



Ocular Presentations of Sickle Cell Disease Patients in a Nigerian Hospital

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Authors' contributions

This work was carried out in collaboration among all authors. Authors CCE and AAO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AU and CCU managed the analyses of the study. Authors OSE and BCO managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Sickle Cell Disease (SCD) is an inherited haemolytic disorder that affects virtually all body systems including the eye. Ocular complications of SCD could have dire consequences if not detected early.

Objectives: We aimed at determining the prevalence of ocular complications of SCD in our patients.

Methods: This study was carried out on patients attending both the adult and Paediatric Sickle cell disease clinic at Chukwuemeka Odumegwu Ojukwu Teaching Hospital, Akwa, Anambra State,

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Nigeria, over an 8 month period. A structured questionnaire was administered to consenting patients to determine their sociodemographic variables and other characteristics. Visual acuity was determined with multiple optotype Snellen's chart at 6 metres in natural daylight. Using pen-torch, the face, external eye examination, anterior segment examination and pupillary reaction to light were assessed. Magnified anterior segment examination was performed with slit-lamp biomicroscope. All subjects underwent dilated fundoscopy (after instillation of tropicamide 0.5% eye drop) using Welch Allyn indirect ophthalmoscope. Results were analysed using SPSS version 22.0 Inc Chicago Illinois and represented in tables. Statistically significant P value was set at < 0.05.

Results: A total of 28 patients with age range of 6-42 years were seen. 17 (60.7%) were males, while 11 (39.3%) were females. 8 (28.6%) had at least one ocular anomaly comprising of refractory errors 3 (10.8%), sickle cell retinopathy 4 (14.3%) and glaucoma 2 (7.1%). Only 2 (7.1%) routinely visit eye clinic. SCD retinopathy was found to increase with age (P value= 0.005).

Conclusion: SCD retinopathy was found more in the older age group despite the small sample size at a prevalence rate of 14.3%. Early initiation of routine ocular examination for SCD patients will be beneficial to avert these complications. More efforts should be made at educating the patients. Larger studies will be required to determine the actual prevalence of ocular anomaly in SCD patients in Anambra State.

Keywords: Sickle cell disease; eye manifestations; early detection.

1. INTRODUCTION

Sickle cell disease (SCD) is an inherited blood disorder that specifically affects hemoglobin in red blood cells. It is characterized by chronic hemolytic anemia, acute episodic pains and various systemic complications affecting many organs in the body including the eye [1].

It is a disease of Public Health Importance and it is estimated that every year approximately 300,000 infants are born with SCD [2]. The disease is found almost exclusively in blacks particularly those in tropical regions of the world like Africa, India, the Mediterranean and the Middle East [1]. It is said to be the most common genetic disorder that affect black race worldwide [3]. However, population migration from high destiny areas of sickle cell disease has led to increase in the incidence in other parts of the world like Europe [4,5].

The sickle hemoglobin 'HbS' can coexist with other abnormal haemoglobin variants such as hemoglobin 'C' as seen in HbSC disease, which is a milder disorder when compared with sickle cell anemia (HbSS). HbSC is also found in blacks while thalassemia, another hereditary disorder of hemoglobin, occurs mainly in people from Mediterranean, North Africa and East Asia [1].

The ocular manifestations of SCD results from vascular occlusion. This occlusion can affect virtually every vascular bed in the eye and has potential to cause blindness in its advanced

stages [5] Ophthalmic manifestations of sickle cell disease include damage of both the anterior and posterior segment tissues including the conjunctiva, iris, the other uveal tissues, and the retina [6,7,8,9].

Retinal changes in patients suffering from sickle cell haemoglobinopathies are primarily caused by retinal hypoxia which results from blockage of small blood vessels by the abnormal-shaped red blood cells [10,11].

Sickle retinopathy can be divided into two; the proliferative and non- proliferative disease [12,13].

The incidence of retinopathy and ocular manifestations are highest in people who are genetically HbSC, less common in people who are S-Beta Thalassemia and least common in HbSS patients [1]. The reason for this may be that HbSS patients have the worse systemic symptoms and are the most anaemic [1]. Anemia lowers the blood viscosity and so reduces vascular occlusions in the retina [14]. Systemic complications are more common in patients with HbSS while visual impairment secondary to proliferative retinopathy is more common in patients with HbSC and Hb-S-Thal [15,16]. This could be due to high blood viscosity in HbSC and Hb-S-Thal but anemia and low blood viscosity in Hbss [1,17].

Sickle cell retinopathy is greatest in adulthood, but some cases have also been described in children [18,19,20]. It has been recommended

that periodic eye examination be carried out on SCD patients from 10 years of age [9].

Although there are similarities in ocular findings in sickle cell disease across the globe, regional variations exist [21]. Several authors have reported various finding on the ocular findings of sickle cell disease some of which include: retinal vein tortuosity, conjunctival signs, visual impairment, central retinal vein occlusion, optic atrophy, myopia, hyperopia, astigmatism etc [11,22,23,24,25,26].

Treatment of sickle cell retinopathy is geared towards prevention of vision loss from vitreous hemorrhage, retinal detachment, and epiretinal membranes. This may be medical or surgical.

Considering the deleterious effects of sickle cell disease on the eyes, we found it necessary to determine the prevalence and patterns of ocular abnormalities and its determinants in our patients. The findings may serve as tools for creating more awareness as well as improving patient management and advocacy in Nigeria.

2. METHODOLOGY

This was a descriptive cross sectional study carried out at Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Amaku Awka, Anambra State. It is a State Government owned tertiary institution. Patients were recruited randomly from the paediatric and adult sickle cell clinic over a period of 8 months. (From February to September 2018).

After informed consent was obtained from the patients' care-givers (for the paediatric age group) and the adult patients, a pre tested structured questionnaire was administered by the ophthalmologist. The questionnaire had two parts: The sociodemographic variables of the patients and brief ocular history including complaints of visual impairment, their habit of routine eye check, as well as findings on ocular examination.

The unaided visual acuity of each eye in each patient was assessed by an ophthalmic nurse using a multiple optotype Snellen's chart at 6 metres in natural daylight. For patients that wore spectacles, their presenting visual acuity with their optical correction were also recorded. Those whose visual acuity improved with pin-hole were refracted subsequently. Using pen-torch the face, external eye examination, anterior

segment examination and pupillary reaction to light were done. Magnified anterior segment examination was performed with slit-lamp biomicroscope, and whenever indicated fluorescein staining of corneal lesions was done.

All subjects underwent dilated funduscopy (after instillation of tropicamide 0.5% eye drop) using Welch Allyn indirect ophthalmoscope. Retinal findings were documented through careful drawings. All ocular examinations were performed separately for each eye in all subjects, and recorded in the questionnaire.

Data analysis was done using statistical package for social sciences (SPSS) version 22.0 Inc Chicago Illinois. Results were represented on tables and P value of < 0.05 was considered statistically significant.

3. RESULTS

A total of 28 (100%) SCD patients with a median age of 16.5 (6-42) were seen during the period of study of these, 17 (60.7%) were males while 11 (39.3%) were females with a male to female ratio of 1.5:1. Most of them (78.6%) were students (Table 1). All the patients seen had haemoglobin phenotype of Hb SS.

Table 1. Demographic variables of the study participants

| Demographics | |
|-------------------|---------------|
| Age | (in years) |
| Mean | 19.68 |
| Median | 16.50 |
| Range (Min – Max) | (6-42) |
| Age group | Frequency (%) |
| <10 | 8(28.6) |
| 10 – 19 | 7(25.0) |
| 20 – 29 | 5(17.8) |
| 30 – 39 | 7(25.0) |
| 40 – 49 | 1 (3.6) |
| Sex | |
| Male | 17(60.7) |
| Female | 11(39.3) |
| HLE | |
| None | 0(0) |
| Primary | 12(42.9) |
| Secondary | 7 (25.0) |
| Tertiary | 9 (32.1) |
| Occupation | |
| Student | 22(78.6) |
| Unemployed | 3(10.7) |
| Self employed | 2(7.1) |
| Civil servant | 1(3.6) |

HLE- highest level of education

Most of the patients (89.3%) did not have difficulty with reading. However, they (92.9%) hardly visit the eye clinic for routine eye check. A total of 9 (32.1%) patients had at least one ocular anomaly. Four (14.2%) patients had some form of retinopathy as evidenced by retinal vascular tortuosity, while 2(7.1%) had glaucoma. Other ocular anomalies seen were myopia, myopic astigmatism and presbyopia, Table 2.

Table 2. Findings on ocular examination

| Eye findings | Frequency (%) |
|----------------------------|---------------|
| Reading problems | |
| • Yes | 3(10.7) |
| • No | 25(89.3) |
| Visit eye clinic | |
| • Yes | 2(7.1) |
| • No | 26(92.9) |
| Refractive problems | |
| ○ Myopia | 1(3.6) |
| ○ Myopic astigmatism | 1(3.6) |
| ○ Presbyopia | 1(3.6) |
| • Retinopathy | 4 (14.2) |
| • Glaucoma | 2 (7.1) |
| • Jaundice | 8(28.6) |

*One subject had both refractive error and retinopathy

Table 3 showed that development of refractory error and retinopathy was affected by patient's age (P value =0.030 and 0.005) respectively). Patients' gender and educational status were not found to be determinants of development of refractory error, retinopathy and glaucoma. Those who were beyond 30 years were found to be at a higher risk of having sickle cell retinopathy (p= 0.03).

4. DISCUSSION

Sickle cell disease (SCD) is the most common genetic disease worldwide. Due to better understanding of the disease and improved quality of care, patients with SCD have an increased life expectancy, which has led to emergence of complications that manifest with aging. Ocular complications when not detected early, can be severe enough to result in blindness, which may be of sudden onset [9].

Most of the patients were below 30 years and this was similar to a study in India [24]. This was probably because more patients were referred from the paediatric clinic. Males were more than

females. There is no sex predilection in sickle cell disease as it is not a sex linked disease. Some other studies have also reported higher number of females [11,22,23,24].

About a 3rd of the patients had an ocular anomaly despite the small sample size. This is higher when compared with other studies [11,23,22]. This suggests a high prevalence of ocular anomaly in our study group. This might be due to the poor habit of routine eye check among our sickle cell patients as documented in our study. It is very important to sensitize them on the need to have routine eye examinations so as to detect ocular anomalies early and prevent its deleterious effects.

Tortuosity of retinal vessels were seen in 14.2% of our patients. This is said to occur due to arteriovenous shunting from the periphery of the retina. Relatively similar findings were made in other studies [11,22].

Retinal vascular tortuosity is a common finding on fundal examination [27]. It is a feature of non-proliferative SCD retinopathy which is said to occur following vasoocclusion, leading to retinal hypoxia, ischemia, infarction, neovascularization and fibrous vascularization [27]. A similar study done at Ibadan reported upto 70% of retinopathy amongst their patients and this was higher in males [28]. We did not find gender as a determinant for retinopathy. SCD retinopathy was common in patients above 30 years and this was found to be statistically significant. Similar reports have also been documented [23,28].

Glaucoma has been reported in SCD patients [29]. Two patients (7.1%) had increased cup to disc ratio and were tagged glaucoma suspects. A glaucoma suspect is defined as a person who has one or more clinical features or risk factors that increase the possibility of developing glaucomatous optic nerve degeneration [30,31] Such patients should be monitored closely depending on clinical judgement [32]. It is said that red cell sickling in the aqueous humour leads to obstruction of outflow channels that could cause raised intraocular pressure leading to glaucoma [33]. Prevalence of glaucoma appeared to be more in our patients, compared to other studies [22,24]. Age, sex and educational status were not found to be determinants of development of glaucoma in this study. Although age and sex have generally been identified as determinants of glaucoma [34],

there is paucity of information on their role in sickle cell disease.

Refractive errors have also been documented in SCD patients [26]. 10.8% of our patients had refractive errors. This is also similar with reports from other studies [25].

In Nigeria, early stages sickle cell disease is not detected early due to lack of facilities for new born screening program for early diagnosis of SCD. This makes it difficult to detect early signs of ocular complications as the disease progresses before diagnosis is made.

Table 3. Demographic variables of respondents and ocular findings

| Refractive error | Yes | No | P value |
|-------------------------|------------|-----------|----------------|
| Age group | | | |
| <10 | 0(0.0) | 8(32.0) | 0.030 |
| 10 – 19 | 1(33.3) | 6(24.0) | |
| 20 – 29 | 1(33.3) | 4(16.0) | |
| 30 – 39 | 0(0.0) | 7(28.0) | |
| 40 – 49 | 1(33.3) | 0(0.0) | |
| Sex | | | |
| Male | 2(66.7) | 15(60.0) | 0.823 |
| Female | 1(33.3) | 10(40.0) | |
| HLE | | | |
| Primary | 0(0.0) | 12(48.0) | 0.151 |
| Secondary | 2(66.7) | 5(20.0) | |
| Tertiary | 1(33.3) | 8(32.0) | |
| Glaucoma | | | |
| Age group | | | |
| <10 | 1(50.0) | 7(26.9) | 0.601 |
| 10 – 19 | 0(0.0) | 7(26.9) | |
| 20 – 29 | 1(50.0) | 4(15.4) | |
| 30 – 39 | 0(0.0) | 7(26.9) | |
| 40 – 49 | 0(0.0) | 1(3.8) | |
| Sex | | | |
| Male | 1(50.0) | 16(61.5) | 0.747 |
| Female | 1(50.0) | 10(38.5) | |
| HLE | | | |
| Primary | 1(50.0) | 11(42.3) | 0.678 |
| Secondary | 0(0.0) | 7(26.9) | |
| Tertiary | 1(50.0) | 8(30.8) | |
| Retinopathy | | | |
| Age group | | | |
| <10 | 0(0.0) | 8(30.8) | 0.005 |
| 10 – 19 | 0(0.0) | 7(26.9) | |
| 20 – 29 | 0(0.0) | 5(19.2) | |
| 30 – 39 | 1(50.0) | 6(23.1) | |
| 40 – 49 | 1(50.0) | 0(0.0) | |
| Sex | | | |
| Male | 1(50.0) | 16(61.5) | 0.747 |
| Female | 1(50.0) | 10(38.5) | |
| HLE | | | |
| Primary | 0(0.0) | 12(46.2) | 0.103 |
| Secondary | 0(0.0) | 7(26.9) | |
| Tertiary | 2(100.0) | 7(26.9) | |

HLE: highest level of education

Table 4. Age and SCD retinopathy

| Retinopathy | Age | | Total n (%) | X ² (p-value) |
|-------------|------------|-----------|-------------|--------------------------|
| | ≤30 n (%) | >30 n (%) | | |
| Yes | 0 (0.0) | 4 (50.0) | 4 (14.3) | 11.667 (0.003) |
| No | 20 (100.0) | 4 (50.0) | 24 (85.7) | |
| Total | 20 (100.0) | 8 (100.0) | 28 (100.0) | |

5. CONCLUSION

In conclusion, 32.1% of sickle cell patients had ocular complications of sickle cell disease, while prevalence of retinopathy was found to be 14.2%. This study was limited by the few number of patients recruited for the study as well as inadequate facilities for more extensive ophthalmologic assessment. That not withstanding, there is a very important need to sensitize the patients and care givers on the importance of routine ocular examination starting from childhood so as to avert the undesirable effects of sickle cell disease on the eyes. Physicians managing these patients also should be encouraged to refer them to Ophthalmologists for regular eye checks.

DISCLAIMER

This manuscript was presented in a Conference. Conference name: 24th Congress of the European Hematology Association. Available link: https://pdfs.journals.lww.com/hemisphere/2019/06001/OCULAR_MANIFESTATION_S_OF_SICKLE_CELL_DISEASE__A.2177.pdf?token=method|ExpireAbsolute;source|Journals;ttl|1579593843699;payload|mY8D3u1TCCsNvP5E421JYK6N6XICDamxByyYpaNzk7FKjTaa1Yz22MivkHZqjGP4kdS2v0J76WGANHACH69s21Csk0OpQi3YbjEMdSoz2UhVybFqQxA7IKwSUIA502zQZr96TQRwhVlocEp/sJ586aVbcBFItKNKo+tbuMfL73hiPqJliudqs17cHeLcLbV/CqjIP3IO0jGHIHQtJWcICDdAyGJMnpi6RibEJaRheGeh5z5uvqz3FLHgPKVXJzdVypCnIIS26ArdAaCL/y0Y768Pcffznrpg1c3zza5AWs=;hash|CWvXB3pL56jsRREA/qsfqA==

CONSENT

As per international standard or university standard written patient consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Ethical approval was obtained for the study from the ethics committee of Chukwuemeka Odumegwu Ojukwu University Teaching Hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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