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## ORIGINAL RESEARCH

# Clinical Profile and Short-Term Outcome of Malaria in Febrile Under-Five Children in a Secondary Health Facility

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### Abstract

**Background:** Malaria remains an essential tropical protozoal disease, affecting both young and old. It manifests in complicated and uncomplicated forms with more grave consequences among Under-five children.

**Objective:** To describe malaria's clinical profile and short-term outcomes in Under-five children in a secondary health facility in southwest Nigeria.

**Methods:** This was a hospital-based and cross-sectional study. Five hundred children under the age of five years who presented with fever at the health facility were recruited into the study. The clinical manifestations were documented, and blood samples were examined for malaria parasitaemia.

**Results:** Forty-eight children (9.6%) of the study subjects were neonates, 195 (39%) were infants, and the remaining 257 (51.4%) were aged 12 months to 5 years. One hundred and two (39.1%) of the 261 children positive for malaria presented with uncomplicated malaria, while 159 (60.9%) of this population had various complications. The overall mortality from malaria was 5.0%.

**Conclusion:** More than 60% of the infected children had complications of malaria, and mortality was mainly due to late presentation. Therefore, malaria preventive strategies should be part of ongoing health interventions.

**Keywords:** *Clinical outcome, Clinical profile, Malaria parasitaemia, Plasmodium, Under-5 Children.*

### Introduction

Malaria is an infectious disease caused by the protozoan parasite of the genus *Plasmodium*. Globally, malaria remains a major cause of morbidity and mortality, especially among children and pregnant women, especially in the developing world. [1-4] Malaria causes severe morbidity and mortality through several pathological mechanisms, which are understood to varying degrees. [5,6] The treatment includes first and second-line antimalarial drugs, adjunctive and supportive measures such as intravenous fluids, blood transfusions, supplemental oxygen, and anti-

convulsant medications. [7] The aims of malaria treatment, as outlined by the World Health Organization (WHO), are to prevent death, prevent long-term deficits, reduce the duration of morbidity of an acute episode of illness and clear the parasites entirely from blood so that the infection does not re-occur. [8]

There were 241 million new cases of malaria worldwide in the year 2020, [9] and there were estimated 627,000 malaria deaths worldwide in that year, representing about 14 million more cases and 69,000 more deaths above the year 2019 figures; indeed, 90% of the deaths occurred in the African region. [10] The threat of

malaria is highest in sub-Saharan Africa. Six countries in that region accounted for more than half of all malaria deaths worldwide in the year 2020: Nigeria (26.8%), the Democratic Republic of the Congo (12%), Uganda (5.4%), Mozambique (4.2%), Angola (3.4%) and Burkina Faso (3.4%).<sup>[8]</sup>

Malaria continues to create a menace in developing countries; malaria accounts for over 60% of outpatient visits and 30% of hospital admissions in Nigeria. <sup>[11]</sup> It is a disease caused by parasites of the genus *Plasmodium*, of which the *P. falciparum* species is responsible for most of the severe forms of the infection.

The southwestern part of Nigeria is one of the worst affected parts of the nation regarding malaria infection because of the thick forest and the characteristic pattern of rainfall and humidity; children and pregnant women are major victims. <sup>[12]</sup>

More data on malaria among under-five children in Akure, southwest Nigeria, needs to be collected. Therefore, it is desirable to profile this infection occasionally to assess its outcomes among under-five children. This may generate a response from the health authorities and health planners. The study, therefore, aimed to describe the clinical profile and short-term outcomes of malaria among under-five Nigerian at the secondary health facility level.

## Methods

### *Study area*

This cross-sectional study was conducted at the Mother and Child Hospital, Akure (MCHA), from January to May 2019. The purpose-built, ultra-modern public facility provides specialised and effective health care services to pregnant women and children aged five years and below in the Ondo State capital, ally communities and neighbouring states in SouthwesternSouthwestern Nigeria.

### *Sample size and recruitment of study subjects*

The sample size was determined using the Raosoft software (Raosoft®, 2019); the calculated sample size based on the year 2019 estimated population of the Akure was 384, but the sample size was rounded up to 500 to allow for non-responses. <sup>[13]</sup> Only under-five children with fever were enrolled into the study while parental refusal to give consent was the exclusion criterion. Five hundred consecutive children aged five years and below were recruited from various entry points into the hospital, vis-à-vis the emergency room, newborn unit, outpatient department (OPD) and the children's ward. The hospital number, data from the case files (age, gender, ethnicity, temperature, presenting complaints, findings on examination) and other information provided by the mothers (birth orders, educational level, occupation of both parents) were entered into the questionnaire and the computer while maintaining confidentiality. The family's first child belongs to birth order 1; the second child belongs to birth order 2; the third child belongs to birth order 3 etc.

### *Socio-economic classification*

This was done using the model described by Ogunlesi *et al.* <sup>[14]</sup>, which considers the parents' income, education and occupation and apportion socioeconomic classes I, II, III, IV and V in descending order. The classes were grouped as upper socioeconomic status (SES) comprising classes I and II, middle SES (Class III) and lower SES (classes IV and V).

### *Sample collection*

Blood samples were drawn by venepuncture from the children after taking consent from the mothers, and the samples were analysed for malaria parasites using the microscopy technique. <sup>[15]</sup> ABO blood typing was done to determine the blood group of the children. Parasite density count was done and was expressed as the number of asexual parasites per  $\mu\text{L}$  of blood-based on an assumed 6,000 white blood cells per  $\mu\text{L}$  of blood. <sup>[16]</sup> Parasitaemia was graded as low intensity (1–999/ $\mu\text{L}$ ), moderate intensity (1000–9999/ $\mu\text{L}$ ), and high intensity ( $\geq 10,000/\mu\text{L}$ ). A slide was

considered negative if no parasites were seen after examining 100 fields. Two to three drops of the blood positive by microscopy test were also placed on a 3mm Whatman filter paper and dried at room air (Dry Blood Sample [DBS]). These were subsequently transported to the Nigerian Institute of Medical Research, Lagos (NIMR) for molecular analysis of DNA PCR to confirm the positivity of malaria parasite infection. Bedside blood glucose level was measured using a glucometer; a full blood count was performed using an automated haematology analyser. Severe malaria was recognised and categorised based on WHO criteria. [16] A packed cell volume of less than 20% was severe anaemia. Demographic data, clinical data and complications observed were documented, and these were entered into the study questionnaire and subsequently transferred into a Microsoft® Excel sheet.

### Data management and analysis

The collected data were checked for errors, and other variables from the laboratory results were entered into the Microsoft® Excel sheet. Data analysis was performed with SPSS statistical software. Associations between variables were tested using the Chi-Squared test, with the level of statistical significance set at 95%.

### Ethical considerations

Ethical approval for the study was sought from the Research and Ethics Committee of the Mother and Child Hospital and the Ondo State Ministry of Health (protocol number - OSHREC/29/04/20/270). Confidentiality was maintained, and only volunteers and consenting mother-child pairs were recruited. Verbal informed consent was obtained from all the mothers.

## Results

A total of 500 mother-child pairs participated in the study. All 500 children (100.0%) had a fever, and 261 (52.2%) were positive for malaria. The parasite species included *Plasmodium falciparum*

and *Plasmodium malariae* in 259 (99.2%) and 2 (0.8%), respectively. The remaining 239 children were negative for malaria parasites. Malaria infection was found across all socioeconomic classes. Forty-eight children (9.6%) of the study subjects were neonates, 195 (39%) were infants and the remaining 257 (51.4%) were aged 12 months to 5 years (Table I). Two hundred and eighty-eight (57.6%) of the children were males, and 212 (42.4%) were females, giving the male-to-female ratio of 1.3:1. Table I also shows that the age-related prevalence rates of malaria infection were 60.4%, 49.2% and 52.9% for neonates, infants and older children, respectively. There was no mortality among the neonates, whereas 3.07% of the infants died of malaria while 1.9% of the older children died. The overall mortality rate was 5.0%. Figure 1 showed a slightly higher prevalence of malaria among male children.

Fever was the only clinical presentation among 217 children, while the remaining 283 had one or more other symptoms besides fever. Eighty (16.0%) of the children presented with the refusal of feeds or loss of appetite, while fever and vomiting were present in 57 (11.4%), and fever and diarrhoea occurred in 58 of the children (11.6%). Other combinations of symptoms included fever and jaundice (8; 1.6%), fever and hepato-splenomegaly (20; 4.0%), fever and weakness (10; 2.0%), fever and difficulty with breathing (10; 2.0%) and excessive crying (2; 0.4%). Table III profiles the complications observed in the children and the case fatality rates. The complications included prostration (10; 2.0%), severe anaemia (42; 8.4%), multiple convulsion (30; 6.0%), hypoglycaemia (2; 0.4%), intravascular haemolysis (4; 0.8%), oliguria (1; 0.2%), hyperparasitaemia (30; 6.0%), metabolic acidosis (10; 2.0%) and cerebral malaria (51; 10.2%). Mortalities occurred in some children who presented with severe anaemia, multiple convulsions and cerebral malaria. Figure 2 shows that the prevalence of severe anaemia was higher among the children who were positive for malaria.

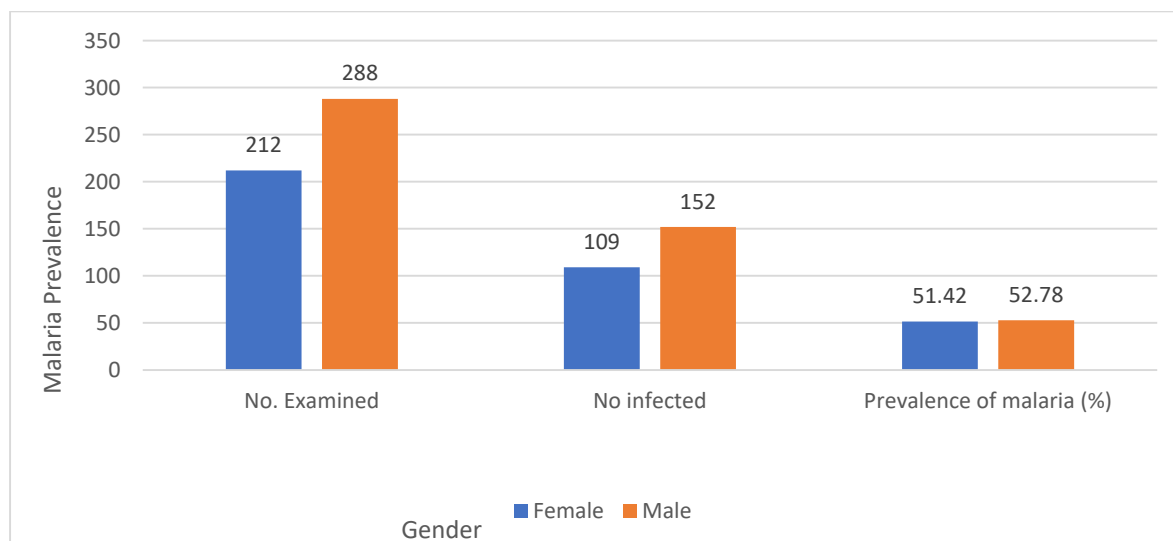


Figure 1: Prevalence of malaria according to gender

Table I: Age distribution, prevalence of malaria infection and outcomes

Age groups (Days/Years)	Number Examined	Number infected	Prevalence of malaria (%)	Mortality (%)
Neonates (1-28 days)	48	29	60.42	0
Infants (29 days – 12 months)	195	96	49.23	3.07
>1 year to 5 years	257	136	52.92	1.95
Total	500	261	52.20	5.02

Total mortality = 11 (5.02%); 6 (3.07%) among the infants and 5 (1.9%) among the older age group

Table II: Clinical presentation of the under-five children

Symptoms	Frequency	Percentage
Fever	500	100
Jaundice	8	1.6
Refusal of feeds/ loss of appetite	80	16.0
Hepato-splenomegaly	20	4.0
Weakness	10	2.0
Vomiting	57	11.4
Diarrhoea	58	11.6
Difficulty with breathing	10	2.0
Cough and catarrh	38	7.6
Excessive cry	2	0.4

Mean temperature was 38.7°C

Two hundred and eighty-three (283) children had fever and one or two other symptoms.

*Parasite Intensity count*

Table IV shows the distribution according to parasite intensity count. Twenty-eight (96.6%) of the 29 infected neonates had low-intensity parasitaemia, 1 (3.4%) had medium-intensity parasitaemia, and none had high-intensity

parasitaemia. Among the infants, 82 (85.4%) of the 96 infected children had low-intensity parasitaemia, while 6 (6.3%) and 8 (8.3%) had medium and high-intensity parasitaemia, respectively. One hundred and twenty-three (80.9%) of the male children had low-intensity

parasitaemia, while 18 (11.8%) and 11 (7.2%) had medium and high-intensity parasitaemia, respectively. Generally, high intensity of the malaria parasite was observed in infants and

older children, but this was absent in neonates. The parasite intensity count among the older children was statistically higher than in, the younger age group ( $\chi^2 = 13.596$ ,  $p = 0.0001$ ).

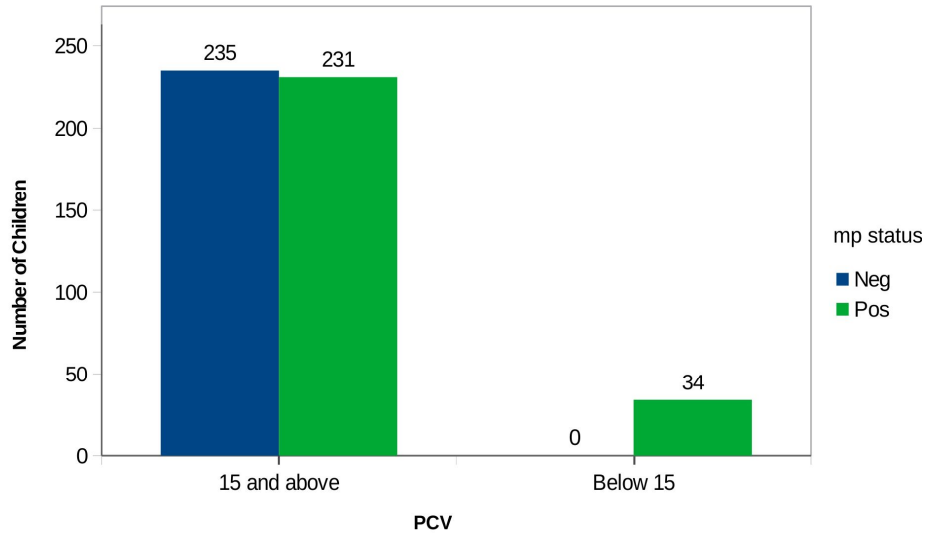


Figure 2: Packed Cell Volume (PCV in percentage) of the under-5 children

Table III: Complications among children with malaria and case fatality rates

Clinical presentation	Frequency	Percentage	Number of deaths	Case fatality (%)
Uncomplicated malaria	102	20.4	0	0.0
Prostration	10	2.0	0	0.0
Severe anaemia	34	6.8	5	14.7
Multiple convulsion	30	6.0	2	6.7
Hypoglycaemia	2	0.4	0	0.0
Intravascular haemolysis	4	0.8	0	0.0
Oliguria	1	0.2	0	0.0
Hyper-parasitaemia	30	6.0	0	0.0
Acidosis / respiratory distress	10	2.0	0	0.0
Cerebral malaria	51	10.2	4	7.8

A few of the children had more than one complication. The children died of anaemia due to late presentation.

Further, of the 109 infected female children, 80 (73.4%) had low-intensity parasitaemia, while 10 (9.2%) had medium intensity and 19 (17.4%) had high-intensity parasitaemia. High intensity of malaria parasite occurred more frequently in females (19; 17.4%) than males (11; 7.2%). The parasite intensity count was statistically higher in the females than the males ( $\chi^2 = 7.722$ ,  $p = 0.030$ ). Eighty-eight (82.2%) children belonging to the first birth order had low-intensity parasitaemia, 14 (13.1%) and 5 (4.7%) had medium and high-intensity parasitaemia,

respectively. The distribution of the remaining children according to birth order and with the corresponding spread of parasite intensities are shown in Table IV. Generally, children belonging to the fifth birth order and above had more cases of high-intensity of malaria parasites in their blood compared to other birth orders with statistical significance ( $\chi^2 = 0.072$ ,  $p = 0.014$ ).

Table IV also shows the distribution of malaria parasite intensity according to the ABO blood

groups of children infected with malaria. The result showed that all the categories of blood groups with either Rhesus positivity or negativity had low-intensity parasitaemia in varying proportions. However, medium-intensity parasitaemia was observed in all blood groups with Rhesus positivity (positive blood group) and in the O Rhesus-negative blood group. In addition, high-intensity parasitaemia was only observed in children with blood group O Rhesus-positive but completely absent in other blood groups ( $\chi^2 = 28.337, p < 0.001$ ).

## Discussion

The prevalence of malaria infection in the present study was 52.2%; this is similar to earlier reports from Kebbi State (52.2%) in the north-western part of Nigeria [18] but higher than the NDHS figures earlier reported from Lagos, southwest (2%), Ebonyi, south-east (30.5%), Akwa Ibom, south-south (23.2%) and Jos (21.2%) North-central, Nigeria. [17]

**Table IV: Parasite Intensity among various groups of children infected with *P. falciparum***

Variables	Number infected	Low intensity (1-999 parasite/ $\mu$ l of blood) (%)	Medium intensity (1000-9999/ $\mu$ l of blood) (%)	High intensity ( $\geq 10,000$ / $\mu$ l of blood) (%)	$\chi^2$	df	p-value
<b>Age Groups</b>							
Neonates	29	28 (96.6)	1(3.4)	0 (0%)	13.596	2	0.01
Infants	96	82 (85.4)	6 (6.3)	8(8.3)			
>12months-5yrs	136	93 (68.4)	21 (15.4)	22 (16.2)			
<b>Gender</b>							
Male	152	123 (80.9)	18 (11.8)	11 (7.2)	7.722	1	0.03
Female	109	80 (73.4)	10 (9.2)	19 (17.4)			
<b>Birth Orders</b>							
1	107	88 (82.2)	14 (13.1)	5 (4.7)	0.072	4	0.014
2	73	56 (76.7)	4 (5.5)	13 (17.8)			
3	59	46 (78)	6 (10.1)	7 (11.9)			
4	14	9 (64.3)	3 (21.4)	2 (14.3)			
$\geq 5$	8	4 (50)	1 (12.5)	3 (37.5)			
<b>Blood Groups</b>							
A+	35	34 (85)	1 (2.5)	0 (0.0)	28.337	7	0.000
A-	5	5 (12.5)	0 (0.0)	0 (0.0)			
B+	51	50(92.5)	1 (1.9)	0 (0.0)			
B-	3	3 (5.6)	0 (0.0)	0 (0.0)			
AB+	14	10 (66.6)	4 (26.7)	0(0.0)			
AB-	1	1 (6.7)	0 (0.0)	0 (0.0)			
O+	135	101 (66.4)	15 (9.9)	19(12.5)			
O-	17	10 (6.6)	7 (4.4)	0 (0.00)			

Numbers in parentheses are percentages of variables with parasitaemia

The disparities can be attributed to seasonality, differences in sample sizes and climatic peculiarities of the country's different regions. An increase in rainfall, temperature and relative humidity of more than 60% is associated with an increased prevalence of malaria, as these factors also shorten the life

cycle of the parasite-carrying vector (female anopheles mosquito). [18] A little over half of the study subjects were males, a pattern that is similar to reports from Mangalore in Karnataka, India.[19] The present study reports a predominance of *P. falciparum* infection, comparable to the 100% *P. falciparum* infection

in Gambia [20] but remarkably higher than the 5.4%, 24.2% and 35.2% reported from different parts of India, respectively. [19, 21, 22]

All the children had their blood tested for malaria parasite compared to 25% tested in an earlier Nigerian report in 2018. [17] The prevalence of neonatal malaria in the current study was 60.4% (29/48); this is comparable to 43.7% in Port Harcourt, Nigeria [23] but higher than figures from Cameroon (17.5%), [24] Gambia (13.3%), [20] and Jos, Nigeria (5.3%). [25] Several studies have discussed the impact of seasonality and diagnostic method on reported prevalence rates. [18, 26, 27] The current study was carried out partly during dry and partially wet seasons, suggesting the endemicity of the infection, and the confirmation of positivity for the malaria parasite was also done by DNA PCR.

The clinical presentations of the children in the present study are not different from known patterns. [28-31] These presentations included refusal to feed/ anorexia, vomiting, diarrhoea, jaundice, respiratory distress, weakness, hepatosplenomegaly and excessive crying. Some children presented with complications (life-threatening manifestations) such as prostration, severe anaemia, multiple convulsions, hypoglycemia, oliguria, intravascular haemolysis, hyper-parasitaemia, metabolic acidosis and cerebral malaria. However, deaths occurred more from severe anaemia due to late presentation, with a case fatality rate of 14.7%, and this is followed by cerebral malaria, with a case fatality rate of 7.8%.

Generally, a high incidence of malaria parasitaemia was observed in infants and older children but not neonates, as most neonates (96.6%) had low parasite intensity. This is not surprising as young infants appear to be relatively protected from clinical malaria, and from the severe consequences of malaria infection, for the first three to six months of life because of the preponderance of foetal

haemoglobin (HbF) in their red blood cells, which are relatively resistant to penetration by the malaria parasite. [28, 29] Furthermore, maternal antibodies such as Immunoglobulin G (IgG) acquired by the foetus via the placenta *in utero*, [30] Secretory IgA and low levels of para-aminobenzoic acid (PABA) [30, 31] found in breastmilk are protective to the neonates. IgG levels are known to decrease variably during the first year of life subsequently. [31] Children are at the highest risk for severe disease and death between six months and five years of age when they would have lost maternal immunity and have not yet developed specific immunity to infection. [31]

Parasite intensity was surprisingly significantly higher among female children despite the previous knowledge that females are doubly endowed with protective genes from their chromosomes XX. [32] Nevertheless, many questions must be answered to assess how gender affects malaria data and outcomes. [33] Generally, children with birth order five and above had higher malaria parasite intensity than other birth orders. There is a link between malaria, poverty, birth orders and family size. When the family size increases above four persons, the incidence of malaria increases. [34] Therefore, it may not be unexpected that malaria incidence also increases with birth order. [35] High-intensity parasitemia was only observed in children with blood group O but completely absent in other blood groups; the possible explanation may be the absence of blood group antigens on the surface of O group red cells. Hence, they have more free receptors and higher chances of attachment to malaria parasites. [36, 37] Regarding outcomes, there was no mortality among the neonates, whereas 3.07% of the infants died, and mortality was 1.9% among the older children.

### *Limitations of the study*

This study was health facility-based and was conducted in a single centre. A multicentre study or community-based study could be more desirable.



## Conclusion

The prevalence of malaria in the current study was 52.2%; many children presented with complications, but there were more deaths among children who presented with severe anaemia. None of the neonates had high-intensity parasitaemia, whereas female children had higher malaria parasite intensity and high-intensity parasitemia was only observed in children belonging to blood group O. Although the overall mortality was 5.02%, malaria preventive strategies should be part of the discussions during interactions with mothers and caregivers in this study area.

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