FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 5 No. 2, June, 2021, pp 511-518
DOI: https://doi.org/10.33003/fjs-2021-0502-664

PREVALENCE AND PATTERN OF SEVERE MALARIA AMONG CHILDREN IN TWO GENERAL HOSPITALS, JIGAWA STATE- NIGERIA

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ABSTRACT

The prevalence and pattern of presentation of severe malaria differ from one area to another, in one age group and gender. A descriptive cross sectional study of children between the ages of one month and fourteen years with symptoms of severe malaria was conducted between July and December 2018 in Dutse and Birnin Kudu Local Government Area of Jigawa State. Venous blood samples were used for parasitological, hematological and biochemical examination following standard procedures. Thick and thin blood films were prepared, stained and examined at x100 magnification. A total of 172 children were considered in which, 73/167(43.7) children had severe malaria. Children less than 5 years of age had the highest percentage of severe malaria (47.1%; 95% CI = 39.5 to 54.7). Hyperpyrexia, prostration, hyper parasitemia and multiple convulsions were the commonest presentations. While metabolic acidosis, jaundice, hypoglycemia and respiratory distress were the least presenting features, no child presented spontaneous bleeding or shock. Furthermore, 21/73 children with severe malaria had only one feature of severity, 32/73 (43.8) had two features of severity, while 14/73 (19.2) of the children had up to three features. Only 4/73 (5.5) children had four of the features of severity. Chi-square analysis showed significant difference (P <0.05) in prostration and multiple convulsions among children less than and above 5 years. The prevalence of severe malaria in less than five years old is high; hence care givers should present symptoms early to the hospital in order to prevent progression to severe life threatening malaria.

Keywords: Cerebral malaria, Children, *Plasmodium falciparum*, Prevalence, Severe Malaria.

INTRODUCTION

Malaria is older than recorded history and probably plagued prehistoric man and is said to have been ravaging humanity for decades (Cox, 2010).It is a mosquito - borne protozoan infection of the red blood cells transmitted by the bite of a female anopheline mosquito.The primary vector across most of the country is *Anopheles gambiae* s.s, because of its high resistance to insecticides and profound adaptation to different climatic conditions (White, 2010). Five human *Plasmodium species* (*Plasmodium falciparum, P. vivax, P. ovale, P. knowlesi, and P. malariae*) are known to cause malaria infection (White *et al*., 2014).The major severity is caused by *P. falciparum in about 99.7% of estimated malaria cases* (WHO, 2017;Trampuz *et al.,* 2003).This is because *P. falciparum* is known to exhibits features like cytoadherence, sequestration, resetting ,and aggregation in the blood vessels with subsequent obstruction to micro-circulation and thus leads to end-organ dysfunction (Magallon *et al*., 2016). The incidence rate of malaria is estimated to have decreased by 27% globally, from 80 in 1000 to 57 cases per 1000 population at risk. In the WHO African Region, the malaria incidence rate however remained at 215 cases per 1000 population at risk in 2019 (WHO, 2018). Children under five years accounted for 67%of all malaria deaths and the WHO African Region accounted for 95% of the deaths with Nigeria (23%), Democratic Republic of the Congo (11%) contributing the most (WHO, 2000).. Nigeria is currently a malaria endemic country with its entire population at risk of been infected, treatment in endemic areas is often less satisfactory and the overall fatality rate for all cases of malaria can be as high as one in ten (Mockenhaupt *et al.*, 2004). Malaria does not only affect the health of the child but, it also causes great drain on the national economy. The cost of daily labour coupled with cost of treatment and high mortality associated with the disease make malaria one of the main diseases retarding development in Africa (Ekpenyong and Eyo, 2008).Severe malaria is acute complicated malaria with signs of organ dysfunction and/or high level of parasitaemia associated with high mortality (White *et al*., 2014).The 2000, WHO criteria for diagnosis of severe malaria includes clinical manifestations and laboratory parameters(WHO, 2000).Studies on African children have centered mostly on the clinical manifestations and factors related to prognostication like genotype, nutrition, blood group etc, but the prevalence, nature and pattern of severity, has been mostly retrospective studies with considerable impact on the outcome (Von Seidlein *et al*,. 2012).Thus,

evaluating the prevalence, clinical pattern and relationship to age, geographic area, gender and outcomes of severe malaria amongst children in our communities may assist in early presentation and diagnosis, appropriate management of cases thereby nipping them early before complications ensue. Information in the literature as regard the prevalence and pattern of presentation of severe malaria in the study area is lacking. This cross – sectional descriptive study therefore was carried out to assess the prevalence and pattern of severe malaria parasite infection among children admitted into the Emergency Paediatric Unit of General Hospitals Dutse and Birnin kudu in Jigawa state. This will therefore be a vital statistic for rational design of interventions and thus a yardstick for effectiveness of any preventive measures knowledge gap filling and for further research.

MATERIALS AND METHODS

Study area

This study was conducted in two General Hospitals: Dutse and Birnin Kudu in Jigawa state. The two hospitals were selected in order to compare incidence of severe *P. falciparum* malaria complications in the areas as they both serves as a secondary care centre for the state, as well as a referral centre for all the primary health centers of their surroudings. Geographically, Birnin kudu is located between altitudes 11.45^0 N and longitude 9.5^0 E, about 474meter above sea level. It has a population of 26,565temperature of 19.3^0C, humidity of 19.4% with wind 2.7m/s N/E, whereas Dutse a Hausa word denoting "Rock" derive its name from the hilly rocks, which encircled the town of Garu and its environs covering an area of about 5 square miles. It is situated at 460 meters elevation above sea level, latitude11.46°North and longitude 9.34° East. It has a projected population of about 335,600 inhabitants as of 2016 (state fact sheet, 2016).

Ethical Clearance

Ethical approval was obtained from State Ministry of Health Jigawa state with Ref; MOH/SEC.3/S/715/1.Informed written consent was given to the parents/guardian of the participants before involvement into the study. A cross-sectional descriptive study design was adopted. The sample size was calculated from the following formula which was adopted from (Araoye *et al*., 2004).

$$N = \frac{Z^2 p\,(1-p)}{d^2}$$

Where: N= Minimum number of subjects required in the sample, Z = a standardized normal deviate value that correspond to a level of statistical significance of $P \leq 0.05$ which is 1.96

P= estimate of proportion of severe malaria parasitemiaamong children, value for p is taken from previous study by Orimadegun *et al*., 2007,where

P= 11.0%. d=margin of error on p or level of precision which is 0.05

Z=standard normal deviation (95%) usually set at 1.96 confidence level

$N = \frac{(1.96)^2 \text{ X } 0.11(1-0.11)}{(0.05)^2}$= 150 + 22.5(allow 15% for missing so as to increase the power of the statistics) = 172 subjects.

A total of 172 children, between the ages of one month and fourteen years were enrolled in the study. This age group was the most affected of the population by malaria and exclusively cover the age group of the hospitals biological definition of a child. It was conducted between July, 2018 to December, 2018 because it falls at the peak of the rain fall and hence period of high malaria transmission in the tropics due to high vegetation and stagnant water during this period. Children that presented to Emergency Pediatric Unit within the study period, that have clinical features, suggestive of severe malaria and meet the world health diagnostic criteria where enrolled,whileChildren that are less than one month and greater than fourteen years and having chronic illnesses like TB, HIV or acute illnesses that mimic malaria infections like meningitis, pneumonia etc, where not included.Clinical and demographic data of study participants with features suggestive of severe malaria were recorded on pre-designed case record form by trained health professionals working at thetwogeneral hospitals thus, body temperature of each child was measured using digital thermometer (Tro-digitherm [water resistant], LOT:12639-05, Troge Medical GMBH, Hamburg Germany, 2018). Hyperpyrexia is considered when body temp is>40.Children with at least one or more symptoms of severe malaria complications set by WHO (2000) were classified as severe malaria cases. 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 parasite anaemia diagnosed either using a rapid diagnostic test (*Malaria Ag.pLDH/HRP2 Combo Card test*), microscopy or both (WHO, 2017).*Impaired consciousness*: A Blantyre coma score <3 in children less than 2 years or A Glasgow Coma Score <11in 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 haematocritof <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. *Acutekidney 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 plasmaor 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 children12 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. Patients

were subsequently managed according to the WHO treatment guidelines and hospital's treatment protocols.(WHO, 2018).

Laboratory procedures

Blood collection and analysis were made using technique of disinfection as described by (Chesbrough, 2006) with the help of experienced laboratory technologists. Drop of blood sample was collected on clean glass slide from lancet pricked finger to prepare thin and thick blood smears per patient for microscopic examination using field's stain A (eosin) and field's stain B (methyl azure). Malaria parasites were identified and parasite load was established by ′Semi Quantitative Counting Method′ (Gupta *et al.,* 2006).The system entails using a code of between one and four plus signs (+ = 1 - 10 parasite per 100 high power fields of thick film, ++ = 11 - 100parasites per 100 high power fields of tick film, +++ = 1 - 10 parasites in every high power field of thick film, ++++ = More than 10 parasites in every high power field of thick film).Blood glucose concentration (Glu) was measured using handheld portable glucose analyzer (Acuu-chek Germany).

Statistical analysis.

The statistical package for social sciences (SPSS) for windows statistical software version 25.0 was used for data analysis. The presence or absence of *Plasmodium* infection (prevalence) was calculated and the significant difference in prevalence across age groups the demographic, socioeconomic, environmental, and behavioural characteristics of the patients were treated as categorical variables and presented as frequencies and percentages. Chi squared test was used to test the associations between malaria prevalence, with the demographic (age, gender, and family size) and socioeconomic factors (educational and employment status), as the explanatory variables. Multivariable logistic regression was conducted to identify the risk factors associated with infection. A $P< 0.05$ was considered statistically significant i.e., at 95% confidence interval.

RESULTS

Socio demographic characteristics of patients

A total of 172 children were proportionately examined from both hospitals and were used for analysis, comprised of 93 (54.1%) from Dutse and 79 (45.9%) from Birnin-kudu. Above half (56.4%) of the children were males. The children were aged from 1 months to 168 months (14 years) with a median age of 3 years (interquartile range = 2 to 5 years). Majority (72.1%) of the children were less than 5 years of age, followed by those between 5 to 10 years, which accounted for 24.4%. Only 6 (3.5%) were above 10 years. Majority of the caregivers had no formal education127 (73.8%), I04 (61%) were petty traders, followed by 64 (37.3%) who were full time house wives. All *Plasmodium* species identified in this study were *P. falciparum*.

Table I: Socio demographic characteristics of children in Dutse and Birnin-Kudu` Local Government, Jigawa State.

Variable	Dutse	B/Kudu	Total
	n (%)	n (%)	n (%)
Gender			
Male	54 (55.7)	43 (44.3)	97 (56.4)
Female	39 (52)	36 (48)	75 (43.6)
Total	93(54.1)	79(45.9)	172(100)
Age (years)			
<5 years	71 (57.3)	53 (42.7)	124 (72.1)
5 to 10 years	21 (50)	21 (50)	42 (24.4)
> 10 years	1 (16.7)	5 (83.3)	6 (3.5)
Level of education of caregivers			
None	66 (52)	61 (48)	127 (73.8)
Qur'anic	4 (80)	1 (20)	5 (2.9)
Primary	11 (57.9)	8 (42.1)	19(11.1)
Secondary	11 (73.3)	4 (26.7)	15 (8.7)
Tertiary	1 (16.7)	5 (83.3)	6 (3.5)
Occupation of caregiver			
Petty traders	66 (63.5)	38 (36.5)	104 (61)
Civil servants	2 (66.7)	1 (33.3)	3 (1.7)
House wives	24 (37.5)	40 (62.5)	64 (37.3)
Farming	0	0	0
Others	0	0	0

Table 2: Prevalence of severe malaria among children in Dutse and Birnin Kudu Local Government Areas Jigawa State.

Frequency	Proportion	Prevalence	5%C.I	*P*
Severe malaria cases	73	43.7	36.2-51.2	
Distribution by local government				**0.91**
Dutse	41	24.5	18.0-31.0	
Birnin kudu	32	19.2	13.2-25.2	

C.I = Confidence Interval

Overall, 73 out of 167 children had severe malaria, giving a prevalence of 43.7% (95% CI: 36.2to51.2%). This implies that about one in every two children in Dutse and Birnin-kudu combined had severe malaria. The prevalence of severe malaria was higher in Dutse (24.5%; 95% CI: 18 to 31%) compared to Birnin-kudu (19.2%; 95% CI: 13.2to25.2%) (Table 2): one in every four children in Dutse local government had severe malaria, while in Birnin-kudu, the ratio was one in every five children. Chi-square statistics showed that severe malaria prevalence between both towns did not significantly differ from each other ($X^2 = 0.01$, $p = 0.91$), in other words, the prevalence of severe malaria in Dutse and Birnin-kudu are comparable Table 2.

Table 3: Comparison between age and severe malaria

Age Range(years)	Frequency (n)	n (%)	95% CI
<5 years	119	47.1%	39.5%-54.7%
5 to 10 years	42	35.7%	28.4%-43.0%
>10 years	6	33.3%	26.2%-40.4%

Table 3 revealed that cases of severe malaria increases with decreasing age. Children below 5 years have the highest percentage of severe malaria (47.1%; 95% CI = 39.5 to 54.7%), followed by those aged 5 to 10 years (35.7%; 95% CI = 28.4 to 43.0%). Children more than years of age had the least percentage of severe malaria cases (33.3%; 95% CI = 26.2 to 40.4%).

Clinical and laboratory assessment revealed that hyperpyrexia, prostration, hyper parasitemia and multiple convulsions were the commonest presentations among children with severe malaria in Dutse and Birnin-kudu Local Government of Jigawa state. Hyperpyrexia was identified in 38.4% of cases, prostration 32.9%, hyper parasitemia 29.6% and multiple convulsion 26%. Among all the features, metabolic acidosis (6.8%), jaundice (5.5%), hypoglycemia (2.7%) and respiratory distress (2.7%) were the least presenting features. No child presented with abnormal spontaneous bleeding or shock (Fig.1).

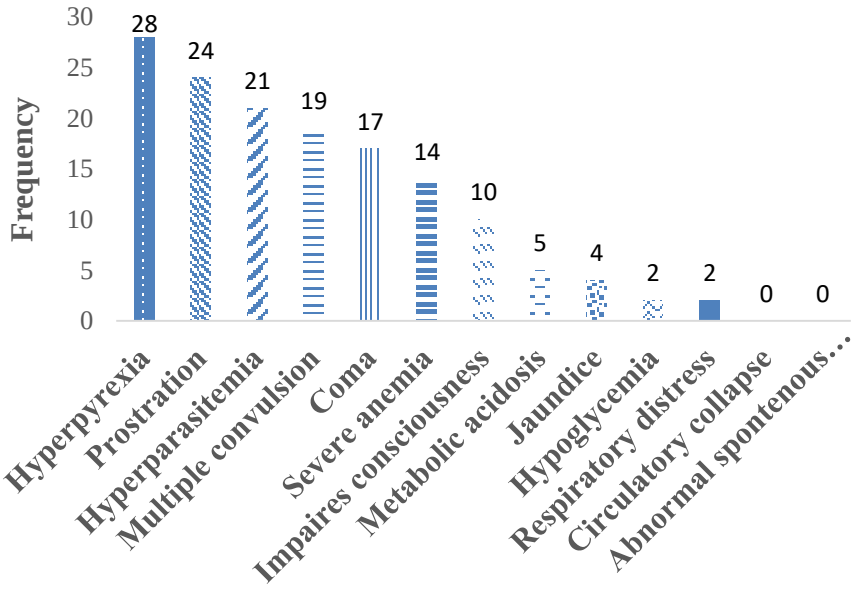

Fig 1: Clinical and laboratory features among children with severe malaria in Dutse and Birnin-kudu local government Jigawa state

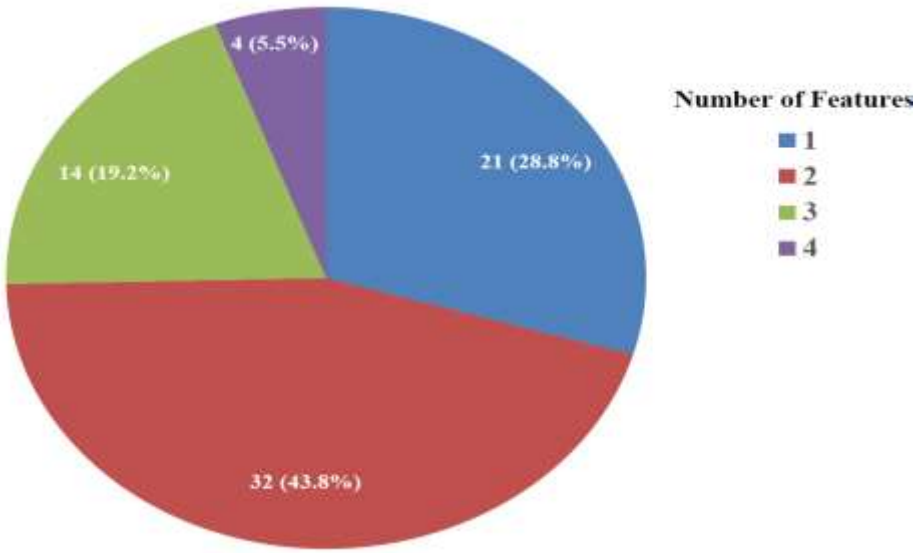

Figure 2: Number of features of severity per child

Figure 2 showed that among 73 children with severe malaria, 21 (28.8%; 95% CI = 18.4 to 39.2%) had only one feature of severity, 32 (43.8%; 95% CI = 32.4 to 55.2%) had two features of severity, while 14 of the children (19.2%; 95% CI = 10.2 to 28.2%) had up to three features. Only 4 children (5.5%; 95% CI = 0.3 to 10.7%) had a four of the features of severity.

Table4: Comparison of prominent features of severity among children with Sever malaria based on age.

Features	**Positive Cases**	**<5 years n (%)**	**≥ 5 years n (%)**	**X^2**	**P- value**
Hyperpyrexia	28	20 (71.4)	8 (28.6)	0.31	0.58
Prostration	24	14 (58.3)	10 (41.7)	5.32	0.02*
Hyperparasitemia	21	14 (66.7)	7 (41.2)	0.80	0.37
Multiple convulsion	19	18(94.7)	1 (5.3)	4.67	0.03*
Coma	17	13 (76.5)	4 (23.5)	0.01	0.98
Severe anemia	14	12 (85.7)	2 (14.3)	0.29	0.59

***Significant at P<0.05**

Cross tabulation between age and prominent features of severity among children with severe malaria (see Table 4) showed that the rate of hyperpyrexia and hyper parasitemia in children less than five years was about twice that in children aged 5 years and above, whereas, the difference in the number of children with multiple convulsion, coma and severe malaria varied greatly between both age groups. Chi-square statistics revealed that the difference in proportion between children less than five years old and those aged five and above were statistically significant for just prostration and multiple convulsions, this implies that in the population, the rate of protrusion and multiple convulsions are higher in children less than five years old.

Table 5 showed that the number of cases of hyperpyrexia and protrusion differed slightly between male and female, however this difference was not statistically significant. Furthermore, the rate of hyper-parasitemia, multiple convulsions, coma and severe anemia was comparable among both genders, hence no statistically significant difference exist.

Table 5: Comparison of prominent features of severity among children with severe malaria based on gender

Features	Positive Cases	Male	Female	X^2	*P*-value
			n (%)	n (%)	
Hyperpyrexia	28	12 (42.9)	16 (57.1)	0.40	0.53
Protrusion	24	9 (37.5)	15 (62.5)	1.36	0.24
Hyperparasitemia	21	10 (47.6)	11 (52.4)	0.01	0.99
Multiple convulsion	19	10 (52.6)	9 (47.4)	0.01	0.95
Coma	17	9 (52.9)	8 (47.1)	0.01	0.99
Severe anemia	14	7 (50)	7 (50)	0.01	0.96

DISCUSSION

The overall prevalence of severe malaria in this study was 43.7%. The prevalence of severe malaria in Dutse and Birnin-kudu, was found to be 24.5%, 19.2%, respectively. It is closely similar to studies carried out in Gusau, Azare and Yemen with prevelance of 19.6%, 25% and 17% respectively (Garba *et al*., 2014; Imoudu *et al*., 2018 ; Al- Taiar *et al*., 2006) but higher than what was obtained in Enugu, Ibadan and Ethopia that have 5.6%, 11% and 9.7% respectively (Eudel *et al.*, 2018 ; Adebola *et al.*,2007; Desta *et al.*, 2016). However, the prevalence in this study was lower than the 56% reported in Sokoto, North west Nigeria and 36.6% in Jos North central Nigeria (Amodu-Sanni *et al*., 2019; Okokon *et al*., 2019). The prevalence of severe malaria was higher in Dutse 24.5% compared to Birnin-kudu 19.2%.This variation may be due to differences in study Location as both towns are border town with a major road connecting the northwest with the northeast region of Nigeria in addition Jigawa has relatively been peaceful, thus serving as focal point for population migration to the state and towns. This migratory population who often abandon some or all malaria preventive measures may have been receiving care more in Dutse been the capital with larger population. Also delay in presentation and initiation of treatment could partly explain the differences.

Findings of this study also revealed that children below 5 years have higher rate of severe malaria and is actually in keeping with similar studies performed in Azare, Enugu and Gusau (Garba *et al*., 2014; Imoudu *et al*., 2018; Eudel *et al.*, 2018).This is due to the fact that immunity against malaria has not been fully developed in age groups less than five years, because they have not been exposed enough to the parasitic infection to develop adequate level of specific immunity to the parasite. This finding underscores the need to have more emphasis placed on malaria preventive measures among the under-5 children.

Hyperpyrexia, prostration, Multiple Convulsion and hyper parasitemia were the commonest features of severe malaria, similar to that seen in Gusau and Mozambique.(Garba *et al*.,2014;Bassat *et al*., 2007) but in contrast to what was found in Enugu (Eudel *et al.*, 2018). This study and the one with similar estimates were performed in secondary facilities or community based studies while the other study is tertiary hospital based thus as the lower cadre health facilities are the first point of contact, the tertiary facilities being referral centers may be seeing patients who might have had previous treatment. Respiratory distress, jaundice, hypoglycemia and metabolic acidosis were the least presenting features similar with earlier studies carried out in Porthacourt and Benin (Yaguo *et al*., 2018 ; Adulugba, 2020).

This study found that most of the children had two of the features of severity 43.8%, while 28.5% had only one feature of severity, and a few 5.5% had four of the features of severe malaria which is similar to Enugu and Portharcourt studies that shows that most of the children presented with multiple rather than single features of severe malaria (Eudel *et al.*, 2018; Yaguo *et al., 2018*). This could be as a result of poor health seeking behaviour, low socio economic status with subsequent delay in presentation and initiation of treatment.

Cerebral malaria was 15% as was the case in Ilorin 11% and Cameroon 8% studies (Olarenwaju and Johnson, 2001; Ikome, *et al*., 2002) However, it was uncommon presentation in Ibadan,2.2% and Malawi,2.5% studies (Orimadegun *et al*., 2007; Nkhoma *et al*., 1999).Convulsions were commoner in under fives in this study 95%, as seen in Gusau 66.8% and Ilorin 65% . (Garba *et al*., 2014; Olarenwaju and Johnson, 2001).

Severe malarial anemia prevalence found in our study is 10% similar to that obtained in Gusau 9.8%, Ibadan 8.5% and Ilorin 9.6% (Garba *et al*., 2014;Orimadegun *et al*.,2007;Olarenwaju and Johnson, 2001) but higher than what was obtained in some African countries like in Malawi

2.5% and Senegal 2.2% (Nwanyanwu,1997;Imbert *et al.*, 1997). Other studies (Oyedeji *et al*., 2010; Edelu *et al.*, 2018; Okafor *et al*., 2012) have however shown higher rates of children presenting with severe anaemia than what was obtained in our study. Furthermore, children less than 5 years (12%) featured severe anaemia more than those aged 5 years and above (2%) Edelu *et al.*, 2018.The high rate in children less than 5 years than those greater than 5 years is comparable to that in Enugu 38% and 11% respectively. These differences in severe anemia among gender and age group was however found not to be statistically significant P=0.96.This is consistent with previous report that have compared data across sites with different transmission intensities (Woolhouse, 2000).Several factors have been documented that predispose the under-five children comorbidity from malaria (Obiano, 2007),because under-five children in endemic malaria areas, have transient resistance to malaria infection from birth to 6months of age due to trans-placentally transferred IgG antibodies from the mother to the child (Nwankwo and Okafor, 2009).

CONCLUSION

The prevalence of severe malaria in the study area was significant especially those that are under 5 years old, which reflects the malaria burden in children despite measures of control been implemented in the region. This study therefore could be useful for rational design of interventions and a yardstick also for effectiveness of any preventive measures or intervention. It could also create and give room for future research as regard prospective studies on malaria mortality, case fatality and possibly genetic diversity.

RECOMMENDATIONS

There is the need for care givers to present children with mild features of malaria early to the hospital, so as to prevent progression to severe malaria. Providing seasonal chemoprevention (SMC) for children less than five years of age, other vulnerable and prompt identification and management of children.

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