

Original Article

Severe Falciparum Malaria in Children in Enugu, South East Nigeria

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ABSTRACT

Introduction: Severe malaria remains one of the leading causes of morbidity and mortality in sub-Saharan Africa and parts of Asia despite several efforts in prevention and management. The prevalence and pattern of presentation may vary from one location to another and from one age group to another. **Objectives:** This study was undertaken to review the prevalence and pattern of severe malaria among children presenting in the two tertiary hospitals in Enugu, south-east Nigeria. **Methods:** The case records of children presenting with malaria in the two tertiary hospitals in the state were retrieved and the necessary information were obtained using a structured questionnaire. **Results:** The children aged from 1 month to 184 months (15 years), with a median age of 36 months and mean age of 49.2 ± 42.7 months. About two-thirds (68/102, 66.7%) of the children were under the age of 5 years, with only 6 of them (8.8%) being 6 months and below. There were significantly more males than females ($\chi^2 = 6.48, P = 0.01$); with a M:F ratio of 1.55:1. The peak of presentation was from August and November. Prostration, respiratory distress and severe anaemia were the commonest features of severe malaria, while shock, acute renal failure and abnormal bleeding were the least presenting features. Of all the features, only severe anaemia was significantly related to age, ($\chi^2 = 5.027, P = 0.02$). Sixty-one (59.8%) of the children had one or more co-morbidities. There were 2 deaths, giving a case fatality rate of 1.96%. **Conclusion:** Early presentation will significantly reduce blood transfusions, prolonged admission and death in children with severe malaria.

KEYWORDS: Children, Enugu, falciparum, malaria, Nigeria

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INTRODUCTION

Severe malaria is acute malaria with signs of organ dysfunction and/or high level of parasitaemia and is associated with high mortality.^[1] It is a medical emergency requiring prompt and effective treatment to prevent death. The World Health Organization (WHO) in 1990 established criteria for the diagnosis of severe malaria.^[2] In 2000, the WHO revised these criteria to include other clinical manifestations and laboratory values that portend a poor prognosis based on clinical experience in semi-immune patients.^[2] Young children and pregnant women are at high risk for severe malaria in endemic areas while older children and adults develop partial immunity after repeated infections and thus have lower risk of severe disease.^[3]

There were around 627,000 deaths from malaria worldwide in 2012, of which about 90% were young

children in sub-Saharan Africa.^[4,5] In Nigeria, malaria remains one of the most important health problems, accounting for 25% of infant mortality, 30% of under-5 mortality and 11% of maternal mortality.^[6] Between 2000 and 2010, at least 50% of the population had one episode of malaria per year, while children below 5 years had two to four attacks.^[7]

Malaria is caused by the obligate intraerythrocytic protozoa of the genus *Plasmodium*.^[8] Humans can be infected with one (or more) of the following four species: *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*.^[8] Severe malaria is mostly caused

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by *Plasmodium falciparum* infection.^[7] However, *Plasmodium vivax* and *Plasmodium knowlesi* are also known to lead to severe and fatal disease.^[7]

Microscopy remains the gold standard and preferred option for diagnosing malaria.^[9] However, where microscopy is unavailable or not feasible, a rapid diagnostic test (RDT) should be used.^[9] RDTs for detecting Histidine rich protein 2 (*p*/fHRP2) antigen can be useful for diagnosing malaria in patients who have recently received antimalarial treatment and in whom blood films are transiently negative for malaria parasites.^[9]

Clinical deterioration of affected children with the involvement of organ dysfunction, usually appears 3–7 days after the onset of fever.^[10] In children less than 5 years of age, late presentation (>48 hours from onset of symptoms) increases fatality.^[10] The major features of severe malaria include cerebral malaria, pulmonary edema, acute renal failure, severe anaemia, and/or bleeding, acidosis and hypoglycemia.^[8] In many patients, several of these complications exist together or evolve in rapid succession within a few hours.^[8]

The management of severe malaria remains challenging. This is because there is need for relatively cost-intensive supportive measures, availability of highly skilled personnel, functional referral systems, blood transfusion services and adequate organization of hospital services.^[11] In addition; the availability of effective parenteral antimalarial drugs may be a challenge.^[11] Severe malaria may mimic other diseases that are also common in malaria-endemic countries. Malaria may also co-exist with other medical conditions such as bacterial sepsis, enteric fever, pneumonia, meningitis, urinary tract infection, otitis media, malnutrition and sickle cell anaemia,^[12-14] necessitating further laboratory investigations and treatment options which may be cost intensive.

The aim of this study therefore is to review the prevalence of severe malaria among children presenting in the two tertiary hospitals in Enugu, south east Nigeria, identify the common presenting feature and outcome.

METHODOLOGY

This was a retrospective study conducted between January, 2016 and December 2016 (one year). The study was conducted at the two tertiary hospitals in the state: University of Nigeria teaching Hospital, Enugu and Enugu State University Teaching Hospital, Park lane, Enugu. Both hospitals receive cases from all over the state and also from nearby communities in the neighbouring states. Ethical clearance was obtained from the two tertiary hospitals.

The admission registers in the two hospitals were used to identify all the children who presented to the children emergency room within the period of study with a diagnosis of malaria. Their case records were retrieved and the necessary information were obtained using a structured questionnaire. These included their biodata, including the occupation and highest educational qualification of parents, presenting symptoms and findings on examination, results of all the laboratory investigations conducted on the patients, any secondary diagnoses and outcome. Those without laboratory diagnosis of malaria were excluded, likewise, those with only fever and parasitaemia but no documented feature of severe malaria.

Data were entered into spss version 20 for analysis. Analysis was mainly descriptive. The age range, sex, distribution socioeconomic class (based on Oyediji),^[15] residence, outcome of presentation of the affected children were described. The clinical features were compared between children below the age of five and those of five years and above. The duration of symptoms before presentation was compared to some confounding variables. Relationship between variables was tested using chi square. A *P* value of <0.05 was regarded as significant. Results were presented as percentages and proportions in forms of prose, tables and charts.

Severe malaria in this study was defined as one or more of the following, occurring in the absence of an identified alternative cause and in the presence of *P. falciparum* asexual parasitaemia diagnosed either using a rapid diagnostic test (*P*/fHRP2), microscopy or both:^[3] *Impaired consciousness*: A Blantyre coma score <3 in children less than 2 years or A Glasgow Coma Score <11 in older children. *Multiple Convulsions*: More than two convulsions in a 24 hour period. *Prostration*: Generalized weakness such that the child is unable to sit, stand or walk without assistance. *Severe malarial anaemia*: A haemoglobin concentration <5 g/dl or a haematocrit of <15% in children <12 years of age, (<7 g/dl or <20%, in children 12 years and above). *Hypoglycaemia*: Blood or plasma glucose <2.2 mM (<40 mg/dl. *Acute kidney injury*: Urine output <0.5ml/kg/hr or plasma or serum creatinine >265 μM/l (3 mg/dl) or blood urea >20mM. *Jaundice*: clinical jaundice or plasma or serum bilirubin >50 μm (3 mg/dl). *Respiratory distress (acidosis/pulmonary oedema)*: oxygen saturation <92% on room air with a respiratory rate >30/min, with laboured breathing. *Shock*: capillary refill ≥3 s or a systolic blood pressure <70 mm Hg in children or <80 mm Hg in children 12 years and above with evidence of impaired perfusion (cool peripheries or prolonged capillary refill). *Haemoglobinuria*: presence

of haemoglobin on urine dipstick. *Abnormal bleeding:* including recurrent or prolonged bleeding from nose, gums or venepuncture sites; haematemesis or melaena.

RESULTS

A total of 1848 children (897 males and 951 females) were admitted during the period, of which 167 were recorded as having been admitted for severe malaria, either alone or with other medical conditions. However, only a total of 139 (83.2%) case records were retrieved, of which only 102 (73.4%) met the criteria for inclusion into the study.

The children were aged from 1 month to 184 months (15 years), with a median age of 36 months and mean age of 49.2 ± 42.7 months. About two-thirds (68/102, 66.7%) of the children were under the age of 5 years, with only 6 of them (8.8%) being 6 months and below. There were significantly more males than females ($\chi^2 = 6.48, P = 0.01$); 62 males and 40 females giving a M: F ratio of 1.55:1. Thirty-two (31.4%) of the children resided in urban areas while 35 (34.3%) each came from rural and semi-urban areas. Information for categorization of the socio-economic class (SEC) was available for 88 (86.3%) children, of which 28 (31.8%), 48 (54.5%)

and 2 (2.3%) were of SEC 3, 4 and 5 respectively, (lower SEC). From the upper SEC, there were 10 (11.4%) from SEC 2 and none was of SEC 1.

Presentation was more in the second half of the year (July to December). The peak of presentation

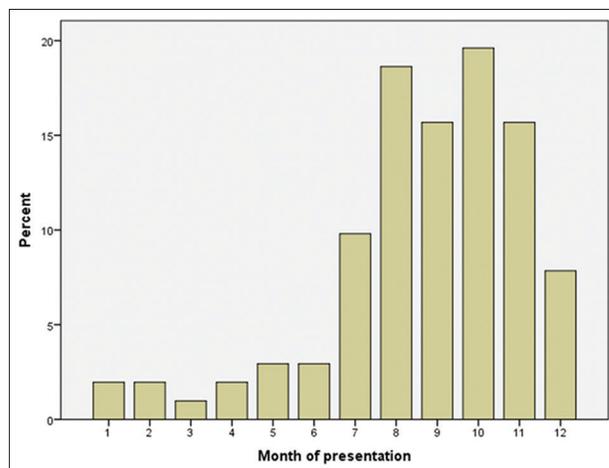


Figure 1: Seasonal variation of severe falciparum malaria presentation among the children

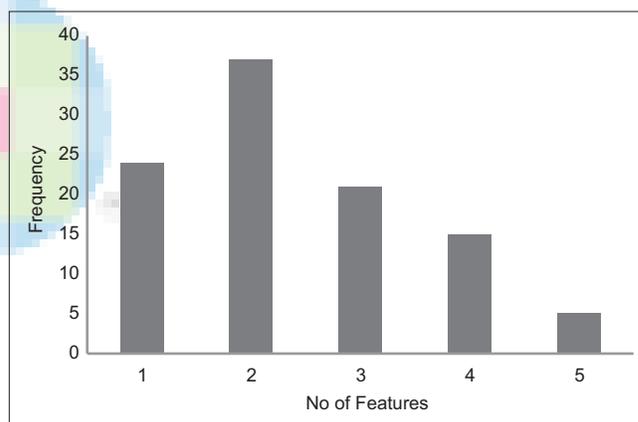


Figure 2: Number of features of severity per child

Table 1: Treatment received before presentation

Types of medications	Frequency (%)
Antimalarials alone or with antipyretics/haematinics	19 (18.6)
Antibiotics alone or with antipyretics/haematinics	5 (4.9)
Both antimalarial and antibiotics alone or with antipyretics/haematinics	35 (34.3)
Antipyretics alone or with haematinics	26 (25.5)
No medication	17 (16.7)
Total	102 (100.0)

Table 2: Comparison of the presenting features of severity among children <5 years and those aged 5 years and above

Features	Frequency (n=102), (percentage of total)	Under-5 years (percentage of frequency)	5 years and above (percentage of frequency)	χ^2	P
Multiple convulsions	28 (27.5)	20 (71.4)	8 (28.6)	0.394	0.53
Altered consciousness	22 (21.6)	17 (77.3)	5 (22.7)	1.420	0.23
Severe anaemia	49 (48.0)	38 (77.6)	11 (22.4)	5.027	0.03
Jaundice	7 (6.9)	4 (57.1)	3 (42.9)	0.019	0.89
Prostration	58 (56.9)	36 (62.1)	22 (37.9)	1.279	0.26
Respiratory distress	51 (50.0)	38 (74.5)	13 (25.5)	2.824	0.09
Shock	1 (1.0)	1 (100.0)	0 (0.0)	0.000	1.00
Acute renal failure	1 (1.0)	0 (0.0)	1 (100.0)	0.126	0.72
Haemoglobinuria	5 (4.9)	2 (40.0)	3 (60.0)	0.657	0.42
Hypoglycaemia	5 (4.9)	4 (80.0)	1 (20.0)	0.026	0.87
Abnormal bleeding	2 (2.0)	2 (100.0)	0 (0.0)	0.064	0.80
Hyperpyrexia	21 (20.6)	12 (57.1)	9 (42.9)	1.004	0.32

Table 3: Co-morbidities found in the children

Condition	Frequency	Percentage of total
Sepsis	39	38.2
Meningitis	8	7.8
Severe malnutrition	4	3.9
UTI	4	3.9
Otitis media	1	1.0
Acute gastroenteritis	1	1.0
Sickle cell anaemia	4	3.9

UTI=Urinary tract infection

was from August and November, accounting for about 70% (71/102) of the total severe malaria presentations, Figure 1. Only 22.6% (23/102) of the patients presented within 2 days of onset of symptoms. The mean duration of symptoms prior to presentation was 5.3 ± 3.6 days, and duration ranged from 1 day to 2 weeks. Presentations from one week of symptoms were 29 (28.4%). A total of 27 (26.5%) patients were referred from other health facilities. There was no relationship between late presentation (>2 days) and referral from other health facilities, ($\chi^2 = 0.342$, $P = 0.98$). Most (83.2%) of the children had received one form of medication either alone or in combination, with 10.8% receiving herbal medications in addition, Table 1. Two (2.0%) children had received blood transfusion from another health facility before presentation.

All the children presented with fever, with 20.6% having axillary body temperatures $\geq 39.5^\circ\text{C}$. Prostration, respiratory distress and severe anaemia were the commonest features of severe malaria, while shock, acute renal failure and abnormal bleeding were the least presenting features. Table 2 compares the presenting features of severity among children <5 years and those aged 5 years and above. Of all the features, only severe anaemia was significantly related to age, ($\chi^2 = 5.027$, $P = 0.02$). The mean haemoglobin concentration for all the children was 5.93 ± 2.51 , but for those with severe malarial anaemia, the mean haemoglobin concentration was 3.96 ± 0.76 . Twenty-four of the children had only one feature of severity, whereas 5 had five of the features of severe malaria, Figure 2.

Other features present in the children included hepatomegaly in 74.5% (76/102) of the children, with 29.4% (30/102) having hepato-splenomegally. Hepatomegally was seen in 95.8% of those with severe malaria anaemia compared to 56.6% of those without severe malaria anaemia ($\chi^2 = 20.812$, $P = 0.00$).

A total of sixty-one (59.8%) of the children had one or more co-morbidities. These include bacterial sepsis (38.2%) for which antibiotics were added to the treatment, Table 3. Sixty-seven (65.7%) received blood

transfusions. These comprised the 49 children with diagnosed severe malarial anaemia and 18 who though had other features of severe malaria did not fulfill the WHO criteria for severe malarial anaemia but clinically required blood. Blood transfusion was significantly associated with late presentation (>2 days from onset of symptoms), ($\chi^2 = 6.968$, $P = 0.008$).

Ninety-two (90.2%) of the children were discharged, eight (7.8%) left against medical advice. There were 2 deaths, giving a case fatality rate of 1.96%. The 2 dead children had delayed presentation and multiple features. The number of children admitted for more than 3 days (prolonged admission) was 54 (52.9%). The presence of co-morbidity did not significantly increase the duration of admission, ($\chi^2 = 3.625$, $P = 0.06$), but blood transfusion significantly prolonged the duration of admission ($\chi^2 = 4.778$, $P = 0.03$). There was also no significant effect of age on duration of admission, ($\chi^2 = 1.594$, $P = 0.21$).

DISCUSSION

From this study, the incidence of severe malaria in this hospital-based study in Enugu was 5.5%. In similar studies conducted over 10 years ago in Nigeria, west Africa^[16] and Yemen,^[17] west Asia, the incidences were 11.3% and 17% respectively. The lower incidence in this current study may be a reflection of the impact of the introduction of artemisinin-based combination therapy for uncomplicated malaria.

The majority of affected children were under the age of 5 years. This is a constant finding in virtually all similar studies.^[16-19] This could be explained by the fact that children less than five years of age have less immunity to malaria since they may not have been exposed to falciparum malaria enough to develop sufficient level of specific acquired immunity to the malaria parasite. Although, majority of the affected children were under the age of 5 years, older children were not spared from severe malaria, even in our malaria endemic region. About a third of the children admitted for severe malaria in this study were above the age of 5 years, thus age is not an absolute factor in the development of severe malaria. Males were significantly more affected. Although most of the previous studies^[16-19] reported more males, none tested for any significance between both genders. The reason for this cannot be explained, it has been suggested that females have better immunity to parasitic diseases which is attributable to genetic and hormonal factors.^[20]

Okeke and Okeibunor^[21] in south-east Nigeria documented a significantly higher number of urban-dwelling mothers seeking treatment for malaria in

hospitals compared to their rural counterparts. However, in our study, the numbers of urban, semi-urban and rural-dwelling children were approximately similar. This may be because of the severity of the illness necessitating a referral to tertiary hospitals from the rural health posts and patent medicine dealers which is the usual first point of care for these rural and semi urban dwellers. Referrals from lower health posts did not significantly affect the time of presentation.

There was a preponderance of children from the lower socioeconomic classes (88.6%), representing the socioeconomic classes that mostly patronize government hospitals in Nigeria. Most people from the upper class prefer private hospitals which though more expensive, offer more friendly services and have better environments, but are more expensive than the government hospitals. Another plausible explanation is that those in the upper SEC reside in better environments with less mosquito infestation and are also more likely to initiate malaria treatment earlier before it becomes severe. Similar pattern of presentation was also documented by Adegoke *et al.*^[22] in their study of severe anaemia in children presenting in another teaching hospital in Nigeria.

The study revealed a peak in the number of children presenting to the emergency room between the months of August and November, accounting for about 70% (71/102) of the total severe malaria presentations. This period coincides with the months when the rains are beginning to thin down in this part of the country so can lead to an increasing collection of stagnant bodies of water and overgrown bushes.

Delay in the initiation of appropriate therapy is one of the main reasons for malaria becoming severe. Only about 22% presented within 48 hours of onset of symptoms, with almost 30% presenting after one week of symptoms. This delayed presentation could be due to the poor health seeking behaviour of our people who prefer initial self-medication.^[23,24] Reasons for this include ignorance of the causes and consequences of the symptoms and more importantly, poverty, since most healthcare financing by Nigerians are out of pocket expenses.

In this study, over 80% of the children had received one drug or another, mostly combinations bought over the counter. A large proportion of the medications prescribed over the counter by unqualified personnel are either wrongly dosed or inappropriate and this may complicate the management of the disease.

Prostration, respiratory distress and severe anaemia were the most common features of severe malaria

among the children, with multiple convulsions, altered consciousness and hyperpyrexia also notably high. All the features, with the exceptions of acute renal failure and haemoglobinuria occurred more in children under the age of 5 years when compared to older children. However, only severe malarial anaemia was significantly higher. In similar African studies,^[18,19] the pattern of presenting features were similar. Among Ghanaian children, severe anaemia, prostration and respiratory distress topped the list of symptoms, with multiple convulsions and altered consciousness following closely.^[18] Similarly, in Gabonese children, severe anaemia, respiratory distress and altered consciousness were the leading features.^[19] Most of children in this study presented with multiple, rather than single features of severe malaria.

Although, severe malarial anaemia significantly prolonged the duration of admission, previous studies^[18,19,25] showed that it did not significantly affect the outcome in places with functional transfusion services. On the other hand, altered consciousness, respiratory distress as well as hypoglycaemia and jaundice have been shown to be predictors of death in severe malaria.^[19,25] In our study, the predictors of death could not be analyzed due to the very small number of deaths recorded. The increased duration of admission in children with severe malarial anaemia were due to the additional time spent in the hospital while waiting to get a donor to replace the blood loaned to the patient for emergency blood transfusion. Early presentation will decrease the rate of blood transfusion and thus the length of time spent on admission.

More than half of the children had one form of co-morbidity, of which bacterial sepsis dominated. The diagnosis was based on the clinical definition of sepsis including a suggestive full blood count. Although, blood culture was not done in most of the cases, this group of children received concurrent parenteral antibiotics followed by oral antibiotics at discharge. Although the presence of co-morbidity increased the duration of admission, it was not significant since those who did not have any co morbidity but were transfused equally had long hospital stay. Previous studies^[12-14] had documented different comorbidities in children with severe malaria. The co-existence of bacteraemia (sepsis) in children with severe malaria has been documented in studies across Africa.^[26,27] The World Health Organization also recognized the high prevalence of malnutrition and sepsis among children with severe malaria and has recommended the concurrent use of broad spectrum antibiotics in children with severe malaria in moderate to high malaria transmission zones, until sepsis can be excluded.^[28]

The case fatality rate of 1.96% was lower than that obtained in other similar studies.^[16-19] This is probably due to the high quality care received at the two tertiary hospitals where the study was conducted. Thus, it is unlikely to be a true reflection of the mortality associated with severe malaria since a good number may die before presentation to these tertiary health facilities. The low case fatality rate in this study gives hope that a good number of children with severe malaria could be saved if they are seen at the tertiary hospitals. This means that efforts at sensitization should be increased to make parents and healthcare providers more aware of features of severe malaria in order to promptly refer such children to tertiary centres and optimize outcomes.

CONCLUSION

Severe malaria, though more prevalent in children under the age of five years, affects children of all age groups in Enugu, Nigeria. Prostration, respiratory distress and severe anaemia are the most common features of severe malaria seen in Enugu. Early presentation will significantly reduce blood transfusion, prolonged admission and death in children with severe malaria.

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Conflicts of interest

There are no conflicts of interest.

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