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Original Research Article

Hyper-Reactive Malarial Splenomegaly among Febrile and Non-Febrile under Ten Children in some Selected Hospitals in South West, Nigeria

Opeyemi O. Adesina[1*], Eunice O. Ajiboye[1], Adebusola A. Shakunle[2], Oluwadamilola A. Sadare[3]

[1]Department of Medical Laboratory Science, Babcock University, Ilishan. Ogun State, Nigeria

[2]Department of Obstetrics and Gynaecology, College of Medicine, Lagos State University, Nigeria

[3]Department of Microbiology, Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria

***Corresponding Author's E-mail: adesinayemi37@gmail.com**

Abstract

Hyper-reactive malarial splenomegaly (HMS) is a significant complication of chronic malaria, particularly in endemic regions. This study aimed to assess the prevalence and associated clinical parameters of HMS among febrile and non-febrile children under ten years of age in selected hospitals in South West, Nigeria. A cross-sectional study was conducted from September to October 2020 in Ifako General Hospital, Lagos State, and State Hospital Ota, Ogun State. A total of 130 children under ten years of age were recruited, with informed consent obtained from their parents. Venous blood samples were collected and analyzed for anti-malarial antibodies using Enzyme-linked Immunosorbent Assay (ELISA), malaria parasite detection via Rapid Diagnostic Test (RDT) and blood film examination, and complete blood count (CBC) using an auto-analyzer. A total of one hundred and thirty (130) questionnaires were administered to respondents and they were all retrieved. Out of the 130 questionnaires administered, only 88 were valid. This was due to irregular, incomplete and inappropriate responses to some questionnaires. Out of these, 9.1% were diagnosed with HMS. The study found significant associations between HMS and abnormal packed cell volume (PCV) (p = 0.023), white blood cell count (WBC) (p = 0.000), and body temperature (p = 0.009). The majority of children with HMS had abnormal WBC counts (87.5%) and low PCV levels (100%). Malaria parasites were detected in 90.9% of the participants, with the prevalence being higher among children with HMS. The study also observed no significant association between HMS and platelet count or lymphocyte levels. The study highlights a notable prevalence of HMS among children in South West Nigeria, with significant associations between HMS and certain hematological parameters. These findings underscore the need for enhanced malaria control efforts and early diagnosis to prevent HMS and related complications.

Keywords: Febrile children, Hematological parameters, Hyper-reactive malarial splenomegaly, Malaria diagnosis, Pediatric malaria, South West Nigeria

INTRODUCTION

Malaria remains a significant public health challenge in Nigeria, particularly among children under the age of ten. Nigeria, which bears the highest burden of malaria globally, accounts for approximately 27% of the world's malaria cases and 24% of malaria-related deaths (WHO, 2023). Malaria is caused by the Plasmodium parasite,

with Plasmodium falciparum being the most prevalent and lethal species in sub-Saharan Africa (Ekeleme et al., 2023). The transmission is primarily through the bite of an infected female Anopheles mosquito, leading to symptoms such as fever, chills, and anemia. In regions of high transmission like Nigeria, repeated exposure to the parasite can result in various complications, including Hyper-Reactive Malarial Splenomegaly (HMS).

Hyper-Reactive Malarial Splenomegaly, formerly known as tropical splenomegaly syndrome, is a severe and chronic complication of malaria. It is characterized by an abnormal enlargement of the spleen due to an exaggerated immune response to recurrent malaria infections. This condition is more prevalent in areas with high malaria transmission, such as sub-Saharan Africa (Anumudu et al., 2021). HMS results from an excessive immunological reaction to Plasmodium antigens, leading to hyperplasia of the reticuloendothelial system and splenomegaly. Clinically, HMS presents with massive splenomegaly, anemia, and an elevated level of serum immunoglobulins, particularly Immunoglobulin M (IgM). The condition poses a significant health risk, especially for children under ten, who are more vulnerable to severe malaria outcomes due to their developing immune systems.

HMS is predominantly seen in malaria-endemic regions, where continuous exposure to malaria antigens triggers the hyper-reactive immune response that leads to splenomegaly. In Nigeria, particularly in the southwest region, malaria transmission is perennial, contributing to the high incidence of HMS (Okafor et al., 2022). The risk factors for HMS include genetic predisposition, the intensity of malaria transmission, age, and immune status. Children under ten are at a higher risk due to their less mature immune systems and the frequent occurrence of malaria episodes, which may lead to a hyper-reactive immune state. Additionally, socio-economic factors such as poverty, limited access to healthcare, and inadequate malaria control measures exacerbate the risk and severity of HMS in this population.

HMS is often underdiagnosed due to its overlapping symptoms with other causes of splenomegaly and the nonspecific nature of its clinical manifestations. Children with HMS typically present with massive splenomegaly, which is often accompanied by symptoms such as fever, weight loss, and pallor. However, the condition can also be asymptomatic, particularly in non-febrile children, making it challenging to identify without proper diagnostic tools. The diagnosis of HMS relies on a combination of clinical findings, laboratory tests showing high levels of IgM, and exclusion of other causes of splenomegaly (Ojo et al., 2023).

Southwest Nigeria, comprising states like Lagos, Ogun, Oyo, Osun, Ondo, and Ekiti, is a region with a high malaria transmission rate. The climate, characterized by a long rainy season, creates an ideal environment for mosquito breeding, thus sustaining the endemicity of malaria (Akinbo et al., 2023). Healthcare facilities in this region, particularly in rural and semi-urban areas, often face challenges such as limited diagnostic capacities and inadequate treatment facilities, which complicate the management of malaria and its complications like HMS. The focus of this study is to assess the prevalence and characteristics of HMS among febrile and non-febrile children under ten years in selected hospitals within this region, aiming to provide insights into the epidemiology, diagnosis, and management of this condition.

MATERIALS AND METHODS

Research Design

This was a cross-sectional study that assessed hyper-reactive malarial splenomegaly among febrile and non-febrile children under the age of ten in some selected hospitals in South West, Nigeria. The study was conducted between September and October, 2020.

Study Area

The study was conducted in some selected hospitals in South West, Nigeria. The selected hospitals used were Ifako General Hospital, Iju Road, Ifako Agege, Lagos State, Nigeria. Ifako General Hospital is located at latitude 6.6434^{o}N and longitude 3.3257^{o}E.State Hospital Ota, Ogun State, Nigeria. State Hospital Ota is located at latitude 6.6818^{o}N and longitude 3.2102^{o}E.

Study Subjects and Population

Children under the age of ten (study subjects) in some selected hospitals in South West, Nigeria (study population), willing to participate in the study without any inducement were recruited after informed consents had been obtained from their parents and the child had read and signed the child assent form.

Sample Size Determination

The sample size will be determined using the Cochran formula for estimating proportions in a population outlined by Airaodion et al. (2023):

$$n = \frac{Z^2(Pq)}{e^2}$$

where n = minimum sample size
Z = 1.96 at 95% confidence level,
P = known hyper-reactive malarial splenomegaly
e = error margin tolerated at 5% = 0.05
q = 1 - p

According to Alkadarou *et al*., (2013), the existing prevalence of hyper-reactive malarial splenomegaly is 9.3%.

P = 9.3% = 0.093

q = 1 – p

= 1 – 0.093

= 0.907

$$n = \frac{(1.96)^2(0.093 \times 0.907)}{(0.05)^2}$$

$$n = \frac{3.8416 \times (0.084351)}{0.0025}$$

$$n = \frac{0.32404}{0.0025} = 129.62$$

A total number of 130 participants were selected from consenting children under the age of ten in some selected hospitals in South West, Nigeria.

Eligibility of Subjects

Inclusion Criteria

1. Febrile children.
2. Children under the age of ten
3. Non-febrile children
4. Children with splenomegaly

Exclusion Criteria

1. Subjects above age 10
2. Subjects below age 1
3. Subjects who are unwilling to provide consent for collection of data

Sample Collection

Five milliliters (5ml) of venous blood were obtained from each subject by a trained phlebotomist via vein puncture and transferred into a plain bottle and a EDTAk_2 bottle and the container were inverted to mix the anticoagulant with the blood.The samples were collected in an EDTAk_2 bottle to prevent clotting of the blood samples and also into a plain bottle to obtain the serum (Ezirim et al., 2024)after which they were transported to the laboratory with the aid of an ice pack for processing.

Laboratory Analysis

Determination of Anti-Malarial Antibodies

The presence of anti-malarial antibodies using Enzyme-linked Immunosorbent Assay (ELISA). The samples were diluted 1+100 with the sample diluent by dispensing 10ul of the sample and 1ml of sample diluent into tubes and they were all mixed.100ul of standards/controls and diluted samples were dispensed into their respective wells. Well A1 was left for the substrate blank. The wells were covered with the foil supplied in the kit.It was then incubated for 1 hour at 37^{o}C.After incubation, the foil was removed and the content of the wells was washed in a microplate washer with washing buffer five times. 100ul of conjugate was dispensed into all the wells except for the substrate blank well A1. The wells were covered with the foil supplied in the kit.It was then incubated for 30 minutes at room temperature. After incubation, the foil was removed and the content of the wells was washed in a microplate washer with washing buffer five times.100ul of TMB substrate solution was dispensed into all the wells.It was then incubated for 15 minutes at room temperature in the dark.100ul of stop solution was dispensed into all the wells and a colour change from blue to yellow was observed. The absorbance was read with an ELISA microwell plate reader at 450nm.

Determination of Malarial Parasite in Subjects

Presence of malaria parasite in the subjects was determined using a rapid diagnostic test kit and examination of blood film.

Rapid Diagnostic Test Kit (RDT) for Malaria

The cassette was labelled with the patient's serial number. A disposable inverted cup provided was used to transfer the blood sample from the EDTAk_2 bottle into the square hole marked "A" and the inverted cup was discarded in a sharp box. Buffer was added to the round hole marked "B". The procedure was timed for 15 minutes after adding the buffer. The result was then recorded. The cassette was discarded in the non-sharps waste container.

Examination of Blood Film

A thick blood film was made on a clean glass slide. The slide was placed in a staining rack and the blood film was allowed to air dry. Giemsa stain diluted 1:10 was used to stain the blood film for 25 minutes. The stain was washed off using clean water. The back of the slide was then wiped clean and placed in a draining rack for it to air dry. A drop of immersion oil was placed on the stained slide which was then viewed under the microscope using x100 objective lens (oil immersion lens).The number of parasites per microliter of blood was then calculated as:

$$\text{Number of parasites per microliter of blood} = \frac{\text{Number of parasites counted}}{\text{Number of WBC counted}} \; x \; \text{Total white cell count}$$

Determination of Complete Blood Count (CBC)

Principle of automation (BC-3200 auto analyser)**:** Blood

cells are diluted in a buffered electrolyte solution after which a calculated volume of the blood sample is aspirated through an aperture tube between two electrodes. There is interruption of the flowing current by the blood cells after which a pulse is produced due to the alteration of the electrical charge. The amplitude of each pulse is proportional to the volume of the cell which caused the interruption of the current. The presence of a threshold circuit then ensures that only those pulses that are greater than the pre-set threshold are counted. The total cell count for each is determined by the total number of pulses counted or obtained in a given blood volume. Hence the cells are counted based on measurable variations in electrical impedance that is produced by non-conductive particles in an electrolyte solution.The tests were done by following the manufacturer's instructions of the operation manual of the automatic analyser.

Disposal of Used Materials

Sharp objects used in blood collection were disposed using sharp containers, all blood samples were treated as potentially infectious samples and all other materials used were disinfected while others were disposed appropriately.

Data Analysis

Collected data were entered into Microsoft Excel. Statistical analysis was then carried out using SPSS (Statistical Package for Social Sciences) software package (version 27.0) and p value ≤ 0.05 was considered statistically significant. Statistical analysis outputs will be presented using tables and graphs.

Ethical Consideration

Ethical clearance was obtained from Babcock University Health Research Ethics Committee (BUHREC) and Lagos State Health Service Commission (LSHSC) before the commencement of the study. Informed consent was obtained from the parent(s) of the participants and child assent form was given to the child before beginning the study. The aim, purpose, objective, nature, benefits of the study was properly explained to each of the parent(s) of the subjects and the subjects. They were assured of confidentiality of the information obtained and their voluntariness to participate in the research. They were also informed of their option to withdraw from the study at any time. The participants were requested to complete a child assent form which were properly endorsed by a signature indicating that they were willing to partake without any form of pressure. The investigation was carried out at no cost to the participants.

RESULTS

A total of one hundred and thirty (130) questionnaires were administered to respondents and they were all retrieved. Out of these, eighty-eight (88) questionnaires were valid. This was due to irregular, incomplete and inappropriate responses to some questionnaires. These 88 questionnaires were cleansed for analysis. Out of these, 56.8% were males and 43.2% were females. The religious distribution was evenly split between Christianity and Islam, each representing 50% of the respondents. Most participants were of Yoruba ethnicity (72.7%), with smaller representations from the Igbo (18.2%) and Hausa (9.1%) tribes. In terms of education, a majority had completed primary education (72.7%), while 11.4% had no formal education. The genotype distribution showed a high prevalence of the SC genotype (59.1%), while the least common was AC at 1.1% (Table 1).

All respondents (100%) had no prior knowledge of splenomegaly. A high percentage (96.6%) had experienced malaria before, and a similar proportion had taken anti-malarial drugs, with 55.7% of these being prescribed by a physician. However, 58% of the respondents did not take any measures to protect themselves from mosquitoes. Only 10.2% had experienced abdominal swelling, and splenomegaly was detected in 10.2% of the respondents (Table 2).

Regarding clinical parameters, 65.9% of respondents had normal neutrophil counts, while 67% had abnormal platelet (PLT) counts. The packed cell volume (PCV) was abnormal in 62.5% of respondents, and the lymphocyte count (LYM) was abnormal in 98.9% of them. Malaria parasites were present in the blood films of 90.9% of respondents. Body temperature was abnormal in 42% of the respondents (Table 3).

A significant association was found between PCV levels and sex, with a higher proportion of females (55.3%) having normal PCV compared to males (24.0%) ($\chi^2 = 9.000$, $p = 0.004$). A notable difference was also observed in the presence of malaria parasites, with 100% of females having parasites compared to 84.0% of males ($\chi^2 = 6.69$, $p = 0.009$) (Table 4).

No significant associations were found between clinical parameters and religion. Both Christian and Muslim respondents had similar proportions of normal and abnormal values across all clinical parameters, including PCV, WBC, and LYM. The presence of malaria parasites was identical between both religious groups, with 90.9% testing positive (Table 5).

A significant association was observed between PLT levels and tribe, with the Yoruba tribe having the highest proportion of abnormal PLT levels (76.6%), followed by Igbo (43.8%) and Hausa (37.5%) ($\chi^2 = 9.71$, $p = 0.008$)

Table 1. Demographic Characteristics of the Respondents

Characteristics	Frequency (n = 88)	Percentage (%)
Sex		
Female	38	43.2
Male	50	56.8
Religion		
Christianity	44	50.0
Islam	44	50.0
Tribe		
Yoruba	64	72.7
Igbo	16	18.2
Hausa	8	9.1
Educational level		
No formal education	10	11.4
Primary	64	72.7
Secondary	14	15.9
Genotype		
AA	10	11.4
AS	14	15.9
AC	1	1.1
SS	11	12.5
SC	52	59.1

Table 2. Distribution of Respondents Experience in Relation to Splenomegaly

Experience	Frequency (n = 88)	Percentage (%)
Heard of splenomegaly before:		
Yes	0	0.0
No	88	100.0
Had malaria before		
Yes	85	96.6
No	3	3.4
Protect self against mosquito		
Yes	37	42.0
No	51	58.0
Taken anti-malarial drugs before		
Yes	85	96.6
No	3	3.4
Prescribed by a physician:		
Yes	49	55.7
No	36	40.9
Anti-malaria drug taken		
Sep-Oct	20	22.7
May-Aug	66	75.0
Normally have abdominal pain		
Yes	14	15.9
No	74	84.1
Abdominal pain		
Always	4	30.8
Often	4	30.8
Sometimes	5	38.5
Side of abdomen normally feel pain		
Left	9	69.2
Right	4	30.8

Table 2. Continue

Had abdominal swelling before		
Yes	9	10.2
No	79	89.8
Splenomegaly		
Present	9	10.2
Absent	79	89.8

Table 3. Distribution of Clinical Parameters

Parameters	Frequency (n = 88)	Percentage (%)
Neutrophil (x10^9/l)		
Normal	58	65.9
Abnormal	30	34.1
MXD (x10^9/l)		
Normal	88	100.0
Abnormal	0	0.0
PLT (x10^9/l)		
Normal	29	33.0
Abnormal	59	67.0
PCV (%)		
Normal	33	37.5
Abnormal	55	62.5
WBC (x10^9/l)		
Normal	67	76.1
Abnormal	21	23.9
LYM (x10^9/l)		
Normal	1	1.1
Abnormal	87	98.9
Blood film (parasites/ul of blood)		
Present	80	90.9
Absent	8	9.1
Temperature (^{o}C)		
Normal	51	58.0
Abnormal	37	42.0

Table 4. Association Between Clinical Parameters and Sex

Parameters	Frequency (%) Sex		Chi-square	P-value
	Female	Male		
PCV (%)				
Normal	21(55.3)	12(24.0)	9.000	0.004*
WBC(x10^9/L)				
Normal	28(73.7)	39(78.0)	0.221	0.801
LYM(x10^9/L)				
Normal	1(2.6)	0(0.0)	1.33	0.432
Abnormal	37(97.4)	50(100.0)		
BLOOD FILM (parasites/ul of blood)				
ABSENT	0(0.0)	8(16.0)	6.69	0.009*
PRESENT	38(100.0)	42(84.0)		
NEUT(x10^9/L)				
Normal	24(63.2)	34(68.0)	0.225	0.656
Abnormal	14(36.8)	16(32.0)		
PLT(x10^9/L)				
Normal	12(31.6)	17(34.0)	0.057	1.000
Abnormal	26(68.4)	33(66.0)		
MXD(x10^9/L)				
Normal	38(100.0)	50(100.0)		

P<0.05 are statistically significant

Table 5. Association Between Clinical Parameters and Religion

Parameters	Frequency (%) Religion		Chi-square	P-value
	Christianity	Islam		
PCV(%)				
Normal	14(31.8)	19(43.2)	1.21	0.379
Abnormal	30(68.2)	25(56.8)		
WBC(x10^9/L)				
Normal	32(72.7)	35(79.5)	0.56	0.618
Abnormal	12(27.3)	9(20.5)		
LYM(x10^9/L)				
Normal	1(2.3)	0(0.0)	1.01	1.000
Abnormal	43(97.7)	44(100.0)		
BLOOD FILM(parasites/ul of blood)				
ABSENT	4(9.1)	4(9.1)	0.00	1.000
PRESENT	40(90.9)	40(90.9)		
NEUT(x10^9/L)				
Normal	30(68.2)	28(63.6)	0.20	0.822
Abnormal	14(31.8)	16(36.4)		
PLT(x10^9/L)				
Normal	15(34.1)	14(31.8)	0.05	1.01
Abnormal	29(65.9)	30(68.2)		
MXD(x10^9/L)				
Normal	44(100.0)	44(100.0)		

P<0.05 are statistically significant

Table 6. Association Between Clinical Parameters and Tribe

Parameters	Frequency (%) Tribe			Chi-square	P-value
	Yoruba	Igbo	Hausa		
PCV(%)					
Normal	24(37.5)	6(37.5)	3(37.5)	0.00	1.00
Abnormal	40(62.5)	10(62.5)	5(62.5)		
NEUT(x10^9/L)					
Normal	39(60.9)	11(68.8)	8(100.0)	4.90	0.086
Abnormal	25(39.1)	5(31.3)	0(0.0)		
PLT(x10^9/L)					
Normal	15(23.4)	9(56.3)	5(62.5)	9.71	0.008
Abnormal	49(76.6)	7(43.8)	3(37.5)		
MXD(x10^9/L)					
Normal	64(100.0)	16(100.0)	8(100.0)		

P<0.05 are statistically significant

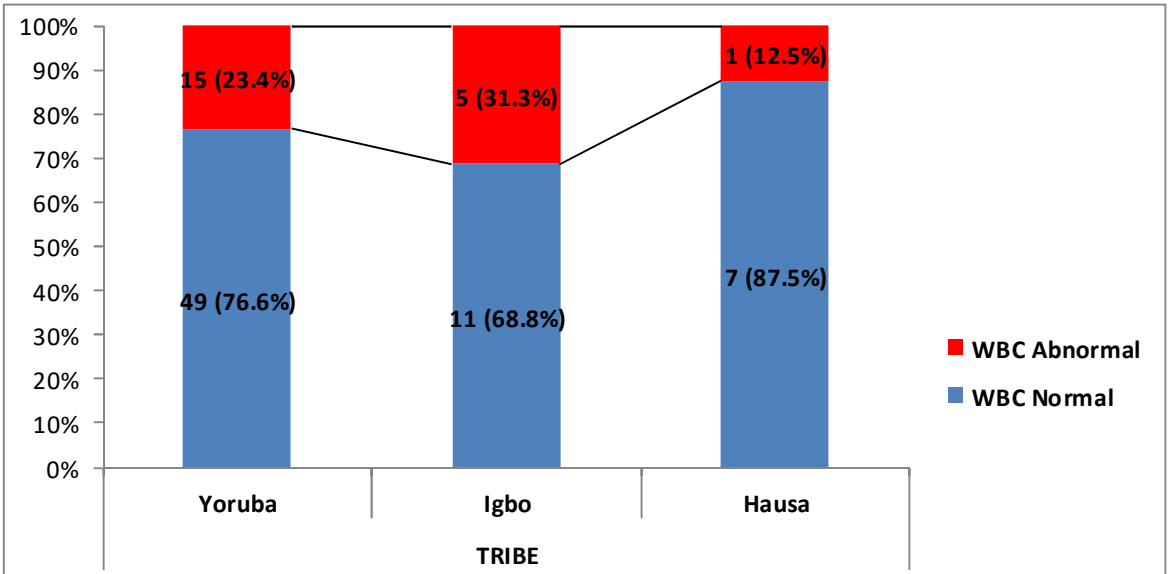

Figure 1. Association of WBC and Tribe

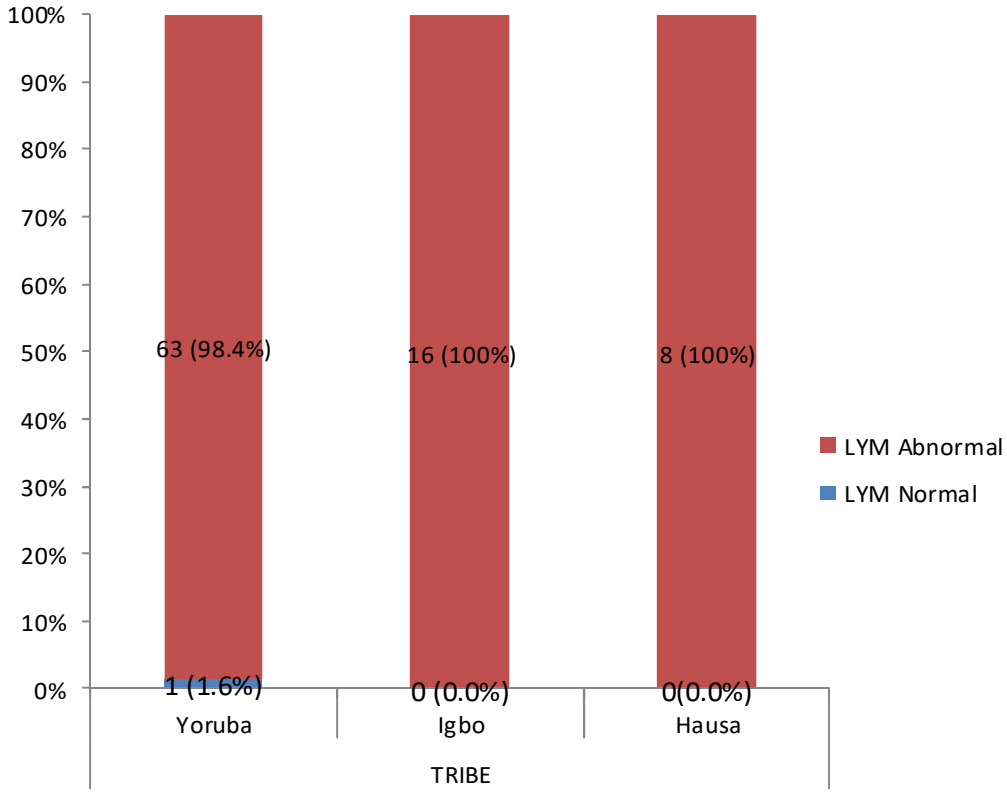

Figure 2: Association of LYM and Tribe

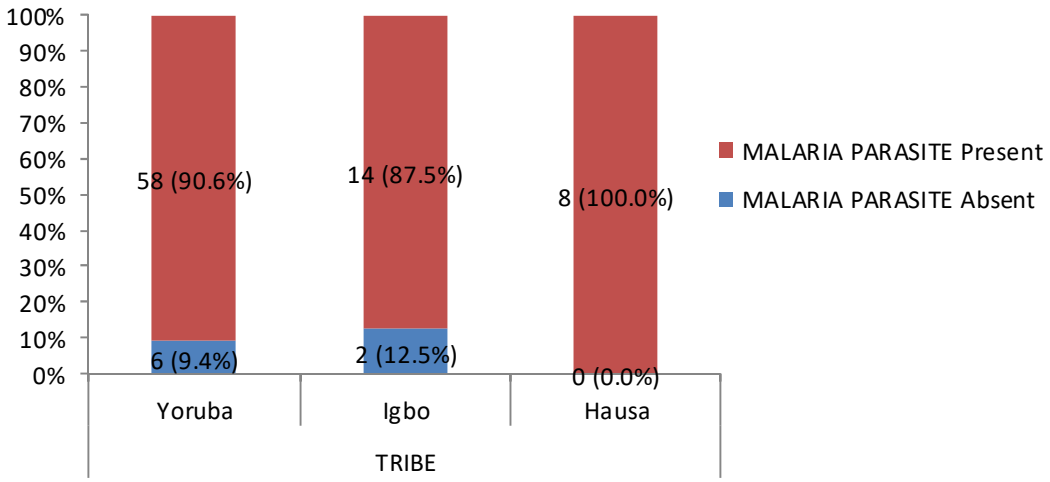

Figure 3: Association of Malaria Parasite presence and Tribe

Table 7. Association Between Parameters and Educational Level

Parameters	Frequency (%) Education		Chi-square	P-value
	No formal education	Educated		
PCV(%)				
Normal	26(40.6)	7(29.2)	0.978	0.459
Abnormal	38(59.4)	17(70.8)		
WBC(x10^9/L)				
Normal	47(73.4)	20(83.3)	0.94	0.409
Abnormal	17(26.6)	4(16.7)		
LYM(x10^9/L)				
Normal	0(0.0)	1(4.2)	2.70	0.273
Abnormal	64(100.0)	23(95.8)		
BLOOD FILM(parasites/ul of blood)				
ABSENT	6(9.4)	2(8.3)	0.023	1.000
PRESENT	58(90.6)	22(91.7)		
NEUT(x10^9/L)				
Normal	37(57.8)	21(87.5)	6.85	0.011*
Abnormal	27(42.2)	3(12.5)		
PLT(x10^9/L)				
Normal	20(31.3)	9(37.5)	0.31	0.616
Abnormal	44(68.8)	15(62.5)		
MXD(x10^9/L)				
Normal	64(100)	24(100)		

P<0.05 are statistically significant

Table 8. Association Between Parameters and Hyper-Reactive Malarial Splenomegaly (HMS)

Parameters	Frequency (%) HMS		Chi-square	P-value
	Yes	No		
PCV(%)				
Normal	0(0.0)	33(41.3)	5.28	0.023*
Abnormal	8(100.0)	47(58.8)		
WBC(x10^9/L)				
Normal	1(12.5)	66(82.5)	19.61	0.000*
Abnormal	7(87.5)	14(17.5)		
LYM(x10^9/L)				
Normal	0(0.0)	1(1.3)	0.10	1.000
Abnormal	8(100.0)	79(98.8)		
NEUT(x10^9/L)				
Normal	3(37.5)	55(68.8)	3.16	0.115
Abnormal	5(62.5)	25(31.3)		
PLT(x10^9/L)				
Normal	4(50.0)	25(31.3)	1.16	0.431
Abnormal	4(50.0)	55(68.8)		
TEMP(^{o}C)				
Normal	1(12.5)	50(62.5)	7.46	0.009*
Abnormal	7(87.5)	30(37.5)		
MXD(x10^9/L)				
Normal	8(100.0)	80(100.0)		

P<0.05 are statistically significant

Table 9. Distribution of Results of Elisa, RDT and Blood Film

Instrument	Frequency	Percentage (%)
ELISA(U)	88	100.0
Positive		
RDT		
Negative	88	100.0
BLOOD FILM(parasites/ul of blood)		
0(no count)	8	9.1
≤1000 parasites/µl of blood	71	80.7
>1000 parasites/µl of blood	9	10.2
HMS		
Yes	8	9.1
No	80	90.9

(Table 6). The Yoruba tribe had the highest percentage of respondents with normal WBC (76.6%) (Figure 1), while all Hausa respondents had abnormal LYM levels (100%) (Figure 2). Malaria parasites were present in all Hausa respondents (100%) and slightly lower in Igbo (87.5%) and Yoruba (90.6%) (Figure 3).

A significant association was found between neutrophil counts and educational level, with a higher percentage of respondents with no formal education having abnormal neutrophil counts (42.2%) compared to educated respondents (12.5%) ($\chi^2 = 6.85$, $p = 0.011$). However, no significant associations were observed for other parameters such as PCV, WBC, and LYM (Table 7).

A significant association was found between HMS and various clinical parameters. All respondents with HMS had abnormal PCV ($\chi^2 = 5.28$, $p = 0.023$), and a significant proportion had abnormal WBC (87.5%) ($\chi^2 = 19.61$, $p = 0.000$). Additionally, 87.5% of those with HMS had abnormal body temperatures ($\chi^2 = 7.46$, $p = 0.009$) (Table 8).

All respondents tested positive for malaria using ELISA, while RDT results were negative for all. Blood films showed a majority (80.7%) with ≤1000 parasites/µl of blood, with a smaller proportion (10.2%) having >1000 parasites/µl. Hyper-reactive malarial splenomegaly was present in 9.1% of the respondents (Table 9).

DISCUSSION

Hyper-reactive malarial splenomegaly (HMS) is a severe and chronic condition that manifests primarily in regions where malaria is endemic. It is characterized by an abnormal immune response to repeated malarial infections, leading to an enlarged spleen (splenomegaly) and potentially severe complications. Children under ten are particularly vulnerable due to their underdeveloped immune systems and frequent exposure to malaria in endemic regions, such as Southwest Nigeria. The present study aimed to examine the prevalence and demographic characteristics associated with HMS among febrile and non-febrile children under ten years old in selected hospitals in Southwest Nigeria.

The study's demographic data reveal a relatively balanced gender distribution among the respondents, with 56.8% male and 43.2% female. This distribution aligns with similar studies in malaria-endemic regions, where no significant gender predisposition to HMS has been reported (Bello et al., 2020). The religious and ethnic diversity observed, with an equal distribution between Christianity and Islam (50.0% each) and a majority of Yoruba participants (72.7%), is reflective of the broader demographic composition of Southwest Nigeria (National Population Commission, 2022). The educational background of respondents shows that a significant majority (72.7%) had attained primary education, indicating a basic level of health literacy, which could influence their understanding and management of malaria (Oladimeji et al., 2019).

The genotype distribution, with a predominance of SC genotype (59.1%) and a notable proportion of SS genotype (12.5%), is particularly concerning given the known vulnerability of individuals with hemoglobinopathies to malaria complications, including HMS (Molina et al., 2021). This finding highlights the need for targeted interventions and monitoring in this subgroup to prevent severe outcomes.

A critical finding in this study is that none of the respondents had prior knowledge of splenomegaly, despite 96.6% having experienced malaria. This lack of awareness may contribute to delays in seeking appropriate medical care, potentially exacerbating the severity of HMS (Njuguna et al., 2019). The high prevalence of malaria history among respondents aligns with previous research that underscores the endemic nature of malaria in Southwest Nigeria (Aina et al., 2018). Moreover, the fact that a majority (58.0%) did not take proactive measures to protect themselves against mosquitoes suggests a gap in public health education and prevention strategies.

The study shows that a substantial majority of the children (96.6%) had taken anti-malarial drugs, with 55.7% of these being prescribed by a physician. This is consistent with the widespread use of anti-malarial medication in endemic areas, yet it raises concerns about the 40.9% who did not have their drugs prescribed by a physician. The lack of medical supervision in the administration of anti-malarial drugs can contribute to suboptimal treatment outcomes and the development of drug resistance, which may indirectly increase the risk of HMS (Dondorp et al., 2020).

Interestingly, the timing of anti-malarial drug administration, with 75.0% occurring between May and August, coincides with the peak malaria transmission season in Nigeria (WHO, 2022). This suggests that seasonal trends in malaria transmission significantly influence the healthcare-seeking behavior of parents and caregivers.

A minority of respondents (15.9%) reported experiencing abdominal pain, with varying frequencies. Of those who experienced abdominal pain, a significant proportion (69.2%) localized the pain to the left side of the abdomen, which is typically associated with splenic enlargement (splenomegaly). The presence of abdominal swelling was reported by 10.2% of the respondents, all of whom were found to have splenomegaly upon examination.

The overall prevalence of splenomegaly in the study population was 10.2%, which is within the range reported in similar studies from malaria-endemic regions, where splenomegaly prevalence among children can vary from 5% to 20% depending on the population and diagnostic criteria used (Kabaghe et al., 2017). This finding underscores the need for routine screening for splenomegaly in children with recurrent malaria, particularly in high-risk groups such as those with hemoglobinopathies.

The results of this study are consistent with previous research in several key areas. For example, the lack of awareness about splenomegaly among respondents mirrors findings from a study conducted in Kenya, where community awareness about the complications of malaria, including HMS, was found to be low (Njuguna et al., 2019). Similarly, the high prevalence of malaria history among children and the seasonal pattern of anti-malarial drug use align with the findings from a study in Ghana, which reported similar trends in malaria incidence and treatment (Owusu-Agyei et al., 2020).

However, the study's findings on genotype distribution and its potential link to HMS are particularly noteworthy and may require further investigation. Previous studies have primarily focused on the relationship between malaria and sickle cell trait (HbAS), with limited research on the SC genotype and its implications for HMS (Molina et al., 2021). The current study's findings suggest that children with the SC genotype may be at a heightened risk for HMS, which warrants further research to explore this relationship in greater detail.

The distribution of clinical parameters (Table 3) highlights several notable findings. A significant proportion of the children had abnormal PLT (67.0%), abnormal PCV (62.5%), and the presence of malaria

parasites (90.9%). These findings align with the typical hematological abnormalities observed in malaria, particularly in children with severe forms of the disease, including HMS. For instance, the study by Ibrahim et al. (2022) observed similar trends in hematological parameters among children with severe malaria in Nigeria, where thrombocytopenia and anemia were prevalent among those with enlarged spleens.

Furthermore, the study identifies that children with HMS had a 100% abnormal PCV, compared to 58.8% among those without HMS (Table 8). This significant association ($p = 0.023$) suggests that anemia is more pronounced in children with HMS, likely due to the chronic hemolysis associated with repeated malaria infections, as supported by findings from Snow et al. (2019), who also reported a strong link between severe anemia and splenomegaly in malaria-endemic regions.

The associations between clinical parameters and demographic factors such as sex, religion, tribe, and educational level were analyzed (Tables 4–7). The data reveal some significant associations, particularly with PCV and sex ($p = 0.004$), where female children were more likely to have normal PCV compared to males. This finding contrasts with the general expectation, as previous studies, such as that by Onwuameze et al. (2020), did not find significant sex differences in hematological parameters among children with malaria. The reasons for this disparity in the present study could be due to differences in sample size, population demographics, or healthcare access between the genders.

The analysis of tribe-related differences (Table 6) showed that children from the Hausa tribe were more likely to have normal neutrophil counts compared to their Yoruba and Igbo counterparts, though this was not statistically significant ($p = 0.086$). Additionally, there was a significant association between tribe and PLT ($p = 0.008$), with the Hausa tribe showing a higher proportion of normal PLT levels. These findings align with observations by Adedoyin et al. (2021), who noted that genetic factors related to ethnicity might influence hematological responses to malaria, potentially affecting the clinical manifestations of HMS.

The diagnostic tools used in this study—ELISA, Rapid Diagnostic Test (RDT), and blood film microscopy—showed a 100% positive rate for malaria by ELISA and a similar rate of parasite detection in blood films for children with HMS (Table 9). This highlights the reliability of ELISA in diagnosing malaria in children with HMS, consistent with the findings of Achidi et al. (2022), who emphasized the superior sensitivity of ELISA over RDTs in detecting malaria in cases with splenomegaly.

Interestingly, while 100% of the children with HMS had a positive ELISA result, the majority also had abnormal WBC counts (87.5%), a significant contrast to children without HMS, where only 17.5% had abnormal WBC counts ($p = 0.000$). This suggests a profound immune dysregulation in children with HMS, which might be due to chronic malaria exposure leading to sustained splenic activation, as discussed by Olumese et al. (2019).

The findings of this study both corroborate and differ from previous research on HMS and its associated hematological parameters. The high prevalence of splenomegaly and anemia among the studied population aligns with earlier works, such as the study by Sowunmi et al. (2018), which documented a high burden of anemia in children with malaria-induced splenomegaly. However, the association between tribe and platelet count observed in this study presents a novel insight not extensively covered in previous literature.

Moreover, the use of multiple diagnostic tools, with ELISA showing a 100% detection rate, contrasts with the findings by Mbanefo et al. (2021), who reported lower sensitivity in RDTs in children with HMS. The present study's emphasis on ELISA's reliability suggests a potential shift in diagnostic approaches in endemic regions, favoring more sensitive tests like ELISA over conventional RDTs.

CONCLUSION

The findings of this study indicate a notable prevalence of HMS with significant associations observed between HMS and various clinical parameters such as abnormal PCV, WBC, and body temperature. Additionally, the study highlights that despite widespread exposure to malaria, a substantial percentage of children presented with abnormal clinical profiles, including elevated levels of lymphocytes and neutrophils, suggesting ongoing immune responses to malaria infection. The research underscores the need for enhanced malaria diagnostic and management strategies, especially in paediatric populations, to reduce the incidence of HMS and associated complications. The associations identified between HMS and key demographic factors, such as sex, religion, and tribe, provide valuable insights that can inform targeted public health interventions. Overall, this study contributes to the growing body of knowledge on the clinical manifestations of malaria in endemic regions and the importance of early detection and management of HMS to improve health outcomes for children in Nigeria.

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