

Original Research Article

Evaluation of impact of COVID-19 pandemic on the burden and pattern of severe malaria in Nigerian children

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ABSTRACT

Background: Malaria is an infectious disease caused by the protozoan *Plasmodium*, accounting for 36% of under-five mortality. About 4.5% of all malaria-infected children reported at least one symptom of severe malaria, with worsening outcome. COVID-19 and malaria shared similar clinical presentation in children this similarity may lead to delay in initiation of treatment for malaria, with progression from uncomplicated to severe forms and consequently high mortality. Thus, we set out to study the extent COVID-19 impacted on the burden and pattern of severe malaria.

Methods: It was a retrospective study of all the children admitted into the children's emergency room severe malaria, from March 2018 to February 2022. The data collected included the total number of admissions within the period, the month and year of admission, age, gender, the component of severe malaria that was the final diagnosis and outcome of management. Data were analysed using NCSS 9 statistical software.

Results: There were 4761 admissions within the study period: males were 54.7%, subjects 1-<60 months were 60.5% and pre COVID-19 period were 63.7%. The prevalence rates of severe malaria in CHER were 2.6%. Among those with severe malaria, the case fatality rate was 10.7%. Severe malarial anaemia was the most common accounting for 49.2% and has predilection for the younger age. Cerebral malaria was predominantly diagnosed during the COVID-19 period.

Conclusions: The prevalence of severe malaria was 2.6% and severe malaria anaemia was the most common mode of presentation while cerebral malaria was diagnosed more during the COVID-19 period.

Keywords: Cerebral, Children, COVID-19, Severe malarial anaemia

INTRODUCTION

Malaria is an infectious disease caused by the protozoan *Plasmodium* species and *Plasmodium falciparum* is the most common specie in many parts of Africa.¹ Malaria accounted for 30.3% of illnesses among children admitted in the children's emergency room of FMC Asaba.² Children under 5 years of age are the most vulnerable group affected by malaria due to lack of specific acquired immunity.¹ With the total malaria death of 77%, about 90% of these deaths worldwide occur in this age group in sub-Saharan African¹ and 36% in Nigeria.³

Severe malaria is defined as one or more life-threatening manifestations, occurring in the presence of *P. falciparum* asexual parasitaemia and in the absence of an identified alternative cause.⁴ In Nigeria, 11.3% cases of severe malaria was reported in Ibadan in 2007, Enugu reported 5.5% in 2018 and 8.4% in Gombe in 2020.⁵⁻⁷

In a survey done between 2015 and 2018 in 19 malaria endemic countries of Africa, 4.5% of all malaria-infected children reported at least one symptom of severe malaria.⁸ The most common presentations of severe malaria reported vary depending on the study site: severe malarial

anemia (SMA), multiple convulsions, cerebral malaria, also, hypoglycaemia haemoglobinuria and acute renal failure were documented.^{5,7,9-12}

Mortality due to severe malaria showed a relatively steady decline with reported case fatality rate of 11.2% in 2004 in Ghana, 9.0% in 2005 in Gabon and 6.9% in 2007 in Ibadan Nigeria, possibly attributable to the series of actively ongoing global interventions against malaria.^{5,9,10}

In March 2020, COVID 19 was declared a global pandemic, with devastating health crisis including decrease in paediatric emergency and outpatient clinic visits.¹³⁻¹⁵ Malaria case incidence increased during the COVID-19 pandemic with 241 million malaria cases globally in 2020 (COVID-19 period), which represents an increase from 227 million in 2019 and this increase was attributed to disruption in all services including health, consequent to the lockdown preventive strategy during the COVID-19 pandemic.¹ The WHO world malaria report of 2021 observed that two thirds of additional malaria deaths were linked to disruptions in the malaria preventive strategies, the COVID-19 period.¹ In Ghana, there was a decline in inpatient and outpatient malaria visits during the COVID-19 period.¹⁶ In Sierra Leone however, the number of diagnosis of malaria in children under five years of age during the COVID-19 period did not change significantly.¹⁷ COVID-19 comorbidity with malaria has been established.¹⁸ Malaria and COVID-19 share similar clinical presentation in children. Because of the similarities in clinical manifestations of COVID and severe malaria, the diagnosis of severe malaria or indeed COVID-19 could be delayed and such issues might be compounded by the disruption to services consequent to the lockdown and disruption of preventive strategy during the COVID-19 pandemic.^{19,20}

Malaria is a major cause of mortality in children admitted in our center, contributing 24.4% of the mortality rate.² We therefore set out to determine the burden and pattern of the severe forms of malaria and to ascertain the outcome of the management of such severe malaria cases. We compared these variables within two time periods; before and during the COVID-19 period. This was to enable us know the extent to which COVID-19 impacted on the burden of the severe forms of malaria.

METHODS

The setting

This was carried out in the FMC Asaba, a tertiary facility located in Asaba, the capital of Delta state. Asaba has 2 major climatic seasons; a dry season which spans from November to March and a rainy season from April to October.

The pediatric department comprises the children outpatient (CHOP) clinic, then the in-patient section: the newborn special care unit (NBSCU), the pediatric general

ward and the children's emergency room (CHER) with bed spaces of 22, 40 and 14 respectively. Children's emergency room is manned by two consultants, who work with 4 resident doctors and 2 house officers on rotation through the unit. Children who are 0 day old (at first day of life) to 18 years, who are acutely ill are triaged at CHER and given emergency care. Side laboratory investigations done in CHER include urinalysis, pack cell volume, blood glucose, serum bilirubin, malaria via microscopic examination of blood film. After stabilization, those patients who are fit to go home are discharged, and the rest who need to continue management are transferred to the children's wards, while the neonates (0-28 days old) are transferred to NBSCU.

Data collection and analysis

This was a retrospective study involving all the admissions at the children emergency room of FMC Asaba over a four-year period, from March 2018 to February 2022, inclusive. This facility started using electronic medical record (EMR) from May 2020 and previously used hardcopy case files were scanned and uploaded to the system but the transition had hitches, as some files got missing in the process. All the case records of children aged 1 month - <18 years (age range admitted in CHER), admitted into the CHER of FMC Asaba were reviewed. The old case records were traced from the admission register and daily bed space summary sheets from the records department and the hardcopy files were then retrieved from the hospital library, also, the records from May 2020 were retrieved from the electronic data base.

Data collected included the total number of admissions within the period, the month and year of admission, age, gender, the component of severe malaria that was the final diagnosis and outcome of management. The children were stratified into 2 different age groups: 1-<60 months (under 5) and 5-<18 years. The 4-year period was divided into 2: March 2018 to February 2020 (pre COVID-19 period) and March 2020 to February 2022 (COVID-19 period). Data were analysed using NCSS 9 statistical software (2013) NCSS LLC, Kaysville, Utah, USA. Nonparametric statistic was used for descriptive analysis and for comparison of median age (data set did not pass normality test using D'Agostino, $p=0.00003$). Mann-Whitney U test was used to compare the median age of those with CM and SMA. Association between CM and SMA with age, gender, the season of admission, COVID-19 category and outcome of management and also comparison between the preCOVID-19 and the COVID-19 periods were done using the chi squared test. Significant levels were set with a p value of <0.05 . Results were presented as tables and charts.

Ethical approval was sought and obtained from the Research and Ethical Committee of FMC Asaba, FMC/ASB/A81 VOL XIII/217.

Definition of some criteria for the diagnosis of severe malaria⁴

We defined severe malaria as one or more of the following, occurring in the absence of an identified alternative cause, and in the presence of *P. falciparum* asexual parasitemia:

Impaired consciousness/cerebral malaria

A Glasgow coma score <11 or a Blantyre coma score <3; malaria with coma persisting for > 30 minutes after a seizure.

Multiple convulsions

It is defined as more than 2 episodes within 24 hours.

Prostration

Generalized weakness so that the patient is unable to sit, stand or walk without assistance.

Hypoglycemia

It is defined as blood glucose <2.2 mmol/l (<40 mg/dl).

Severe malarial anemia

Hematocrit ≤15% in children less than 12 years and <20% in those older and with a parasite count >10 000/μl,

Renal impairment

serum creatinine of >265 μmol (3 mg/dl) or blood urea of >20 mmol/l.

RESULTS

General characteristics of the study population

There were 4761 admissions within the study period: M:F ratio of 1.2. Those with severe malaria were 125, giving a prevalence rate of severe malaria during the study period as 2.6% (125/4761) (Table 1).

General characteristics of the study population with severe malaria

Table 2 shows that severe malaria accounted for 2.8% admissions among all children below five years and contributed 6.8% of all mortalities recorded in CHER within the study period.

Most of the cases of severe malaria were admitted during the rainy season and the odds of diagnosing severe malaria in the rainy season, was 2.27 ($p<0.001$) and the odds of a patient dying from severe malaria was 2.66

($p<0.001$), with a case fatality rate 10.6%, (13/122), (Table 3).

Table 1: General characteristics of the study population.

Parameters (n=4761)	Frequency	Percentage
Age group	1-<60 months	2881
	5-18 years	1880
Gender	Male	2605
	Female	2156
Season of admission	Rainy	2372
	Dry	2389
COVID-19 era	Pre-COVID	3033
	COVID	1728
Severe malaria	Yes	125
	No	4636
Outcome	Discharged	4087
	DAMA*	484
	Died	190

*DAMA= Discharge against medical advice

Table 2: General characteristics of subjects with severe malaria within the total study population.

Parameters	Number admitted	Number with severe malaria (% admitted)
Age group	1-<60 months	2881
	5-18 years	1880
Gender	Male	2605
	Female	2156
Season admitted	Rainy	2372
	Dry	2389
COVID-19 era	Pre-COVID	3033
	COVID	1728
Outcome	Discharged	4087
	DAMA	484
	Died	190

Table 3: Comparison of prevalence of severe malaria within age groups, gender, the season of admission and COVID-19 periods of admission.

Variables	Cases with severe malaria	Odds ratio	P value
Age group	1-<60 months	81 (63.9)	1.21
	5-18 years	44 (36.1)	0.83
Gender	Male	68 (54.9)	0.99
	Female	57 (45.1)	1.01
Season admitted	Rainy	86 (68.0)	2.27
	Dry	39 (32.0)	0.44
COVID-19 era	Pre-COVID	71 (55.7)	0.74
	COVID	54 (44.3)	1.35
Outcome	Discharged	110 (89.4)	0.38
	Died	13 (10.6)	2.66

2 cases of DAMA excluded from the analysis of "outcome".
SMA=Severe malaria anaemia. CM = cerebral malaria

Severe malaria criteria

Only 122 were analysed for this section as 3 cases were excluded because we could not ascertain their severe malaria criteria. These cases were 2 females and 1 male, all under five years of age, who presented during the rainy season of the pre COVID-19 period. Severe malarial anemia (SMA) was the most common presentation of severe malaria seen during the study periods, 49.2% (60/122) (Figure 1).

As shown in Table 4, six children <5 years had both CM and SMA, the term “others” represents multiple convulsions (7), both SMA and prostration (2), then a case with SMA, hemoglobinuria and jaundice (1). The seven cases with comorbidity comprise SMA and sepsis (4), SMA and acute kidney injury AKI (2), SMA and RVD (1) and CM and sepsis (1).

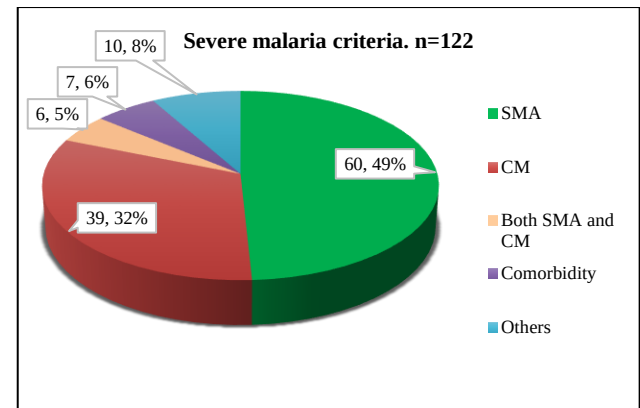


Figure 1: Pie chart showing the different severe malaria criteria seen during the study period.

Others = renal impairment/acute kidney injury, jaundice, prostration, multiple convulsions. SMA = Severe malarial anaemia. CM = cerebral malaria.

Table 4: Distribution of all the severe malaria criteria across age groups, gender, season, COVID 19 era and outcome.

Variables (n)		SMA	CM	Both CM and SMA	Others	Co-morbidity
Age group	1-<60 months (78)	41	19	6	8	4
	5-18 years (44)	19	20	0	2	3
Gender	Male (67)	29	25	5	5	3
	Female (55)	31	14	1	5	4
Season of admission	Rainy (83)	43	23	4	9	4
	Dry (39)	17	16	2	1	3
COVID-19 era	Pre-COVID (68)	40	17	4	7	0
	COVID (54)	20	22	2	3	7
Outcome	Discharged (107)	54	33	4	10	5
	DAMA (2)	0	1	1	0	0
	Died (13)	6	5	1	0	1

3 with incomplete data were excluded. 122 analysed. SMA = severe malarial anaemia. CM = cerebral malaria. DAMA= discharge against medical advice.

Cases of severe malarial anemia and cerebral malaria

Of the 122 cases of severe malaria with criteria, 99 cases had either SMA or CM. One case that DAMA, a CM case, was excluded so as to analyze only the two outcomes of either “died or not” thus, 98 cases with either SMA or CM, were analysed. The median age (IQR) was 48 (48) months and those with CM were older, $p=0.007$, Table 5. Cerebral malaria is commoner in older age, $p=0.009$, with odds ratio of 2.85. The odds of a child under five years of age or a male child dying from SMA was 2.52 and 2.32 respectively.

Severe malaria and the COVID 19 pandemic era

During the pre-COVID period, 36.9% (1119/3033) of admissions were children above five years of age while during the COVID-19 period, 44.0% (761/1728) were above five years of age. As shown in Table 6, during the COVID period more cases of severe malaria presented with comorbidity, ($p<0.0001$) and the odds of presenting with CM was 3 times higher ($p=0.009$). Respective CFR was 13.2% and 7.4% for pre COVID and the COVID period.

Table 5: Relationship between SMA and CM with age, gender, the season of admission, COVID era and outcome of management.

Variables		SMA n=60	Cerebral malaria n=38
Median age (IQR, 95% CI)		33.5 (43, 24-48)	60 (51, 48-60)
Mann-Whitney U		0.007	
Age group	1-<60 months	41 (68.3)	18 (47.4)
	5-18 years	19 (31.7)	20 (52.6)
	P value	0.341	0.009

Continued.

Variables		SMA n=60	Cerebral malaria n=38
Gender	Male	29 (48.3)	25 (65.8)
	Female	31 (51.7)	13 (34.2)
	P value	0.142	0.168
Season of admitted	Rainy	43 (71.7)	22 (57.9)
	Dry	17 (28.3)	16 (42.1)
	P value	0.330	0.318
COVID-19 era	Pre-COVID	40 (66.7)	17 (44.7)
	COVID	20 (33.3)	21 (55.3)
	P value	0.017	0.096
Outcome	Discharged	54 (90.0)	33 (86.8)
	Died	6 (10.0)	5 (13.2)
	P value	0.769	0.577
Mortality within age group	1-<60 months	5 (83.3)	2 (40.0)
	5-18 years	1 (16.7)	3 (60.0)
	P value	0.405	0.723
Mortality within gender	Male	4 (66.7)	5 (100.0)
	Female	2 (33.3)	0 (0.0)
	P value	0.344	0.084

SMA = severe malarial anaemia. CM = cerebral malaria.

Table 6: Comparison of median age, different severe malaria criteria and other variables malaria between the preCOVID and COVID-19 periods.

Variables		Pre COVID	COVID-19	P value
Median age (IQR, 95% CI)		36 (36, 24-48)	48 (80, 24-60)	0.430
Age group	1-<60 months	47	31	0.523
	5-18 years	21	23	0.027
Gender	Male	37	30	0.146
	Female	31	24	0.255
Season of admission	Rainy	47	36	0.176
	Dry	21	18	0.199
Severe malaria criteria	SMA	40	20	0.631
	CM	17	22	0.009
	Both CM and SMA	4	2	0.880
	Others	7	3	0.679
	Comorbidity	0	7	<0.0001
Outcome	Discharged	58	49	0.039
	DAMA	1	1	0.687
	Died	9	4	0.678

SMA = severe malarial anaemia. CM = cerebral malaria. DAMA= Discharge against medical advice.

DISCUSSION

The prevalence rate of 2.6% for severe malaria documented in this study was similar to works done in Nigeria: in 2012, Ajetunmobi et al in Ibadan found 3.05% and in 2018 Edelu et al in Enugu reported a prevalence rate of 5.5%.^{6,12} These studies, like index study were tertiary hospital-based, done retrospectively and involved all the admissions in CHER but the similarity in the findings was most likely due to the period of the studies, as they were recently done, long after implementation of several malaria preventive strategies which effectively causes reduction in malaria burden.^{1,6,12} In contrast, however, Orimadegun et al, at a similar setting in Ibadan,

Nigeria, in 2005 found a higher prevalence of 11.3%, Al-Taiair et al in Yemen documented 17.0%.^{5,11} Their higher prevalence rate may be attributed to the fact that the impact of several malaria control measures such as widespread use of insecticide treated net (ITN) and availability and effective use of artemisinin-based combination therapy for the treatment of malaria, was yet to be felt as those were not readily available and affordable for use at those years. The impact of these malaria control measures was supported by Jalo et al in Gombe whose study was in 2020, but although they still reported a high prevalence rate of 8.4%, this was attributed partly to very low usage of ITN (27.8%).⁸

Most (63.9%) of the children with severe malaria in the index study were less than 5 years, the finding that was similarly documented by several other studies.^{5,6,9-11,20} The comparable higher prevalence in children less than 5 years was due to their lack of specific acquired immunity that gives some degree of protection to older children who are likely to have acquired the specific immunity.¹

Severe malaria was slightly more in males than females, similar to other studies,^{5-7,20} possibly because they are all hospital-based studies, and boys are more likely to be taken to hospital during ill health because the prevalent health-seeking attitude of African parents is still skewed positively towards male children.

Severe malaria showed significant seasonal predominance, occurring more in the rainy season. More than half (55.7%) of the cases of severe malaria in this study were recorded in the months of August through November. This finding was comparable with a report by Edelu et al in Enugu where they reported that 70% of the total severe malaria presentation in their study occurred between August and November.⁶ The seasonal predilection follows malaria season as this rainy period are often characterized by widespread collection of stagnant water bodies and overgrown bushes which provide a good habitat for the mosquitoes to proliferate. The two study sites share the same seasons which may explain the similar seasonal preponderance. Al-Taiar and colleagues in Yemen also reported seasonal predilection in tandem with malaria transmission season in their study areas.¹¹

Severe malarial anemia was the most common form of severe malaria seen among the children in our center, followed by cerebral malaria. This pattern of presentation is not different from what has been reported in other studies in Nigeria and other countries.^{1,5-7,9-12,20,21} Orimadegun and Ajetunmobi with their coworkers, both in Ibadan, Mockenhaupt et al in Ghana and Al-Taiar et al in Yemen reported severe malarial anaemia topping the list followed by cerebral malaria.^{5,7,10,11} This could be attributed to the fact that, these studies like the index study, involved more of the younger children and it has been shown that severe malarial anaemia predominantly occur in younger children.^{5,6,11} This trend is not surprising as this age cohort corresponds to the age with higher prevalence of anaemia and notably iron deficiency anaemia due to insufficient intake coupled with rapid growth.^{22,23} In contrast, Jalo et al observed preponderance of multiple convulsion and CM in their study subjects who were comparatively older children.⁷ Coincidentally, CM was commoner in the cohort of older children in this study whereas SMA was commoner in the younger children. Both SMA and CM showed no gender predilection.

The case fatality rate (CFR) of 10.7% of severe malaria in this study is comparable to other similar studies in different parts of Nigeria that reported a CFR of 6.9% in

2007 in Ibadan, 7.3% in 2020 in Gombe, 8.0% in 2012 in Ibadan and 8.2% in 2017 in Bauchi.^{5,7,12,20} Probably so because the subjects in the other studies like index study are younger and children less than 5 years have been shown to be more severely affected by malaria.^{1,12,20} Even in Mozambique, where admission for severe malaria was comparably higher in older children, most of the deaths from malaria still occurred in children aged under 5 years of age.¹ In contrast to index study, CFR of 1.96% was documented by Edelu et al and 3.2% by Al-Taiar and coworkers despite the predominantly younger children in their study.^{6,11} Thus, other predictors of mortality such as availability of blood products, may have impacted the index study and these other studies at varying degrees.^{5-7,11,12,20} Both SMA and CM had significant good outcome.

This study did not demonstrate that age and gender had any significant impact on case fatality of either SMA or CM, similar to the study by Jalo et al.⁷ However, in the index study, the odds of a child under five years of age dying of SMA was 2.5 and 2.3 for that of a male child dying of SMA. Case fatality rate was higher for CM than SMA as reported by Jalo et al in Gombe, Al-Taiar et al in Yemen, and Ajetunmobi et al in Ibadan.^{7,11,12} These studies documented that cerebral malaria was an independent factor associated with mortality in severe malaria.^{7,11,12} Orimadegun, in Ibadan on the other hand found that SMA was associated with higher number of deaths, while Mockenhaupt et al in Ghana noted that SMA did not contribute to mortality.^{5,9,10}

There was a decrease in the total number of admissions and number of cases of severe malaria during the COVID-19 period, slight increase in proportion of children above five years that were admitted, although these were not significant. A similar finding was documented by Heuschen et al in Ghana, who observed overall decline in outpatient visits and malaria cases in paediatrics and adults.¹⁶ This decline could be the result of the lockdown in Nigeria that span from April through July 2020, in a bid to contain the COVID-19 pandemic. The prevalence of severe malaria did not vary between the preCOVID-19 and the COVID-19 periods and there was no difference in the median ages of the children with severe malaria in both periods under study. The pattern of presentation of severe malaria varied between the preCOVID-19 and the COVID-19 periods with predilection for older children. This was similar to the finding by Mehrotra et al in their study which demonstrated that the decline in hospital attendance affected children under the age of five years, with older children more in attendance.²⁴ This index study also documented a preponderance of CM cases during the COVID-19 period and this could be attributed to the predominance of older children with severe malaria during the COVID-19 period and CM has been shown to be commoner in older children.¹ Jalo et al also attributed the preponderance of CM in their study subjects to their relatively older age.⁷ The increased CM diagnosis during the COVID-19 pandemic could not have been

misdiagnosis because although malaria and COVID-19 share similar symptoms such as fever, body aches, arthralgia, myalgia, none of the symptoms can be mistaken for cerebral malaria. Unlike the WHO world malaria report of 2021, this index study did not find any increase in the case fatality rate from severe malaria during the COVID-19 period.¹ The period of movement restriction could have resulted in out-of-hospital mortalities that were not possible to capture. However, all the cases of comorbidity with sepsis and retroviral disease, diagnosed during the period of study were documented during the COVID-19 period. Nevertheless, no respiratory illness was part of the comorbidity.

CONCLUSION

In conclusion, the prevalence of severe malaria was 2.6% and case fatality rate was 10.7%. Severe malarial anaemia was the most common mode of presentation and cerebral malaria was diagnosed more during the COVID-19 period.

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