ORIGINAL ARTICLE

Predictors of poor outcome in children with severe malaria at a tertiary health facility in Northern Nigeria

Abubakar Sani Lugga, Olayinka Rasheed Ibrahim, Nuraddeen Ibrahim, Olumide B. Ajide, Ashurah Armayau Abubakar, Olajide Aladesua, Mohammed Bashir, Fatima F. Nasir, Amina O. Ibrahim, Sakiru Abiodun Yekinni, Lawal Magaji Ibrahim, Bello M. Suleiman, Muutassim Ibrahim[1]

Department of Paediatrics, Federal Medical Centre, Katsina State, [1]Department of Paediatrics, Aminu Kano Teaching Hospital, Kano State, Nigeria

ABSTRACT

Background: Malaria is a major cause of mortality among children. **Objective:** This study determines the clinical profile, outcome (discharge and death), and factors associated with poor outcome in children with severe malaria in a tertiary health facility in Northern Nigeria. **Methods:** We conducted a descriptive retrospective study of all children (≤14 years) admitted with severe malaria based on positive malaria parasite on thick film and or rapid diagnostic test and the World Health Organization guideline for severe malaria. We extracted relevant data from patients' case files and departmental records and analyzed with the Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0. (IBM Corp, Armonk, NY). **Results:** A total of 483 children with severe malaria were admitted with median age interquartile range of 4.0 (2.5–8.0) years. Males were 261 (54.0%). Underfives were 258 (53.4%). Common forms of presentation were cerebral malaria 169 (35.0%), prostration (102; 21.1%), and multiple convulsion (86; 17.8%). Cerebral malaria and prostration were significantly higher among children aged 5 years and older. The mortality rate was 4.3% (21). Multivariate logistic regression analyses showed that impaired consciousness (adjusted odds ratio [aOR] 8.5, 95% confidence interval [CI]: 2.345, 30.484), hypoglycemia (aOR: 21.4, 95% CI: 2.766, 165.410), presence of two or more components (aOR: 4.5, 95% CI: 1.630, 12.522), and duration of hospitalization of 24 h or less (aOR: 4.6, 95% CI: 1.621, 12.782) were independent predictors of poor outcome. **Conclusion:** Our study showed that cerebral malaria was the most common form of severe malaria with a significant burden in children above 5 years. The presence of impaired consciousness, hypoglycemia, multiple components, and duration of <24 h on admission were predictive of death.

Keywords: Children, hospitalization outcome, predictors of poor outcome, severe malaria

INTRODUCTION

Despite improvements in control efforts, malaria remains a major cause of mortality among children in sub-Saharan Africa.[1] The estimated global incidence of malaria in 2017 was 63/1000 population at risk.[2] About 83% of the global burden of malaria occurs in Sub-Saharan Africa with 15 countries including Nigeria, accounting for 80% of malaria deaths.[2] In 2018, there were about 228 million cases of malaria worldwide, 50% of which occurred in the 11 high burdens to high impact countries, with Nigeria and the Democratic Republic of

Corresponding Author: Dr. Abubakar Sani Lugga, Department of Paediatrics, Federal Medical Centre, Katsina State, Nigeria.
E-mail: aslugga21@gmail.com

Submitted: 20-Jul-2020 **Revised:** 29-Sep-2020
Accepted: 24-Feb-2021 **Published:** 30-Apr-2024

Access this article online	
Quick Response Code:	Website: https://journals.lww.com/SHMJ
	DOI: 10.4103/smj.smj_90_20

Cite this article as: Lugga AS, Ibrahim OR, Ibrahim N, Ajide OB, Abubakar AA, Aladesua O, *et al*. Predictors of poor outcome in children with severe malaria at a tertiary health facility in Northern Nigeria. Sahel Med J 2022;25:109-15.

Congo accounting for the highest burden.[1] Nigeria has a stable transmission of malaria, with 76% and 24% of the population living in high and low malaria transmission areas, respectively.[3]

Available studies from Nigeria indicated variation in the reported manifestations and outcome of severe malaria in children.[4-6] A study in Osogbo, south-western Nigeria, found the most common manifestations to be multiple convulsion, severe anemia, and persistent vomiting with a case fatality rate of 5.2%. A similar study in Zamfara, northwestern Nigeria, reported the most common manifestation of children with severe malaria to be multiple convulsions, hyperpyrexia, and prostrations with a case fatality rate of 8.5%. In contrast, the most common manifestations found among children with severe malaria in Enugu; southeastern Nigeria included prostration, respiratory distress, and severe anemia with a case fatality of 2.0%. A systematic review and meta-analysis also found significant variations in the common manifestations and outcome of severe malaria in children in the different geographical regions of Africa and Asia despite declining global deaths.[7]

Hence, we report the profile, outcomes (discharge and death), and factors associated with poor outcome (death) in children with severe malaria in a tertiary health facility in Northern Nigeria.

METHODS

This study was a descriptive retrospective study of all children aged 14 years and less admitted into the Emergency Paediatric Unit (EPU) of the hospital between July 2016 and August 2017 and fulfilled the World Health Organization (WHO) criteria for severe malaria.[8]

Data collection

We extracted relevant data from patients' case files and departmental records. Information extracted included the age and sex of the patients, symptoms, and clinical signs at presentation, duration of hospitalization, outcome (discharge or death), and results of laboratory investigations (including a rapid diagnostic test for malaria, thick film for malaria parasite, packed cell volume, and random blood glucose).

Inclusion criteria

The study included children with positive thick film for malaria parasite or rapid diagnostic test for malaria (done with CareStart™ Malaria Pf-HRP2 antigen detection rapid diagnostic kit, Access Bio, United States) and at least one index of severity of malaria.

Exclusion criteria

Those with alternate diagnoses (such as positive bacterial cultures from the blood, urine, cerebrospinal fluid, or other specimens) were excluded from the study.

Clinical features and diagnosis

Diagnosis of malaria was made when the thick blood film and/or the rapid diagnostic test for malaria were positive. Severe malaria and its indices were defined based on the WHO guidelines, 2015 as follows:[8]

- Severe *falciparum* malaria: One or more life-threatening complications occurring in the absence of an identified alternative cause and the presence of asexual *Plasmodium falciparum* parasitemia
- Impaired consciousness (cerebral malaria): A Glasgow coma score <11 in adults or a Blantyre coma score <3 in children
- Prostration: Generalized weakness with inability to sit, stand, or walk without assistance
- Multiple convulsions: More than two episodes of convulsions in 24 h
- Acidosis: A base deficit of more than 8 mmol/L, plasma bicarbonate level of <15 mmol/L, or venous plasma lactate ≥5 mmol/L (manifests clinically as rapid, deep, and labored breathing)
- Hypoglycemia: Blood or plasma glucose <2.2 mmol/L (<40 mg/dL)
- Severe malarial anemia: Hemoglobin concentration of 5 g/dL or less or a hematocrit of 15% or less in children <12 years of age (<7 g/dL and <20%, respectively, in adults) with a parasite count more than 10,000/μL
- Renal impairment: Plasma or serum creatinine more than 265 μmol/L (3 mg/dL) or blood urea more than 20 mmol/L
- Jaundice: Plasma or serum bilirubin >50 μmol/L (3 mg/dL) with a parasite count >100,000/μL
- Pulmonary edema: Radiologically confirmed or oxygen saturation <92% on room air with a respiratory rate >30/min, often with chest in-drawing and crepitations on auscultation
- Significant bleeding: Recurrent or prolonged bleeding from the nose, gums, or venepuncture sites; hematemesis or melena
- Shock: Compensated shock defined as capillary refill ≥3 s or temperature gradient on the leg (mid to proximal limb) but no hypotension. Decompensated

shock defined as systolic blood pressure <70 mmHg in children or <80 mmHg in adults, with evidence of impaired perfusion (cold peripheries or prolonged capillary refill)
- Hyperparasitemia: *P. falciparum* parasitemia >10%.

All children with impaired consciousness or multiple convulsions had a cerebrospinal fluid analysis done to rule out meningitis. We excluded those with results suggestive of meningitis.

All the patients received treatment with at least three doses of intravenous artesunate, followed by oral artemether-lumefantrine according to the WHO protocol. The children received supportive treatments based on the index of severity of malaria and included anticonvulsants, blood transfusion, glucose, intravenous fluids, and oxygen therapy as appropriate.

Outcomes measure

The primary outcome of this study was hospitalization outcomes (defined as death or discharged). The secondary outcomes included the descriptions of indices of childhood severe malaria and factors predictive of death.

Statistical analysis

We analyzed the data extracted with the Statistical Package for Social Sciences (SPSS) version 20.0 for Windows® (IBM software, USA). The continuous variables (age and duration of hospitalization) were not normally distributed and expressed as median with interquartile range (IQR) and categorical variables were summarized using frequencies and percentages. Relationship between variables was tested using Chi-square and Fisher's exact test as appropriate. Odds ratio with 95% confidence interval (CI) was used to evaluate factors associated with poor outcome. Variables with $P < 0.25$ were entered into multivariate (binary logistic regression) to determine the predictors of poor outcome. The level of the statistical significance was $P < 0.05$.

Ethical approval

The Federal Medical Center Katsina ethical review committee (ERC) gave approval for the study (FMCNHREC. REG.N003/082013) on February 18, 2018. The ERC also granted waivers for the informed consent for being a retrospective study, and all the patients were anonymous during the data collection and analyses. We have carried all the procedures out as per the guidelines given in the Declaration of Helsinki, 2013.

RESULTS

A total of 1733 children were admitted into the EPU over 14 months, out of which 483 had severe malaria giving a prevalence of 27.9% (95% CI: 25.8%–30.1%). The median age (IQR) of children with severe malaria was 4 (2.5–8) years with a range of 5 months to 14 years. There were 261 (54.0%) males and 222 (46.0%) females with a male-to-female ratio of 1.2:1. The underfives were 258 (53.4%), as shown in Table 1.

As shown in Figure 1, the most common indices of severity were cerebral malaria and prostration with 169 (35.0%) and 102 (21.1%) cases, respectively, while the least form of severe malaria observed was acute kidney injury with only two cases (0.4%).

As shown in Table 2, cerebral malaria and prostration were significantly higher among children aged 5 years and older. Conversely, multiple convulsions and severe anemia were significantly higher among children <5 years of age. The other components of severe malaria did not differ significantly among the two groups.

The duration of hospitalization ranged from 1 day to 32 days with a median (IQR) of 2 (1 to 3) days. Out of the 483 children with severe malaria managed, 21 died with a mortality rate of 4.3% (95% CI: 2.9%–6.6%). Out of 424 with a single component, 12 died with a case fatality rate of 2.8% (95% CI: 1.6%–4.9%). Out of 59 with two or more components, nine died with a case fatality rate of 15.3% (95% CI: 8.2%–26.5%).

Cerebral malaria had a case fatality of 5.9%. The case fatality rate in children with cerebral malaria and hypoglycemia was 75.0%. The case fatality rate in those with shock and multiple organ dysfunctions was 33.3% and 50.0%, respectively [Table 3].

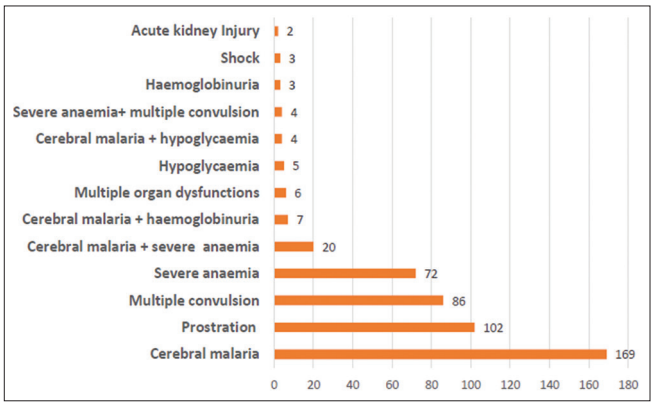

Figure 1: Components of severe malaria

The factors associated with poor outcome (death) include impaired consciousness (odds ratio [OR] 4.1, 95% CI: 1.562, 10.752), hypoglycemia (OR: 13.3, 95% CI: 3.066, 57.263), presence of two or more components (OR: 6.2, 95% CI: 2.481, 5.396), and duration of 24 h or less (OR: 3.7, 95% CI: 1.400, 9.645) on admission [Table 4].

Table 1: Clinical characteristics of the children with severe malaria

Variable	Frequency, *n* (%)
Age (months)	
<6	5 (1.0)
7-12	29 (6.0)
13-60	258 (53.4)
61-120	140 (29.0)
>120	51 (10.6)
Gender	
Male	261 (54)
Female	222 (46)
Clinical features	
Fever	472 (97.7)
Convulsions	144 (29.8)
Passage of dark colored urine	10 (2.1)
Loss of consciousness	209 (43.3)
Pallor	152 (31.1)
Reduce urine output	2 (0.4)
Prostration	104 (21.5)

Multivariate logistic-regression analyses of the four covariates that were significant on univariate analysis showed that, after adjustment for the remaining factors, impaired consciousness (adjusted odds ratio [aOR]: 8.5, 95% CI: 2.345, 30.484), hypoglycemia (aOR: 21.4, 95% CI: 2.766, 165.410), presence of two or more components (aOR: 4.5, 95% CI: 1.630, 12.522), and duration of hospitalization of 24 h or less (aOR: 4.6, 95% CI: 1.621, 12.782) were independently associated with poor outcome/death [Table 5].

DISCUSSION

The prevalence of severe malaria among children in Katsina from this hospital-based study was 27.9%. This is higher than the prevalence observed in Enugu,[6] Ibadan,[9] Osogbo,[10] and Mozambique.[11] The prevalence in this study is higher even though Katsina state has one of the highest household ownership (97%) of the long-lasting insecticide-treated nets in Nigeria.[12] This may be attributed to the peculiar weather conditions of Northwestern Nigeria where Katsina is located, and the fact that home treatment of malaria using artemisinin combination therapy is lower in Katsina when compared

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

Index of severity of malaria	Frequency			χ^2	*P*
	Under 5 years	5 years and above	Total		
Cerebral malaria	73	96	169	13.28	0.000
Prostration	40	62	102	12.102	0.000
Multiple convulsions	61	25	86	11.46	0.000
Cerebral malaria and severe anemia	13	7	20	0.936	0.333
Severe anemia	52	18	70	12.98	0.000
Cerebral malaria and hemoglobinuria	4	3	7	0.021	0.885
Cerebral malaria and MODS	5	1	6	2.043*	0.227
Hypoglycemia	2	3	5	0.42*	0.663
Severe anemia and multiple convulsion	3	1	4	0.687*	0.629
Shock	1	2	3	0.542*	0.594
Hemoglobinuria	1	2	3	0.542*	0.594

*Fisher's exact test. MODS: Multiple organ dysfunctions

Table 3: Index of severity and outcome

Component	Frequency (*n*=483), *n* (%)	Deaths	Case fatality rate (%)
Cerebral malaria	169 (35.0)	10	5.9
Prostration	102 (21.1)		0
Multiple convulsion	86 (17.8)	2	2.3
Severe anemia	72 (14.9)	1	1.4
Cerebral malaria + severe anemia	20 (4.1)	1	5.0
Cerebral malaria + hemoglobinuria	7 (1.4)		0.0
Multiple organ dysfunction	6 (1.2)	3	50.0
Hypoglycemia	5 (1.0)		0.0
Cerebral malaria + hypoglycemia	4 (0.8)	3	75.0
Severe anemia + multiple convulsion	4 (0.8)		0.0
Hemoglobinuria	3 (0.6)		0.0
Shock	3 (0.6)	1	33.3
Acute kidney injury	2 (0.4)		0.0

Table 4: Univariate analysis of factors associated with poor outcome in children with severe malaria

Variables	Discharge	Death	χ^2	OR	95% CI	*P*
Impaired level of consciousness≠						
Yes	183	15	9.492	4.1	1.562-10.752	0.004
No*	300	6				
Multiple convulsions						
Yes	84	2	0.880	0.5	0.114-2.188	0.500
No*	399	19				
Anemia						
Yes	94	2	1.289	0.5	0.100-1.903	0.2693
No*	399	19				
Hemoglobinuria						
Yes	10	0		1.1	0.060-18.493	0.974
No*	473	21				
Hypoglycemia						
Yes	6	3	19.523	13.3	3.066-57.263	0.000
No*	477	18				
Index of severity						
Two or more components (59)	50	9	19.223	6.2	2.481-5.396	0.001
Single component (424)*	412	12				
Age group (years)						
≤5 (292)	279	13	0.019	1.1	0.433-2.622	1.000
>5 (191)*	183	8				
Gender						
Male (261)	254	7	3.789	0.4	0.162-1.032	0.072
Female (222)*	208	14				
Duration on hospitalization (h)						
≤24 (202)	187	15	7.909	3.7	1.400-9.645	0.006
>24 (281)*	275	6				

*Reference; ≠GCS below 12 (older children) or a Blantyre coma score <3 in younger children. GCS: Glasgow coma score, OR: Odds ratio; CI: Confidence interval

Table 5: Multivariate analyses of factors associated with poor outcome in children with severe malaria

Variables	Categories	*n*	aOR	95% CI for (aOR)	*P*
Impaired level of consciousness≠	Yes*	198	8.455	2.345-30.484	0.001
	No	285			
Hypoglycemia	Yes*	9	21.392	2.766-165.410	0.003
	No	474			
Index of severity	Two or more components*	59	4.518	1.630-12.522	0.004
	Single component	424			
Gender	Male	222	2.192	0.798-6.026	0.128
	Female*	261			
Duration of hospitalization (h)	≤24*	202	4.552	1.621-12.782	0.004
	>24	281			

*Reference; ≠GCS below 12 (older children) or a Blantyre coma score <3 in younger children. GCS: Glasgow coma score; aOR: Adjusted odd ratio; CI: Confidence interval

to the other regions.[12] The prevalence is, however, lower than 36.7% observed in Kaduna[13] probably because the study in Kaduna was a community-based study and included children with uncomplicated malaria. Furthermore, unlike the present study which included only subjects with positive microscopy for malaria parasite or positive rapid diagnostic test for malaria, the case definition for malaria in the Kaduna study was based on presumptive diagnosis raising the possibility of false-positives among the children.[14]

The median age (IQR) was 4 (2.5–8) years. This is comparable to the median age of 49 months observed in Enugu[6] and 52 months in Gusau[5] but lower than 96 months in Kinshasa.[15] Most of the subjects were under 5 years of age (53%), which affirmed the previous findings that the malaria burden is common among children <5 years.[5,6,15] The preponderance of severe malaria among children <5 years of age may be attributed to the fact that, in areas of high malaria transmission, acquired immunity builds up as the child gets older following repeated exposure to the malaria parasite.[16] This study also showed that only five subjects (1%) were <6 months of age, which conforms with the fact that malaria infection is uncommon in infants <6 months in endemic regions. The reason for low malaria burden in infants younger than 6 months include the protective effects of transplacentally transferred immunoglobulin-G against malaria from mother to child in malaria endemic areas.[17] Other reasons include factors that inhibit parasite growth

such as hemoglobin F, lactoferrin (which binds iron), and secretory immunoglobulin-A in breast milk, as well as low levels of paraaminobenzoic acid in breast milk, a metabolic substrate for parasite growth.[18]

Most of the children in this study (87.7%) had a single component of severe malaria. This is contrary to 23.3% observed in Enugu.[6] The most common indices of severity were cerebral malaria and prostration with 35.0% and 21.1% of cases, respectively, which is contrary to findings from other parts of Nigeria.[5,6] While there is no clear-cut reason for cerebral malaria being the most common finding among the studied children, the finding may be due to some factors. Katsina state has a marked seasonal weather forecast including the rainfall (June to August) with a marked seasonal variation in reported malaria cases.[7,19] Children may be exposed to malaria infection for a shorter period with subsequent wanes of protection against malaria, which is an important part of the protection against the severe form of the disease including cerebral malaria. We also observed that acute kidney injury, shock, hemoglobinuria, and hyperbilirubinemia were uncommon in this study, similar to the findings of other studies.[5,20,21] These are generally rare manifestations of severe malaria among children.[5]

Our study also showed that cerebral malaria and prostration were significantly higher among children aged 5 years and older. This is in contrast to earlier studies that showed that cerebral malaria was commoner among children younger than 5 years. This is a bit of concern considering the fact that partial immunity against malaria is acquired in children as they grow old. The observation of multiple convulsions and severe anemia among children <5 years of age is similar to the finding in Enugu.[6] This may be due to the inadequate feeding practices, micronutrient deficiencies, and increased parasitic infestations as well as increased immune dysregulation that contribute to severe anemia in under-five children with malaria.[22]

In this study, severe malaria among children had a mortality rate of 4.3%. This is similar to the mortality of 4.4% in Mozambique.[11] It is, however, lower than 8.5% in Gusau[5] and 5.2% in Osogbo[10] but higher than 1.96% in Enugu.[6] The variation in outcomes of severe malaria between the present study and previous studies may be explained by the differences in epidemiological and immunological factors among the different regions, the malaria-related health practices of primary caregivers as well as the promptness of interventions at the health facilities such as antimalarial administration and other services such as blood transfusion.[6,23]

Our study also showed that the presence of more than a single component of severe malaria increased the odds of death by six times. The presence of multiple components has been documented to be associated with increased risk of death in children with severe malaria.[6] The other factors associated with death from severe malaria in this study included an impaired level of consciousness, hypoglycemia, and duration of 24 h or less. In a large cohort of children with severe malaria in India, factors associated with death included respiratory distress, cerebral malaria, multiple organ dysfunctions, and hyperparasitemia. The other predictors of death in severe malaria described in previous studies include respiratory distress and jaundice.[24,25] Higher mortality within the first 24 h of admission has also been observed in previous studies.[26-29] The high risk of dying within the 24 h of admission indicates the needs to focus on this period in children with severe malaria.

Limitation of the study

Despite the large sample size of 483 children with severe malaria, our study is limited because it was retrospective in design and there were 13 missing case files that were excluded from the final data analyses.

CONCLUSION

Our study showed that severe malaria remains an important cause of childhood morbidity and mortality in Katsina. Cerebral malaria is the most common form of severe malaria with a significant burden in the children above 5 years of age. The risk factors predictive of death among children with severe malaria included an impaired level of consciousness, hypoglycemia, multiple components of severe malaria, and duration of 24 h or less on admission.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. World Health Organization. World Malaria Report 2019. Geneva: World Health Organization; 2019.
2. World Health Organization. World Malaria Report 2017. Geneva: World Health Organization; 2017.
3. World Health Organization. World Malaria Report 2016: Country

Profiles. Geneva: World Health Organization; 2017.
4. Odey F, Esu E, Effa E, Udoh E, Oduwole O, Chibuzor M, *et al*. Management of severe malaria in children under 5 years of age in private and public health facilities in Cross River State, southeastern Nigeria : An audit of current practices. Clin Audit 2013;5:43-8.
5. Garba BI, Muhammad AS, Edem BE, Adeniji AO, Aghadueki S, Kolawole T, *et al*. Prevalence and pattern of severe malaria seen in children at a specialist hospital in Gusau, Nigeria. IJBR 2014;5:351-4.
6. Edelu BO, Ndu IK, Igbokwe OO, Iloh ON. Severe falciparum malaria in children in Enugu, South East Nigeria. Niger J Clin Pract 2018;21:1349-55.
7. Seasonal malaria chemoprevention programme start up guide. Nigeria: Malaria consortium; 2015. Available from: https://www.malariaconsortium.org/resources/publications/add-2015/. [Last accessed on 2018 Apr 10].
8. World Health Organization. Guidelines for the Treatment of Malaria. Geneva: World Health Organization; 2018.
9. Orimadegun AE, Fawole O, Okereke JO, Akinbami FO, Sodeinde O. Increasing burden of childhood severe malaria in a Nigerian tertiary hospital: Implication for control. J Trop Pediatr 2007;53:185-9.
10. Oyedeji OA, Oluwayemi IO, Afolabi AA, Bolaji O, Fadero FF. Severe malaria at a tertiary paediatric emergency unit in South West Nigeria. Res J Med Sci 2010;4:352-6.
11. Bassat Q, Guinovart C, Sigaúque B, Aide P, Sacarlal J, Nhampossa T, *et al*. Malaria in rural mozambique. Part II: Children admitted to hospital. Malar J 2008;7:37-9.
12. National Malaria Elimination Program (Nigeria), and ICF International. The 2015 Nigeria Malaria Indicator Survey: Atlas of Key Indicators. Rockville, Maryland, USA: Federal ministry of health, Nigeria; 2015.
13. Bajoga UA, Balarabe HS, Olufemi AA, Dalhat MM, Sule IB, Ibrahim MS, *et al*. Trend of malaria cases in Kaduna State using routine surveillance data, 2011-2015. Pan Afr Med J 2019;32:8.
14. Wogu MN, Nduka FO. Evaluating malaria prevalence using clinical diagnosis compared with microscopy and rapid diagnostic tests in a tertiary healthcare facility in Rivers State, Nigeria. J Trop Med 2018;3:1-4.
15. Kunuanunua TS, Nsibu CN, Bodi JM, Tshibola TK, Makusi Bura M, Magoga K, *et al*. Severe malaria in children: A descriptive report from Kinshasa, the democratic republic of Congo. J Trop Pediatr 2015;61:272-8.
16. Custodio E, Descalzo Ma, Villamor E, Molina L, Lwanga M, Bernis C, *et al*. Nutritional and socio-economic factors associated with *Plasmodium falciparum* infection in children from Equatorial Guinea: Results from a nationally representative survey. Malar J 2009;8:225.
17. Schofield L, Grau GE. Immunological processes in malaria pathogenesis. Nat Rev Immunol 2005;5:722-35.
18. Federal Ministry of Health. National Guidelines for Diagnosis and Treatment of Malaria 2015. Abuja, Nigeria: Federal Ministry of Health; 2015.
19. Bello E, Aganbi B, Gbode E, Aremu O. Monthly rainfall forecast over the sahel region using Sarima Models. Open Access Toxicol Res 2018;1:13-26.
20. Desta KM. Pattern of severe and complicated malaria in children admitted to Gondar medical college hospital during 1995-2000. Ethiop J Heal Dev 2000;16:53-9.
21. Kaushik JS, Gomber S, Dewan P. Clinical and epidemiological profile of severe malaria in children from Delhi, India. J Health Popul Nutr 2012;30:113-6.
22. Perkins DJ, Were T, Davenport GC, Kempaiah P, Hittner JB, Ong'echa JM. Severe malarial anemia: Innate immunity and pathogenesis. Int J Biol Sci 2011;7:1427-42.
23. Iloh GU, Orji UN, Amadi AN. Malaria morbidity among under-five Nigerian children: A study of its prevalence and health practices of primary care givers (mothers) in a resource-poor setting of a rural hospital in Eastern Nigeria. EJPM 2013;1:50-7.
24. Marsh K, Forster D, Waruiru C, Mwangi I, Winstanley M, Marsh V, *et al*. Indicators of life-threatening malaria in African Children. N Engl J Med 1995;332:1399-404.
25. Dzeing-Ella A, Nze Obiang PC, Tchoua R, Planche T, Mboza B, Mbounja M, *et al*. Severe falciparum malaria in Gabonese children: Clinical and laboratory features. Malar J 2005;4:1.
26. Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO, *et al*. Mortality after fluid bolus in African children with severe infection. N Engl J Med 2011;364:2483-95.
27. Berkley JA, Ross A, Mwangi I, Osier FH, Mohammed M, Shebbe M, *et al*. Prognostic indicators of early and late death in children admitted to district hospital in Kenya: Cohort study. BMJ 2003;326:361.
28. Kendjo E, Agbenyega T, Bojang K, Newton CR, Bouyou-Akotet M, Pedross F, *et al*. Mortality patterns and site heterogeneity of severe malaria in African children. PLoS One 2013;8:e58686.
29. Kazembe LN, Kleinschmidt I, Sharp BL. Patterns of malaria-related hospital admissions and mortality among Malawian children: An example of spatial modelling of hospital register data. Malar J 2006;5:93.