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OCULAR MANIFESTATIONS OF CHILDREN WITH SICKLE CELL DISEASE IN IBADAN, NIGERIA

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ABSTRACT

Background: **Children with sickle cell disease can present with ocular complaints. Regular eye examination can detect sight threatening conditions amenable to treatment. The aim of the study was to describe ocular manifestation of children with sickle cell disease attending the Pediatric Outpatient Department of the University College Hospital Ibadan.**

Methodology**: Children 15 year and below diagnosed with sickle cell disease at the Pediatric Outpatient of the University College Hospital were examined in detail by the Ophthalmologist to document ocular findings.**

Results**: One hundred and five (105) patients were examined. Mean age was 3.22 ± 2.49 years with a male to female ratio of 1.2: 1. Ninety children (85.7%) had Hemoglobin SS while HB SC had 15(14.3%). The commonest ocular finding was retinal vascular tortuosity in 15(14.3%). Other important findings were central retinal artery occlusion in 2 (1.9%) patients; black sunbursts pigmentation 2(1.9%); chorioretinal atrophy 3(2.8%), salmon patch retina hemorrhage 1(0.95%); retina holes1(0.95%) and retina coloboma1(0.95%). The only anterior segment finding was jaundice in all the patients. No conjunctiva vascular abnormalities were found.**

Conclusion**: Retinal vascular tortuosity is the commonest ocular manifestation of children with sickle cell disease in Ibadan. Central retinal artery occlusion, a devastating condition is an emerging manifestation. Regular eye examination for sickle cell retinopathy in children less than 15 years of age is not recommended.**

INTRODUCTION

Sickle cell disease (SCD) is common genetic disorder in Sub Saharan Africa.[1]The prevalence of the hemoglobin S gene which causes the disease is 24% in Nigeria and the prevalence of sickle cell anemia is 20 per 1000 live births.[2]In the presence of oxidative stress, the red blood cells of sickle cell disease patients take on a sickle shape instead of the normal bi-concave disc. They become trapped in the small vessels leading to ischemia, hypoxia, and tissue necrosis. The hypoxia leads to more sickling and a cycle is created.SCD is a systemic disease that is often associated with varying complications such as infections, painful crises and severe anaemia.[2]Ocular manifestations have been described in the literature [3-13]and Abiose in Lagos, Nigeria, described ocular findings in children with the homozygous disease.[14]

Among individuals with SCD, those with Haemoglobin SS (Hb SS) have the worst systemic complications while S-thalassemia and SC patients have the most severe ocular problems. The blood is more viscous in the latter group as small retinal arterioles occlude more easily.

Retinal abnormalities in SCD may be proliferative or non-proliferative. Non-proliferative retinal findings include salmon-patch hemorrhages and black sunburst pigments. These are retinal pigment epithelial layer reaction to hemorrhage and choroidal infarction.14 Others abnormalities are intraretinal refractile bodies, and silvering of peripheral arterioles. Proliferative abnormalities include sea-fan neovascularization, vitreous hemorrhages, and retinal detachments.

Other associated findings include venous tortuosity, retinal holes, Central retina artery occlusion, and angioid streaks.14There is inadequate data on ocular manifestations of SCD in children in Nigeria. The objectives of this study were to describe the pattern of ocular abnormalities, frequency of retinopathy and risk factors in children with sickle cell disease attending the children outpatient clinic of the University College Hospital, Ibadan. It is hoped that findings from this study would contribute to the knowledge of ophthalmic manifestations of sickle cell disease in the pediatric population, identify risk factors for these manifestations and inform guidelines for early detection and management. Methodology.

The study took place in the Children Out patient and Eye Clinics of the University College Hospital, Ibadan, Nigeria. It involved children aged less than 15 years diagnosed with sickle cell disease and attending the Hematology/Oncology clinic of the Department of Pediatrics of the Hospital. Following parental consent, children were initially seen at the children's clinic by a pediatrician and subsequently referred to the Eye clinic of the hospital where they were examined by ophthalmologists. In the children's clinic, the parents or caregivers were interviewed, examined and investigations were done on each patient. Information obtained included demographic variables, hemoglobin phenotype, age at onset of symptoms of sickle cell disease, use of folate and prophylactic anti-malarials as well as history of trauma to the eye.

All patients had their Hemoglobin genotype (Hb) properly ascertained. Morbidity information obtained include frequency of painful crises, frequency of blood transfusions and steady state hematocrit (from their case notes). At the Eye clinic, a detailed ophthalmic examination was carried out. Visual acuity was done using a Snellen chart placed 6 meters from the participant in a well illuminated area. Preschool children were assessed based on standard procedures.

Anterior segment examination was carried out with a slit lamp and each patient had his intraocular pressure determined by Goldman's tonometer or Perkins tonometer for younger patients. Indirect ophthalmoscopy was done after the pupil was dilated with tropicamide 0.5%. Findings were documented on a proforma and where ocular abnormalities where detected, appropriate treatment was recommended.

RESULTS

A total of 105 patients were included in the study. Their mean age at diagnosis of genotype status was 3.2 ± 2.6 years with a range of 6 months to 12 years while the mean age of patients recruited into the study was 7.6± 4.3 years with a range of 1.4 to 15.0 years. There were 61 males (58.1%) and 44 females (41.9%).

Hematological Features

Out of the 105 patients 90 (85.7%) had the HbSS genotype while 15 (14.3%) had the HbSC genotype. Forty-six (43.8%) patients had been transfused with blood during the course of the disease while 59(56.2%) patients had never been

transfused. Eighty-six (81.9%) patients were using routine and regular proguanil while 11 (10.5%) patients were not compliant with the use of their routine medications. Folic acid was used regularly and routinely in 89 (84.8%) of patients while 11 (10.5%) were not compliant with the use of their routine medications. The packed cell volume (PCV) ranged from 17-35% with a mean of 24.6±3.6%. Ninety-seven (92.4%) of the patients had a PCV of less than 30% while 8 (7.6%) had values of ≥ 30%.

OCULAR FEATURES

Visual acuity was carried out in 91 patients (86.7%) out of a total of 105 patients. The remaining 14 patients (13.3%) were too young to co-operate for visual acuity. Out of the 91 patients, 63 patients (69.2%) had a visual acuity of 6/6 or better in both eyes while 11 patients (12.1) had a visual acuity(V/A) of 6/9 in both eyes. Two patients (2.2%) had V/A of 6/12 in both eyes. The remaining 15 patients (30 eyes) had different visual acuities in both eyes. Twelve eyes had visual acuity of 6/6, 10 eyes had V/A of 6/9, 3 eyes had V/A of 6/12, 2 eyes had 6/18, 1 eye had 6/24, 1 eye had 6/36 and one eye had no light perception (NLP). The 2 eyes with markedly poor vision of 6/36 and NLP are the left eyes of 2 patients who had central retinal artery occlusion (CRAO). All the other patients who had visual acuity between 6/9-6/24 had refractive error and their visual acuities were corrected with refraction. Among the 53 male children assessed for visual acuity (VA), 14 (26.4%) had a VA worse than 6/6 in at least one eye compared with 15 (39.5%) out of the 38 females. There was however no statistically significant association between a VA of less than 6/6 and gender (Chi-square 1.738, p=0.187). Similarly, VA was worse than 6/6 in 25 (32.5%) of the 77 children with HbSS compared with 4 (28.6%) of the 14 children with HbSC (Fisher's Exact test p=1.000). Visual acuity was also less than 6/6 in 11 (25%) of the 44 children with a history of blood transfusion compared with 18 (38.3%) of 47 children with no history of blood transfusion (chi-square 1.851, p= 0.174) Analysis of relationship between VA of worse than 6/6 and age of children, frequency of painful crises and steady state packed cell volume did not reveal any statistically significant differences between children with VA 6/6 and those with less VA (Table I).

TABLE I

Relationship between visual acuity and age, packed cell volume and frequency of painful crises

Parameter	Visual acuity 6/6		Visual acuity less than 6/6		T	P value
	N	Mean parameter	N	Mean parameter		
Mean age (years)	62	7.6	29	7.7	1.302	0.199
Mean Packed Cell Volume (%)	62	24.6	29	24.5	0.222	0.825
Mean† number of painful crises / year	43	2.4	20	1.9	1.264	0.212

Data of number of painful crises not available for some child

Anterior Segment features

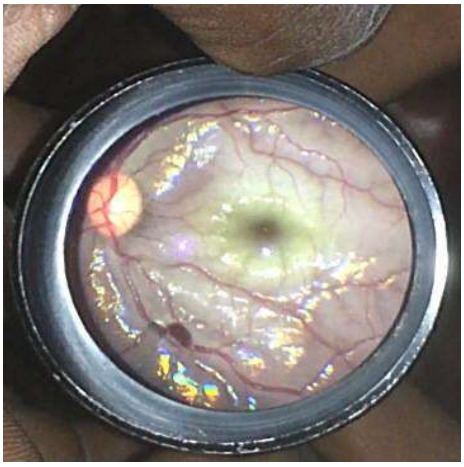
All the patients had a yellowish conjunctival tinge. No conjunctiva vascular abnormality was found.

Posterior segment features

Vascular abnormalities such as tortuosity of the vessels was found in 15 patients (14.3%) and 30 eyes, while two patients (1.9%) had central retinal artery occlusion (CRAO) in the left eyes with severe disc pallor (Figure 1).

Figure 1

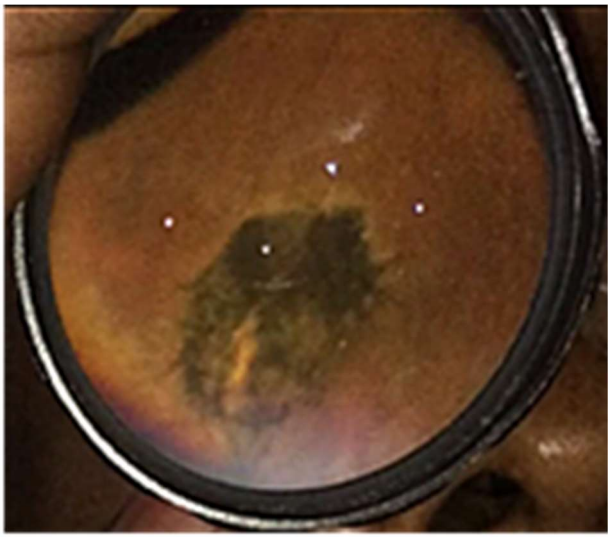
Central retinal artery occlusion in a child with sickle cell disease



acuity in the affected eyes were 6/36 and No light perception respectively. Three patients had chorioretinal atrophy and 2 patients had black sunbursts (pigmented chorioretinal scars) at the periphery.(Figure 2)

Figure 2

Black sunburst in a child with sickle cell disease



The two patients with CRAO were both boys aged 7 and 7.5 years respectively and visual Other abnormalities found were bilateral coloboma, retinal holes in the periphery and salmon patches (Table 2). There was no age or gender predilection.

Table 2

Ophthalmic manifestation of children with sickle cell disease in Ibadan, Nigeria

Features	Frequency	Percentages
Anterior segment		
Yellowish conjunctiva tinge	105	100
Posterior segment		
Retina vascular tortuosity	15	14.3
Chorio retinal atrophy	3	2.8
Central retina artery occlusion	2	1.9
Black sunburst retina scar	2	1.9
Retina holes	1	0.95
Salmon patch hemorrhages	1	0.95
Retino choroidal coloboma	1	0.95
Optic disc cupping (borderline,physiologic)	10	9.5

Combining all manifestations of retinopathy such as retinal vascular tortuosity, central retinal vascular occlusion, black sunburst retinal scars, retinal holes and salmon patch haemorrhages, retinopathy was present in 23 (21.9%) of the 105 children studied.

Among the 61 male children, retinopathy was present in 17 (27.9%) compared to 6 (13.6%) of the 44 females studied (p=0.082). Similarly, retinopathy was present in 21 (23.3%) of the 90 Hb SS children compared to 2 (13.3%) of the 15 children with HbSC (Fisher's Exact test p=0.514). Retinopathy was present in 12 (26.1%) of the 46 children with a history of blood transfusion compared with 11(22.4%) of 49 children with no history of blood transfusion (chi-square 0.837, p= 0.360).

Analysis of relationship between retinopathy and age of children, frequency of painful crises and steady state packed cell volume did not reveal any significant differences between children with retinopathy and those without (Table 3). Retinopathy was present in 17 (23.9%) of the 71 children aged ≤10 years compared to 6 (17.6%) of the 34 children aged >10 years (Chi-square 0.533, p=0.465).

Optic disc examination revealed normal disc with a cup to disc (CDR) ratio of 0.3-0.4 in 95 patients (90.5%) while 7 patients (6.6%) had borderline cupping with CDR of 0.5. There was physiological cupping in three patients (2.8%) who had CDR of 0.6-0.7.

These patients had pink neuro-retinal rims and normal intraocular pressures. There was no clinical feature to suggest glaucoma. There was no association between non-proliferative retinopathy observed and gender (p=0.08. pearson chi square =3.02 (OR 0.14-1.14), haemoglobin phenotype p=0.38; Pearson Chi square=0.17 (OR= 0.1-2.4) and frequency of painful crises.

Table 3

Relationship between retinopathy age, packed cell volume and frequency of crises

Parameter	Retinopathy		Absence of Retinopathy		T	P value
	N	Mean parameter	N	Mean parameter		
Mean age (years)	23	7.9	82	7.5	0.387	0.701
Mean steady state Packed Cell Volume (%)	23	24.1	82	24.7	-0.626	0.536
Mean† number of painful crises / year	20	2.3	47	2.2	0.227	0.822

DISCUSSION

Sickle cell disease is prevalent in south western Nigeria1. Ophthalmic manifestations have been described in adults and children with sickle cell disease in Nigeria.3-13 The most common manifestation in this study was retinal vascular tortuosity. This feature has been observed in adults and children by previous workers4,5,12 and reported to be due to sluggish blood flow, ischemia, stasis and vasodilatation associated with sickle cell disease.14The second most common feature was chorio-retinal atrophy which may not be unconnected to the chronic degeneration associated with ischemia. Central retinal artery occlusion was found in two children. This is a devastating condition resulting from the sickled cells blocking the central retinal artery which is an end artery. It usually results in irreversible visual loss. In the present study, it was associated with impaired visual acuity and no light perception. Black sunburst represents retinal pigment epithelial proliferation in response to retinal hemorrhage from retinal ischemia and requires no treatment. Retino- choroidal coloboma may be an incidental finding in our patient because it is not known to be a complication of SCD and to the best of the authors knowledge, there has been no previous report of its occurrence in SCD.Optic disc changes noted included borderline cupping of the discs. The association of glaucoma and sickle cell disease appear possible, but previous studies showed no association between the two diseases.15Normal tension glaucoma may be common and vascular insufficiency may explain the findings. Conjunctiva vascular abnormalities have been described in SCD by previous authors.4,5 In our study, the only anterior segment finding in our study was jaundice. In the southern part of Nigeria, previous workers found conjunctiva vascular abnormalities to be declining in children due to improved health seeking behavior of caregivers. 16None of our patients had conjunctiva vascular anomalies. Our study did not reveal proliferative sickle retinopathy in any of the children. This is in keeping with findings of Tantawy et al17 in children and adolescents in Cairo and supports the reports by other workers that clinically detectable retinal disease is found most commonly between 15 and 30 years of age.

This finding therefore do not support the need for routine screening of children for sickle retinopathy in our environment. However, the occurrence of central retinal artery occlusion with its attendant visual impairment underpins the need to elucidate its risk factors in order to screen children at risk with a view of implementing preventing measures. The present study found no association between non-proliferative retinopathy observed and gender hemoglobin phenotype and frequency of painful crises. In contrast, proliferative sickle retinopathy (PSR) is known to increase with age and occurs more frequently in HbSC than in HbSS.19The most important ocular finding in these children was CRAO and fortunately this was found in only two patients with SCD. These patients were about7 years old,
had been transfused at least twice within one year and had ≥2 painful crises within the year.
Further studies are needed to further elucidate other predisposing risk factors so that such patients can be screened regularly.

CONCLUSION

This study adds to existing knowledge about ocular findings in patients with sickle cell disease in the pediatric age group. Based on our findings and literature we do not recommend routine and regular examination of patients with SCD for sickle cell retinopathy however at risk patient for retinal vascular occlusion will need to be followed up regularly.

Conflict of Interest

The authors have no conflict of interest regarding the present study.

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