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Factors associated with ocular features in children with Malaria in the University of Benin teaching hospital, Benin City. A cross-sectional study.

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ABSTRACT

Background:
The study aims to assess the factors associated with ocular features in children with Malaria in the University of Benin teaching hospital.

Methods:
A case control study at the UBTH in which Data were analysed using the Statistical Software Package SPSS, version 21. Quantitative variables were summarised using descriptive statistics. The relationship between ocular features and the identified factors was presented as bivariate frequency tables and charts where applicable.

Results:
The ages of the subjects ranged from 11months to 16 years for cases and 3 years to 17 years for controls. The mean age for the cases and control were4.08±3.85and 4.04±2.49, respectively.
The prevalence of any ocular features of malaria was seen to be higher in males (25%) than in females (21.1%) in this study, although the difference was not statistically significant (p= 0.490). The highest prevalence of ocular features of severe malaria was seen in children in the < 5-year age group (26.8%). Prevalence of ocular features of malaria (any retinopathy) was higher in children who had convulsed (54.8%) than in those who did not (45.2%). Retinopathy is significantly associated with high malaria parasite density (p=0.002). Prevalence of retinopathy in patients with 3 plus (+++) *Plasmodium falciparum* malaria parasite was higher than in children with 2 plus (++). There was a statistically significant increase in the prevalence of ocular features of malaria with a decrease in the social class of subjects and vice versa (p=0.000).

Conclusion:
The ocular features of malaria are more frequently found in patients with more severe malaria infestation. Ocular features of malaria were higher in the children who had convulsed.

Recommendations:
The Ophthalmologist should be consulted in the co-management of children with malaria complications. This will aid diagnosis and institution of appropriate treatment modalities.

Keywords: *Ophthalmologist, Factors, ocular features, Children with Malaria, University of Benin teaching hospital.*
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Background
Malaria, when severe, can affect all organs of the body, including the eyes. Doctors, irrespective of whatever speciality, are faced with the challenging diagnosis and treatment of malaria, especially in under- fives. The ophthalmologist is often invited to evaluate the ocular status

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of a patient during or after an attack of malaria. Chuka Okosa[1] highlighted the ocular complications of malaria and antimalarial treatment in a review of several literature and internet searches in December 2006 in UNTH, Enugu, and reported that blindness or visual impairment could arise from malaria infection. Therefore, she recommended that frequent evaluation of the eyes in patients with severe malaria be carried out in the course of management of the disease. In a study by Biswas *et al.*, [2] presented at the International Uveitis Symposium, Montreal, Canada, in May 1995, anterior segment findings of ocular lesions of malaria were reported to include bilateral anterior uveitis, secondary glaucoma, subconjunctival and episcleral haemorrhage. Posterior segment findings that were reported include retinal haemorrhage, retinal whitening, perimacular whitening and opacifications, papilloedema, exudates, and cotton wool spots.[2] Biswas[2] suggested that patients with unexplained blotchy retinal haemorrhages should be investigated for malaria infection, especially if they reside or have travelled to endemic areas. The most common ocular manifestation seen in severe malaria is malaria retinopathy, which consists of a set of retinal abnormalities that is unique to children with malaria, especially cerebral malaria.[3] The presence of retinal haemorrhage and retinal whitening as a result of retinal ischaemia in malaria infection has been predicted to be pathognomic of severe malaria. A description of the full constellation of retinal findings was first published in 1993 when a group of 56 children from Malawi who had cerebral malaria were studied, and findings were shown to have prognostic significance.[3] Lewallen *et al*[3] reported that the presence of malaria retinopathy in severe malaria suggested a very high risk of death and prolonged length of coma in malaria patients. Although the pathophysiologic connection is yet unknown, the retina and central nervous system share the same embryonic origin, have similar cellular structure and blood tissue barrier; therefore, the retinal signs seen in malaria retinopathy correlate significantly with the coma and death in children with cerebral malaria.[4] The study aims to assess the factors associated with ocular features in children with Malaria in the University of Benin teaching hospital.

METHODOLOGY

Study Design

This is a hospital-based case-control study.

Study Area/Location

The University of Benin Teaching Hospital is a tertiary health establishment located in Benin City, Edo State, South-south geopolitical zone of Nigeria. It provides diverse specialised healthcare for patients in Edo state and neighbouring States of Ondo, Delta, Kogi, and Bayelsa. The majority of these states are within the tropical rain forest, where malaria transmission is holoendemic and stable throughout the year, especially in under-fives. Egor Local Government Area is one of the three LGAs within the Benin metropolis and consists of ten political wards. It has its headquarters in the town of Uselu and has an area of 93 km^2 with a population of 339,899. The University of Benin Teaching Hospital is also located in this Local Government Area. Egor was chosen because it is centrally located in Benin metropolis and cuts across various socioeconomic strata, in addition to the fact that UBTH and the UBTH STAFF school are also situated in this LGA.

This study was carried out at the Children's Emergency Room, General Practice Clinic, and Paediatric wards of the University of Benin Teaching Hospital (UBTH), Benin City. The CHER is a complex with a total bed capacity of 25 and an average in-patient load of 80 per month, and a casualty room where out-patient paediatric cases are seen. The GPC has a paediatric patient load of about 20 per day and operates from 8 am to 4 pm on weekdays.

StudyDuration

This study was carried out within six months, from 5th October 2017 to 13th March 2018.

Study Population

The study was conducted in children of consenting parents or caregivers, who presented with signs and symptoms of malaria according to WHO criteria, and in those patients with severe malaria who were screened and admitted by a paediatric physician into the children's emergency and paediatric wards of the University of Benin Teaching Hospital (UBTH).

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Selection Criteria

Inclusion Criteria

Subjects

Children below 18 years for whom a diagnosis of malaria was made by parasite microscopy

Children below 18 years with features of malaria according to the WHO criteria.

Exclusion Criteria

Children who were on management for other known causes of coma, e.g., recent head trauma or hypoglycaemia, meningitis and encephalitis, and other causes of non-malarial fever.

Children in whom the malaria parasite was negative, whether or not they had features of malaria.

Children with a history of or on treatment for sickle cell disease.

All children whose birth was before 37 weeks of gestation or birth weight < 1.5kg because these children are at risk of Retinopathy of prematurity.

All undernourished children were excluded since severe undernutrition is associated with increased morbidity and ocular features.

Controls

Healthy age and sex matched children who attend the University of Benin Teaching Hospital Staff School and who were below the age of 18 years without a history of fever in the past 3 months were screened for *Plasmodium falciparum* malaria using the WHO standard laboratory tests and screening criteria for malaria. Those who tested negative for the parasite were included in the study for control by the following method:

After consultations with the Principal and Head Teacher of the UBTH Staff School, consent forms explaining the research procedure were distributed to the pupils and students to take home to their parents/ caregivers. One hundred and seventy-eight apparently healthy age-group and sex matched children (control) were selected from those whose parents gave informed consent. The children whose parents gave informed consent had their blood samples taken and screened for *Plasmodium falciparum* parasite by the WHO-certified microbiologist of the Department of Child Health, UBTH. Children who were positive for the malaria parasite were not included in the control group. Those who were negative for malaria parasite were recruited into the study from the classrooms, and their eyes were examined.

Sample Size Determination

The sample size was determined by using the Kish and Leslie 20 formula. A similar number of apparently healthy children who were age and sex matched were included as controls.

This is expressed as $n = \frac{Z^2 pq}{d^2}$

Where;

n =minimum sample size

Z = 1.96 (standard normal deviate when α is 0.05)

p = prevalence of having any ocular feature of malaria amongst children below 18 years in a 2002 study in Mali = 11.8% (Schemann *et al*[21])

therefore;

p =11.8/100= 0.118 = 0.12

q = 1-p = 1 - 0.12

d = degree of accuracy or level of precision = 5% (0.05)

Therefore,

$n = \frac{[(1.96)^2 \times 0.12 \times (1 - 0.12)]}{(0.05)^2} = 162$

Allowing for a 10% non- response rate,

110/100 x 162 = 178

This calculation gave a minimum sample size of 162. Allowing for a non- response rate of 10%, the minimum sample size calculated is 178. Therefore, Group A will contain 178 patients, and Group B (standard control) will contain 178 patients.

These will be age-group and sex matched.

Sampling Technique (for cases)

All children aged below 18 years with a diagnosis of malaria (uncomplicated and severe) using the WHO criteria were recruited consecutively in the study until the minimum sample size was achieved.

Sampling Technique (for control)

Sampling per classroom was done using the method of "Proportionate allocation" as shown by the formulae below: Both nursery, primary, and secondary schools consist of classes 1-5 and JSS 1- SS3.

Primary 1 - 5 consists of classes A-C, JSS 1 –SS3 had classes A-D, respectively. Class 'A' was chosen through all the arms for the purpose of convenience.

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Number of students selected from JSS 1A =
Number of students in JSS 1 'A' x 178
Total number of students in the school: 1
that are in all classes 'A.'
(i.e Nursery 1A, Pry 1A-5A and
JSS 1A –SS3A)

UBTH STAFF school consists of nursery, primary, and secondary units and is located in Egor Local Government Area, Edo State.

Ethical Considerations

Ethical approval was sought from and granted by the Ethics and Research Committee of the University of Benin Teaching Hospital. Also, permission was sought from the Heads of Departments involved (Childhealth and Ophthalmology) and the Consultants whose patients were recruited for the study.

Informed Consent

Written informed consent was obtained from parents or primary caregivers of all participants after verbal explanation of the study. Assent was obtained from children who are of age and can communicate before their inclusion into the study.

Subjects and their primary caregivers were assured of the strict confidentiality of information volunteered. Assent was obtained from the children who are verbal and able to communicate.

Data Collection

The survey team consisted of
An ophthalmic senior registrar (principal investigator)
Two ophthalmic registrars
A Paediatric registrar
An ophthalmic nurse
A paediatric nurse

Questionnaire Description

A structured questionnaire was used to obtain data. It was an interviewer- administered data collection. The questionnaire was developed to consist of relevant, short, structured questions necessary to obtain relevant and useful information specifically for the study.

Questionnaire Pre-test

The questionnaire was pre-tested among patients diagnosed with malaria in the Children's Emergency and Paediatric wards in Central Hospital, Benin City, which is a centre that has similar patient demographics to the University of Benin Teaching Hospital (UBTH) and is located about 10 km away from UBTH. A correction was made before the final questionnaire for the study was printed out. These patients were not included in the final analysis.

Research Materials

Questionnaire (interviewer-administered)
Snellen visual acuity chart, Kay-picture charts (literate and illiterate)
Pen torch
Meter rule
Keeler Pulsair non-contact tonometer – intellipuff
Keeler direct ophthalmoscope
Zeiss Portable Slitlamp Microscope
Mydriatic eye drops – Tropicamide (1%) and phenylephrine (2.5%)
Binocular indirect ophthalmoscope (BIO) (Appasamy) – model AAIO
+ 20D non contact lens (Volks)
iPhone 6 (Apple) model A1586
Eye swabs
Weighing scale with extendable meter rule – health scale RG2- 12
Mechanical bench Scale (SALTER model 180 England)
Mechanical floor Scale (SECA model 761)

Data Collection Procedure

Data collection procedure was done at the Children's Emergency Ward, GPC, and Paediatric ward of the University of Benin Teaching Hospital. Questionnaires designed specifically for the study were administered by the study, assisted by the ophthalmic registrars. General examination was done, and vital signs of subjects were taken by the Nurses. Ocular examination was carried out for both subjects and controls by the author, as the lead researcher, assisted by the ophthalmic resident doctors. The findings were recorded in relevant sections of the form. The presenting visual acuity (PVA) was assessed by the principal researcher uniocularly and then binocularly in patients who are conscious and oriented, unaided first, then with the subject's present spectacles or visual aids, where his or her unaided VA was less than 6/9. Fixation and following light and behavioural pattern to occlusion of the good eye was employed for preverbal children, picture charts for verbal children, and Snellen's visual acuity charts and E charts were employed for older children as appropriate. Under normal daylight supplemented with

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fluorescent electric light, the chart was placed at a distance of 6m, and the subject was asked if he/she could see and read. When a subject was unable to see the largest print (6/60), the chart was moved 1m closer to the subject until he/she was able to see the largest optotype. This was recorded as 6/60, 5/60, 4/60, 3/60, 2/60, or 1/60. When a subject was unable to see/ read the largest optotype or count fingers at a distance of 1m, hand movement (HM) was tested by waving the hand in front of the eye. This was recorded as HM when identified. When not attainable, perception of light (PL) was tested by shining a pen torch into the eye. This was recorded as PL when correctly visualised, but if not, the visual acuity was recorded as nil perception of light (NPL). Examination of the ocular adnexa and anterior segment was done using a pen torch, a magnifying (binocular) loop (x2.5), and a Zeiss portable handheld slit lamp microscope. Intraocular pressure measurement was done with a Keelers pulsair non- contact tonometer.

Children who were 18 years and below and diagnosed with malaria (Study participants) had dilated fundus examination by direct and indirect ophthalmoscopy and were assessed by the study for ocular and retinal signs of malaria. Fundus examination was carried out using the wireless binocular indirect ophthalmoscope after pupillary dilatation (with commercially available 1% tropicamide and 2.5% phenylephrine eye drops). This was carried out by the study, and findings were recorded in relevant sections of the form. Laboratory investigations were requested by the Paediatric physician and registrar for children presenting with symptoms suggestive of malaria.

Laboratory microscopy

Microscopic detection and identification of Plasmodium parasites was done by the microbiologist using Giemsa-stained thick and thin blood films**.** Haemoglobin was measured using the 18-parameter automatic haematology analyser (System KX -21, Japan). Screening for sickling was done by the haematologist using the sodium metabisulfite method in patients who presented with features suggestive of sickle cell disease. Cerebrospinal fluid examination was done by the paediatrician via lumbar puncture to rule out meningitis. These results were retrieved from the case files of patients who have had these investigations done and documented already.

Confirmation of malaria in study participants.

Diagnosis of malaria parasite

Diagnosis of malaria was done by the demonstration of malaria parasites on microscopy.

Procedure for microscopy

Blood film was prepared for all the study participants from blood obtained from a peripheral vein of each child. Blood samples were stored in ethylene diamine tetraacetate (EDTA) anti-coagulant bottles before being taken to the laboratory for analysis.

Limb veins (preferably the hand for comfort) were used for sample collection. The sample was collected after skin preparation on the anatomical site with a wet swab (cotton wool with methylated spirit). Each specimen bottle was labelled with the child's identification number as recorded on the questionnaire administered at recruitment, and then sent to the Department of Child Health, UBTH Research Laboratory for preparation of thick and thin films. The thick and thin films were used for determining malaria parasite density (parasite count) and species identification, respectively. Samples were collected at presentation and sent to the laboratory immediately. Analyses were done within 2 hours of presentation in the hospital.

Technique for blood film for malaria parasite

Thick smear

One or two drops of blood from a blood pipette were placed at the center of the pre-cleaned, labelled slide.

Using the corner of another slide or an applicator stick, the drop of blood was spread in a circular pattern or the size of a coin (1.5cm ^{2}).

The slide was then laid flat and allowed to dry.

After a minimum of 30 minutes, the slide was stained with Giemsa stain and viewed under the microscope at X100 magnification.

Thin smear

A drop of blood was placed on a pre-cleaned, labelled slide, near the frosted end.

A smear of the blood sample was made on the slide.

The smear on the slide was allowed to air- dry for about 10 minutes by placing the slide in a horizontal position.

The smear was then fixed by dipping the slide in absolute methanol solution and allowing it to dry in air for 1-2 minutes.

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The slide was then stained at pH 7.1 – 7.2 using Giemsa stain and was viewed under the microscope for malaria parasite species.

The malaria parasite identification was done by the WHO-certified Chief laboratory scientist who currently works at the Paediatric microbiology laboratory of the Department of Child Health, UBTH.

A high-power (100X objective) microscope field for each slide was examined, and the malaria parasite was recorded as positive or negative. Parasite count for each patient was obtained using the formula proposed by Greenwood and Armstrong, 49 and as cited by Cheesebrough. This was done by multiplying the average number of parasite trophozoites counted per high-power field (100X objective) by 500. This method has been observed to be more accurate and quicker in determining parasite count and has been recommended by the WHO in malaria-endemic regions.

As per institutional practice at this time of the study, patients with severe malaria were managed using the current University of Benin Teaching Hospital treatment protocol (WHO Standard Treatment Protocol):

Children with severe anaemia were transfused with whole blood or fresh frozen plasma. Those who had severe anaemia and respiratory distress were placed on humidified oxygen by facemask or nasal prongs. Hypoglycemia was corrected with an intravenous 10% dextrose solution. This treatment was administered by the Paediatrician in the Department of Child Health, UBTH.

Data Management

Data collected was cross-checked for completeness. Any incomplete data was discarded. Analysis of data collected was done using a computer and the Statistical Package for the Social Sciences (SPSS) version 21 software. The children's ages were stratified into less than 5 years, 5 to 9 years, and 10 years and above (below 18 years). Quantitative variables in the study were summarised using means and standard deviations or medians and ranges, where applicable. Frequency tables and charts were constructed as appropriate, such as the demographic characteristics and ocular features identified in the subjects and control groups. The relationship between ocular features and the identified factors was presented as bivariate frequency tables and charts where applicable. The association between ocular features seen and the common clinical syndromes of malaria infection was analysed using the chi-square test, where applicable. The level of significance of each test was set at $p < 0.05$ and 95% confidence level.

RESULTS

A total of one hundred and seventy-eight (178) children with malaria met the inclusion criteria for the study; for the control group, a hundred and ninety-two (192) children who attend the UBTH STAFF school, whose parents gave informed consent, were also registered for the study, from which 178 were selected to meet the sample size. A total of 33 ethnic tribes/ languages were represented among the subjects for both cases and controls. However, the majority were from the Bini ethnic group, which had the highest frequency of 72 subjects (40.4%) for cases and 91 subjects (51.1%) for controls. This was followed by the Igbo ethnic group, who had 32 subjects (18%) and 17(9.6%) for cases and control, respectively, and the Etsako 12(6.7%) and 7(3.9%) ethnic group for cases and control, respectively. The majority of the subjects (159) with malaria (cases) resided in Edo state, while 19 had come in from the surrounding states of Ondo, Delta, Kogi, and Bayelsa. All the subjects that were used for control resided in Benin City, Edo State.

Table 1: Socio-demographic characteristics of cases and controls

Variable	Cases (%) N=178 n=178	Controls (%) N=178	χ^2	P
Sex				
Male	102(57.3)	98(55.1)	0.183	0.669
Female	76(42.7)	80(44.9)		

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Age group				
<5yrs	112(62.9)	117(62.6)	0.163	0.922
5-9yrs	48(27.0)	53(28.3)		
10yrs and above	18(10.1)	17(9.1)		
Mean age (yrs)	4.08±3.85	4.04±2.49	0.116	0.907

Analysis of the 178 children recruited for this study shows that 102(57.3%) were males, while 76(42.7%) were females. For cases, 98(55.1%) were males, while 80(44.9%) were females for controls. (Table 1). Giving a male-to-female ratio of 1.34:1 for cases and 1.225:1 for controls. The ages of the subjects ranged from 11months to 16 years for cases and 3 years to 17 years for controls. The mean age for the cases and control were4.08±3.85and 4.04±2.49respectively, while the modal age for both groups was 4years.The median (IQR) age of the children in this study is 2.0(1.0 – 6.0) yrs. The age of the children was divided into 3 groups: <5yrs, 5-9yrs, and >10yrs. The majority of the children are in the < 5-year age group. There was no significant statistical difference between the sex and age of the cases and control groups ($p > 0.05$).

Table 2: Other sociodemographic factors of children with malaria in UBTH.

Variable	Subjects N=178(%)	Controls N=178 (%)	χ^2	p
Social Status				
Upper	112(62.9)	162(91.0)	46.441	0.000
Middle	37(20.8)	16(9.0)		
Lower	29(16.3)	0(0.0)		
Tribe				
Bini	72(40.4)	91(51.1)	25.438	0.000
Delta	10(5.6)	0(0.0)		
Etsako	7(3.9)	12(6.7)		
Igbo	17(9.6)	32(18.0)		
Yoruba	12(6.7)	7(3.9)		
Others	60(33.7)	36(20.2)		
Level of education of the mother				
Primary	33(19.4)	6(3.4)	51.772	0.000
Secondary	42(24.7)	12(6.7)		
Tertiary	95(55.9)	160(89.9)		

Social status, ethnicity, and level of education of the mother were significantly different for the control and the cases (p=0.000). The control group had mothers who were significantly better educated and belonged to higher social classes (p=0.000). Significantly more of the control subjects were of Bini, Etsako, and Ibo extraction (p=0.000).

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Table 3: Association between convulsion and prevalence of retinopathy in children with malaria in UBTH.

	Retinopathy			
	Absent	Present	χ^2	p
No convulsion	10(55.6)	19(45.2)	0.537	0.464
Convulsion	8(44.4)	23(54.8)		

Prevalence of ocular features of malaria (any retinopathy) was higher in children who had convulsed (54.8%) than in those who did not (45.2%), but this was not statistically significant (p=0.464). Eight children out of 23 children who convulsed did not show any ocular features of malaria (Table 9).

Table 4: Factors associated with ocular features of malaria in children in UBTH.

	Ocular features			
	Absent(%)	Present(%)	χ^2	P
Sex				
Male	76(74.5)	26(25.5))	0.476	0.490
Female	60(78.9)	16(21.1)		
Age group				
<5yrs	82(73.2)	30(26.8)	2.969	0.227
5-9yrs	41(85.4)	7(14.6)		
10yrs and above	13(72.2)	5(27.8)		
Social Status				
Upper	95(84.8)	17(15.2)	24.215	0.000
Middle	29(78.4)	8(21.6)		
Lower	12(41.4)	17(58.6)		
Mother's education				
Primary	4(22.2)	14(77.8)	0.416	0.812
Secondary	5(26.3)	14(73.7)		
Tertiary	6(31.6)	13(68.4)		
Father's education				
Primary	1(11.1)	8(88.9)	1.438	0.487
Secondary	8(29.6)	19(70.4)		
Tertiary	6(31.6)	13(68.4)		
Tribe				
Bini	55(76.4)	17(23.6)	8.994	0.091

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Delta	5(50.0)	5(50.0)		
Etsako	7(100.0)	0(0.0)		
Igbo	11(64.7)	6(35.3)		
Yoruba	11(91.7)	1(8.3)		
Others	47(78.3)	13(21.7)		
Mode of feeding				
Exclusive breastfeeding	83(74.8)	28(25.2)	1.844	0.398
Supplementary feeding	48(81.4)	11(18.6)		
Formula feeding	3(100.0)	0(0.0)		
Is the child fully immunised for their age?				
Yes	130(76.0)	41(24.0)	0.350	0.554
No	6(85.7)	1(14.3)		
Any delay in the milestone				
Yes	5(83.3)	1(16.7)	0.165	0.684
No	131(76.2)	41(23.8)		

There was a statistically significant increase in the prevalence of ocular features of malaria with a decrease in social class of subjects and vice versa (p=0.000). Prevalence of ocular features of malaria was higher in male subjects (25.5%) than in female subjects (21.1%); however, this was not of any statistical significance.

Table 5: Association of malaria parasite density and retinopathy

	Retinopathy	
Malaria parasite density	*Absent* *n (%)*	*Present* *n (%)*
+	118(0.0)	0(0.0)
++	10(29.4)	24(70.6)
+++	0(0.0)	26(100.0)

$\chi^2 = 12.17$; $p = 0.002$

Retinopathy is significantly associated with high malaria parasite density (p=0.002). Prevalence of retinopathy in patients with 3 plus (+++) *Plasmodium falciparum* malaria parasite was higher than in children with 2 plus (++)

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Table 6: Association between ocular features and common clinical syndromes of malaria infection in Children in UBTH

	Severe non-cerebral malaria (n=16)	Severe malaria/ anaemia (n=17)	Cerebral malaria (n=27)	χ^2	P
Retinal whitening	2(12.5)	6(35.3)	6(22.2)	25.71	0.00
Papilloedema	2(12.5)	0(0.0)	8(29.6)	22.95	0.00
Macular whitening	3(18.8)	6(35.3)	11(40.7)	37.33	0.00
Macular haemorrhage	3(18.8)	0(0.0)	3(11.1)	12.72	0.00
Retinal haemorrhage	4(25.0)	1(5.9)	9(33.3)	27.93	0.00
Vessel abnormalities	7(43.8)	10(58.8)	17(63.0)	69.30	0.00
Disc Pallor	2(12.5)	3(17.6)	6(22.2)	18.57	0.00
Any retinopathy*	8(50.0)	12(70.6)	22(81.5)	95.48	0.00

**one or more of any retinal features*

Prevalence of retinal whitening was highest with malaria infested children that have severe malaria/anaemia (35.3%), less in those with severe non-cerebral malaria. Prevalence of papilloedema (29.6%), macular whitening (40.7%), and retinal haemorrhage (33.3%) was highest in children with cerebral malaria. The highest prevalence of vessel abnormalities (63.0%), disc pallor (22.2%), and any retinopathy was recorded in subjects with cerebral malaria.

Ocular features of malaria encountered in the study (81.5%) increased in prevalence in children with cerebral malaria when compared to the uncomplicated, severe non-cerebral, and severe malaria anaemia groups.

There was a statistically significant relationship between ocular features and the clinical syndromes of malaria (p= 0.00).

Table 7: Association of ocular features of malaria and convulsion in UBTH.

	Convulsion			
	Absent	Present	χ^2	P
Retinal whitening	6(42.9)	8(57.1)	0.219	0.640
Papilloedema	2(20.0)	8(80.0)	3.853	0.050
Macular whitening	8(40.0)	12(60.0)	0.834	0.361
Macular haemorrhage	2(33.3)	4(66.7)	0.601	0.438
Retinal haemorrhage	5(35.7)	9(64.3)	1.164	0.281
Vessel abnormalities	15(44.1)	19(55.9)	0.558	0.455
Disc Pallor	4(36.4)	7(63.6)	0.773	0.379

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$\chi^2 = 2.16; p = 0.602$

The most frequent ocular feature seen in children who had experienced one or more episodes of convulsion was papilledema, where 8(80.0%) children out of 10 who had convulsed had papilledema present, and 2(20.0%) children did not. This was followed by macular haemorrhage 4(66.7%) and retinal haemorrhage 9(64.3%). Convulsion was not statistically significantly associated (p>0.05) with any of the ocular features.

Table 8: Association of ocular features of malaria and coma in children in UBTH.

	Coma			
	Absent	**Present**		
Retinal whitening	2(14.2)	12(85.7)		
Papilloedema	1(10.0)	9(90.0)		
Macular whitening	9(45.0)	11(55.0)		
Macular haemorrhage	4(66.7)	2(33.3)		
Retinal haemorrhage	3(21.4)	11(78.5)		
Vessel abnormalities	18(52.9)	16(47.1)		
Disc Pallor	1(9.1)	10(90.9)		

$\chi^2 = 14.916; p = 0.016$

The ocular feature most commonly seen in children who had severe malaria and had become comatose was disc pallor (90.9%), followed closely by papilledema (90%). Retinal whitening (85.7%) and retinal haemorrhage (78.5%) were also commonly seen. There was a significant relationship between ocular features of malaria and coma (p=0.016).

Discussion

Ocular features of malaria (mostly posterior segment) were seen in all types of severe malaria in this study, which is similar to previous studies[3,5,6,7]. The prevalence of any ocular features of malaria was seen to be higher in males (25%) than in females (21.1%) in this study, although the difference was not statistically significant (p= 0.490). The highest prevalence of ocular features of severe malaria was seen in children in the < 5-year age group (26.8%). This was also not significant (p = 0.227).

The prevalence of ocular features was seen to increase with decreasing levels of education of parents or caregivers and with decreasing socioeconomic status, and vice versa. This may be explained by the fact that there is a higher level of ignorance about health issues in this group and a tendency for poor health practices that are detrimental to these children's health. There may also be negligence in the healthcare of these children due to ignorance, even when they begin to manifest early symptoms of malaria infestation. The mothers, therefore, may not practice preventive measures that protect these children from having malaria, and they may also not understand the urgency in presenting early to the hospital for immediate intervention and care. These parents or caregivers may also experience severe poverty, which makes it difficult to make up their minds to seek timely intervention since they cannot afford to pay for the health services. This is because out-of-pocket payment is the predominant form of payment for health services in Nigeria, as uptake of health insurance among the populace is low. Therefore, these children develop late stages of the disease (complicated malaria) and develop ocular features of malaria, which have been documented to be very common at the late stages of the disease. Due to ignorance and poverty, these parents may fail to provide adequate nutrition for these children, and therefore, they may suffer malnutrition, which reduces their immunity and ability to fight malaria and other common infections. These may contribute to the disease severity and therefore make

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them prone to developing more of these ocular complications of *Plasmodium falciparum* malaria.

In this study, the prevalence of any ocular feature of malaria seen was found to be higher in cerebral malaria than in the other clinical syndromes of malaria, 50.0%, 70.6%, and 81.5% for severe non-cerebral malaria, severe malaria anaemia, and cerebral malaria, respectively. This is similar to the findings of previous studies.[5,6,7,9] This may reflect the greater severity of cerebral malaria. The ocular feature with the highest prevalence seen in the cerebral malaria group was vessel abnormalities (63.0%) (which were engorged and tortuous veins with yellowish-whitish discolouration), followed by macular whitening (40.7%) and retinal haemorrhages (33.3%).

Prevalence of ocular features, any retinopathy, macular whitening, macular haemorrhage, retinal haemorrhage, and vessel abnormalities increased generally with delay in seeking effective result-oriented treatment intervention for malaria. Analysis of ocular features of malaria in this study showed that there was a relationship between delay before seeking treatment intervention in hospital and the frequency of occurrence of ocular features of malaria encountered, although this was not statistically significant (p= 0.667); it was similar to the study in Mali, where the frequency of ocular signs increased with delay for consulting.[8]

Conclusion

The ocular features of malaria are more frequently found in patients with more severe malaria infestation. Ocular features of malaria were higher in the children who had convulsed.

Limitations

Because of the short duration of the study, the long-term effect of malaria on the vision of these children could not be ascertained.

Recommendations

The Ophthalmologist should be consulted in the co-management of children with malaria complications. This will aid diagnosis and institution of appropriate treatment modalities.

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List of abbreviations

UBTH: University of Benin teaching hospital.
WHO: World Health Organisation

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The author did not declare any conflict of interest.

Data availability

Data is available upon request.

Author contribution

Dr Johnpaul Oshorenua Okolo collected data and drafted the manuscript of the study.
Prof. A.E. Omoti supervised the study
Dr O.M. Uhumwangho supervised the study
Dr D.U Nwaneri supervised the study

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