it was found that the mortality was high even after blood transfusion. In low resource settings, where screened blood is available it may be necessary to transfuse early before more complications ensue [25].

Although the WHO encourages rational blood transfusion use at Haemoglobin level of 4 - 5g/dl (i.e. PCV of 12-15%) in the presence of respiratory distress in high malaria transmission settings and has a lower threshold of 7g/dl for low transmission settings [26,27], this may not be very practicable in settings where there is paucity of monitoring facilities, adequate health personnel and strict adherence to follow up. A study in Kenya [28], demonstrated haematological recovery and survival in children with severe anaemia who were discharged with moderate to severe anaemia, however the adaptability of this method of management to all low resource settings may be in question.

The findings of this study about the Haemoglobin electrophoretic pattern and blood group of those affected being mainly AA genotype and 'O' blood group respectively are in consonance with the study from Ilorin [10]. The pattern of mortality also reflects the type of severe complication mainly co-existent cerebral malaria among the study population.

In conclusion, severe malarial anaemia is an important cause of childhood mortality in the study area. Prompt evaluation and early transfusion may reduce mortality. One of the strengths of this study is that it is among the first to document the problem of severe malarial anaemia amongst children in Northern Nigeria while also highlighting the problem of moderate anaemia amongst these patients. It has also highlighted a problem faced in some health facilities where clinical judgements have to be made early enough to transfuse patients who have not reached the threshold of SMA to avoid undue morbidity and mortality.

Conflict of Interest

None.

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