Original research article

Ocular Manifestations in Sickle Cell Patients at a Tertiary Care Set up of Western Odisha: Cross Sectional Study

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Abstract

Introduction: Sickle cell disease (SCD) is the most common genetic disease worldwide. SCD can affect virtually every vascular bed in the eye and can cause blindness in the advanced stages. **Objectives:** To determine the prevalence and patterns of ocular manifestations in patients of sickle cell disease attending VIMSAR, Burla and to correlate these manifestations with haematological parameters. **Methods:** The study was conducted among 51 subjects in four months duration. The sickle cell patients with disease duration of more than 10 years and indoor patients admitted for sickle cell crisis in General Medicine and Pediatrics ward were included in the study. Hematologic investigations were done and ophthalmic investigations such as visual acuity, silt lamp bio-microscopy and fundoscopy was done and compared. **Results:** The study depicts that out of 51 study subjects, prevalence of positive Proliferative Sickle Cell Retinopathy (PSR) in the study population was 13.72%. The hematocrit values were lower in positive PSR cases and higher in negative PSR cases. These difference in values were statistically significant ($p < 0.05$).**Conclusion:** Sickle cell retinopathy is a significant health problem, hence routine awareness campaign should be organized in sickle cell institute regarding the need of early interventions which could protect them from dreadful complications.

Keywords: Sickle Cell Disease, Proliferative Sickle Cell Retinopathy, Hematocrit, Fundoscopy

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] The cumulative gene frequency of haemoglobinopathies in India is 4.2%. With a population of over 1 billion and a birth rate of 28 per 1000, there are over 42 million carriers and over 12,000 infants are born each year with a major and clinical significant haemoglobinopathy.[2,3,4] 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] The other ocular manifestations are secondary

glaucoma, angoid streaks, retinopathy, and retinal artery occlusion. Autoinfarction of the orbital bones has been reported rarely. It can lead to acute proptosis, periorbital pain, limited motility, potentially compressive optic neuropathy, and orbital compression syndrome (OCS).[10,11] Vascular occlusion in the peripheral retina in sickle cell disease results in peripheral arteriolar obstruction with the development of arterio-venous fistulae and proliferative retinopathy.[12] SCD is widely prevalent in Western Odisha and VIMSAR caters to a large group of such patients. Considering the deleterious effects of sickle cell disease on the eyes, we felt it necessary to determine the prevalence and patterns of ocular manifestations in patients of sickle cell disease attending VIMSAR, Burla and to correlate these manifestations with hematological parameters. These findings may serve as tools for creating more awareness as well as improving patient management of ocular manifestations in SCD patients.

Materials and Methods:

(a)*Study type:* Cross sectional study
(b) *Place of study:* VSS Institute of Medical Sciences and Research (VIMSAR)**,** Burla, Odisha
(c)*Study setting:* Department of Opthalmology in collaboration with Sickle Cell Institute, Community Medicine, Pediatrics and General Medicine Department of VIMSAR, Burla.
(d) *Study duration*: Four months, November 2019- February 2020
(e)*Study subjects*: The sickle cell patients with disease duration of more than 10 years coming to Sickle Cell Institute for follow up were included in the study. The indoor patients admitted for sickle cell crisis in General Medicine and Pediatrics ward were also included in the study.
(f) Sample size and sampling technique: 51 patients were recruited by consecutive sampling method over a period of four months.
(g)*Method of data collection*: The study subjects were those who had Sickle Cell Disease for more than 10 years and had come for a routine checkup at Sickle Cell Institute and patients admitted for sickle cell crisis in Medicine and Pediatric ward. These patients were advised for regular blood investigations and routine eye checkup in the Department of Ophthalmology. An informed consent was obtained from the patients' care-givers (for the paediatric age group) and the adult patients. A pre-tested semi-structured questionnaire was administered to the study subjects by the interviewer. The questionnaire had two parts: The socio-demographic 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.
(h) *Inclusion criteria*: All the sickle cell patients with 10 years disease duration coming regularly to sickle cell institute for follow up and the patients admitted for sickle cell crisis in General Medicine and Pediatric ward were included in the study.
(i) Exclusion criteria:
Patient with Sickle cell trait, Thalassemia and haemoglobinopathies other than sickle cell disease were excluded from the study.
(j) *Study tools and techniques*: Routine blood investigation like CBC,HPLC.
OPD evaluation- Slit lamp, Fundoscopy, Optical Coherence Tomography(OCT), Perimetry, Fundus Fluorescein Angiography (FFA).
(k) *Exposure variables*: Hemoglobin (Hb%), Total RBC count, Red Cell Distribution Width (RDW), Total White Blood Cell Count (TWBC), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Platelet count.
(l) *Outcome variables*: (i). Anterior segment (ii) Posterior segment

Anterior segment

- Conjuctiva- linear enlargements, truncated vascular segments
- Iris- vascular occlusions, atrophic scars, neovascularization of optic disc

Posterior segment

- Retina- venous tortuosity
- Epiretinal membrane, Angiod streaks, Arterial occlusions,Venous occlusions.
- Haemorrhage- Salmon patches
- Proliferative Retinopathy: new vessels presenting characteristics fan shape structure.

(m) ***Statistical analysis-*** Percentages of various ocular manifestations in SCD patients and their hematological parameters were collected and put into a statistical format and SPSS software was used for statistical analysis of the data.

Results:

Table 1: Age and Sex distribution of Sickle Cell Retinopathy patients (N=51)

Female					Male			
Age (in years)	**No. of female**	**% from total female**	**No. of + *PSR**	**% female in total +PSR**	**No.of male**	**% from total male**	**No.of + PSR**	**% male in total +PSR**
10-19	8	30.76%	1	14.28%	14	56	2	28.57%
20-29	5	19.23%	1	14.28%	5	20	1	14.28%
30-39	7	26.93%	0	0	0	0	0	0
40-49	2	7.69%	0	0	3	12	0	0
50-59	4	15.38%	0	0	3	12	2	28.57%
Total	**26**	100	2	28.57%	**25**	100	5	71.42%

(*PSR- Proliferative Sickle Cell Retinopathy)

Table no 1 depicts that out of 51 study subjects, prevalence of positive PSR in the study population was 7(13.72%). 26 (49.01%) of study subjects were female and 25 (50.98%) male.Out of total positive PSR patients, 5(71.42%) were found to be male. It was observed that equal prevalence (28.57%) of positive PSR was seen in males of (10-19years) and (50-60 years) age group.

Table 2: Proliferative Sickle Cell Retinopathy (PSR) and Hematological parameters (N=51)

Parameters	PSR	N	Mean	Std. Deviation	Std.Error Mean	t-value	p-value
Hb%	Positive	7	6.83	4.15	1.57	2.45	0.02,S,p<0.05
	Negative	44	9.182	1.67	0.257		
Total RBC	Positive	7	2.35	0.73	0.27	2.012	0.047,S,p<0.05
	Negative	44	4.81	0.79	0.119		
RDW	Positive	7	22.83	3.64	1.37	2.3	0.045,S,p<0.05
	Negative	44	18.56	3.19	0.48		
Total WBC	Positive	7	6	3.62	1.37	2.36	0.33,NS,p>0.05
	Negative	44	7.489	2.48	0.37		
MCV	Positive	7	101.47	12.134	4.58	2.364	0.014,S,p<0.05
	Negative	44	93.67	8.77	1.322		
MCH	Positive	7	30.6	1.41	0.53	2.063	0.636,NS,p>0.05
	Negative	44	30.975	3.81	0.57		
MCHC	Positive	7	33.1	3.08	1.16	2.361	0.018,S,p<0.05
	Negative	44	33.925	2.05	0.31		
Platelet Count	Positive	7	217.43	78.18	28.54	2.228	0.77,NS,p>0.05
	Negative	44	227.54	108.56	40.82		

Table no.2 suggests that the hematological parameters were found to be directly related to the sickle cell retinopathy status of the patients. The hematocrit values were lower in positive PSR cases and higher in negative PSR cases. These difference in values were statistically significant ($p < 0.05$).

Table 3: Ocular changes in positive Proliferative Sickle Cell Retinopathy *(n=7)

Ocular manifestations Fundus in general	Sickle Cell disease (No. of cases with ocular changes)	Percentage (%)
Major retinal changes	4	57.14%
Hemorrhages in the periphery	0	0
Neovascularization	2	28.57%
Iridescent glistening vessels	0	0
Peripheral vessel deposits	1	14.28%
Choroiditis	0	0
Total (51 study subjects)	7	100%

(* *Out of 51 study subjects (N), 7 subjects (n) had positive PSR with ocular manifestations)*

In Table no 3, out of all positive PSR patients, 57.14% developed major retinal vessel changes. Neovascularization and Peripheral vessel deposits were seen in 28.57% and 14.28% patients respectively. The major retinal changes found in positive PSR cases were AV crossing, Vascular sheathing, Arterial narrowing and Venous tortuosity.

Table 4: Ocular changes and haemoglobin concentration (N=51)

Haemoglobin range	Total cases (N=51)	No. with ocular changes (n=7)	Percentage (%)
0-5 gm/dl	3	3	100
6-10 gm/dl	32	3	9.375
11-15 gm/dl	16	1	6.25

Table no 4 represents that positive PSR patients having very low haemoglobin level were more susceptible for ocular changes.

Discussion:

Sickle cell haemoglobinopathy is widely prevalent genetic disorder in Western Odisha. 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. [16]

The present study was conducted amongst the 51 sickle cell disease patients in four months duration at VIMSAR, Burla. Out of 7 positive PSR patients, 5(71.8%) were male which shows male suffered more from ocular manifestation than female and this kind of similar observation was found in study conducted by Efobi CC etal.[17] 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. [18,19,20,21] Most of the patients in our study who had +PSR were below 30 years and this finding was similar to a study conducted by Efobi CC etal [17] and Rautray K . [21]

In the present study, major retinal vessel changes 4 (57.14%); neovascularization 2 (28.57%) and peripheral vessel deposits 1 (14.3%) were found in patients with positive PSR. Study conducted by Condon PI and Serjeant GR [13] reported peripheral vessel disease 93.4% and major retinal vessel changes in 10.5% of Hb. SS cases, retinal hemorrhage (2.6%) and tortuosity and dilatations of capillary network with micro-aneurysmal formation and

neovascularisation (39.5%) in the Hb-SS cases of his study. In contrast there were no cases of retinal hemorrhages in the present study. Roy MS etal [22] in his study found that the MCHC was generally higher in severely affected patients, this association was not statistically significant (p=0.08). But in the present study MCHC values were lower in positive PSR cases and higher in negative PSR patients and this difference in value was statistically significant(p= 0.018).

Conclusion:

In the present study, out of 51 Sickle Cell Disease patients, 7 (13.7%) patients had Proliferative Sickle Cell Retinopathy with ocular manifestations. VIMSAR, Burla is an apex healthcare institution, hence it is difficult to follow up each and every sickle cell disease patient for sickle cell retinopathy .So proper administrative measures should be taken to channelize these patients between Department of Ophthalmology and Sickle cell Institute. It is a wake up call to understand the 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. Early initiation of routine ocular examination for SCD patients will be beneficial to prevent these complications. Counseling by Sickle Cell Institute professionals, General Practitioners and Pediatricians, to sickle cell disease patients (SS) should be done for regular ophthalmologic examinations even if there are no external signs and symptoms.

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