Research Article

Ocular manifestations in sickle cell disease (SCD) in children

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Abstract

Introduction: Sickle cell disease (SCD) is autosomal recessive inherited condition characterized by presence of anomalous haemoglobin **'S'** in the erythrocytes. Patients with SCD inherit an abnormal haemoglobin which becomes insoluble when deoxygenated and so distorts the red cells and cause tissue infarction[1,2,3]. The organs mainly affected are spleen, the bones, the kidney, the lung and the skin. But any organ may be involved and the eyes are not exemption. Hence the study is taken up to find ocular manifestation in SCD in children. **Aims and Objectives:** To find out prevalence, nature and outcome of ocular manifestation in SCD in children's. **Material and Methods:** This prospective study was conducted in pediatrics department of tertiary care hospital from Oct 2000 to April 2002. The study group includes SCD patients admitted in pediatrics ward and patients attending SCD speciality clinics, who were electrophoretically confirmed for diagnosis of sickle cell haemoglobinopathy. A detail history, clinical examination and routine investigation were done in each case. A systematic ophthalmological examination was meticulously done in every case which includes visual acuity, intraocular tension measurement, slit lamp examination and fundus examination**.** **Observation and Results:** A total of 204 cases of SCD, who were electrophoretically confirmed for diagnosis of sickle cell haemoglobinopathy were enrolled during study period, out of which 120(58.82%) patients were homozygous **"SS"** and 84(41.17%) patients were heterozygous **"AS"** for SCD. 95(46.56%) of the patients were between age group of 9 to 12 years, 58(28.43%) were between 6-8 years and 58(28.43%) were between 2-5 years, male to female ratio of 1.4:1. Out of total 204 cases, 165 (80.88%) were from Buddhist community and less number of patients were from Kunbi, Teli, Gonda, Kosthi, Gowari, Sonar, Thakur and Muslim community. The most common type of crisis in both Haemoglobin 'SS" and Haemoglobin'AS' patients was Vasoocclusive crisis followed by haemolytic and sequestration crisis. No patient had Aplastic crisis in the present study. 166(81.37%) had pallor, 83(40.68%) patients had icterus, 88(43.13%) patient had hepatomegaly and 94(46.07%) of patients had splenomegaly. Out of 204 cases, 49(40.83%) homozygous"SS" and 15 (17.85%) heterozygous "AS" were symptomatic for eye and the most common type of symptom in both "SS" and "AS" was headache followed by pain in eye. In the present study, 168(82.35%) patients had normal vision in both eyes, 22(10.78%) patients had refractive error and 13(6.37%) patients were not cooperative. 30% SS patients and 2.38% AS patients had conjunctival sign. Raised intraocular tension was found in one case of homozygous SCD patient.1 patient of sickle cell trait had central retinal artery occlusion which later developed to complicated cataract. Fundus abnormality was found in 6 patients. Fluoroscein angiography done in 7 patients, out of which 6 were normal and 1 had central retinal artery occlusion. **Conclusion:** The prevalence of ocular manifestation was more in Homozygous "SS" patients compared to Heterozygous "AS" patients. The most common age group was 9-12 years with male to female distribution of 1.4:1. Among Community, Buddhist was most commonly and vasoocclusive crisis was most common presentation. Headache was most common symptom and Conjunctival sickling sign was found to be most common sign in ocular manifestation in SCD in childrens.

Keywords: Sickle Cell Disease (SCD), Ocular manifestation, Homozygous 'SS', Heterozygous 'AS'.

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Sickle cell disease (SCD) is autosomal recessive inherited condition characterized by presence of anomalous haemoglobin **'S'** in the erythrocytes. Patients with SCD inherit an abnormal haemoglobin which becomes insoluble when deoxygenated and so distorts the red cells and cause tissue infarction[1,2,3]. The organs mainly affected are spleen, the bones, the kidney, the lung and the skin. But any organ may be involved and the eyes are not exemption. The ocular manifestation of SCD is

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manifestation of sluggish blood flow, intravascular sickling and occlusion of vessels[4]. The sickling sign were described right from the conjunctiva to the retina. The effects on ocular tissue include dilatation and segmentalization of conjunctival vessels, segmental iris atrophy with occluded vessels and neovascularization, vitreous haemorrhages that become organized by fibrovascular proliferative membrane from retinal vessels[4]. Retinal changes can be categorized as non-proliferative or proliferative changes. Non proliferative changes include retinal vessels tortuosity, salmon patch haemorrhages, deposits of glistening iridescent granules and black sunburst lesions. Proliferative changes include sea fans, vitreous haemorrhages and retinal detachement[5]. The retinopathy of sickle cell disease is a striking feature of the SCD[6]. The conjunctival sign (multiple, short, comma shaped or curlicued capillary segments towards lower fornix) is almost pathognomic of clinically significant sickle cell disease and was most prevalently seen in in patient with homozygous sickle cell anaemia and was absent in heterozygous sickle cell trait[7,8].

MATERIALS AND METHODS

This prospective study was conducted in pediatrics department of tertiary care hospital from Oct 2000 to April 2002. The study group includes SCD patients (either homozygous sickle cell anaemia or heterozygous sickle cell trait) admitted in pediatrics ward and patients attending SCD speciality clinics, who were electrophoretically confirmed for diagnosis of sickle cell haemoglobinopathy. A detail history, clinical examination and routine investigation were done in each case. A systematic opthalmological examination was meticulously done in every case which includes external ocular examination with help of torch light, visual acuity, intraocular tension measurement, slit lamp examintion and fundus examination. The details of ocular examination were recorded in predesigned and pretested performa.

OBSERVATION AND RESULTS

A total of 204 cases of SCD who were electrophoretically confirmed for diagnosis of sickle cell haemoglobinopathy were enrolled during study period.

Table 1: Age, Sex and Haemoglobin Electrophoresis distribution

Sr. No	Age Group (yrs)	Sex		Haemoglobin Electrophoresis		No of patients
		Male	Female	SS	SA	
1.	2-5	32	26	36	22	58(28.43%)
2.	6-8	26	25	25	26	51(25%)
3.	9-12	61	34	59	36	95(46.56%)

In present study 58 patients (28.43%) were in age group of 2-5 years, out of which 32 were male and 36 females. 51 patients (25%) were in age group of 6-8 years, out of which 26 were males and 25 females. 95 patients (46.56%) were in age group of 9-12 years, out of which 61 were males and 34 females. The above table also shows that 120 patients (58.83%) had homozygous and 84 patients (41.17%) had heterozygous sickle cell disease. (Table 1)

Table 2: Caste distribution

Sr. No	Caste	No of patients(n=204)	Percentage (%)
1.	Buddhist	165	80
2.	Teli	8	3.92
3.	Kunbi	11	5.39
4.	Gonda	3	1.47
5.	Kosthi	3	1.47
6.	Gowari	1	0.49
7.	Sonar	2	0.98
8.	Thakur	1	0.49
9.	Muslim	10	4.90

In the present study out of 204 cases, 165 (80.88%) were from Buddhist community and less number of patients were from Kunbi, Teli, Gonda, Kosthi, Gowari, Sonar, Thakur and Muslim community.(Table 2)

Table 3: Type of crisis

Sr. No	Type of Crisis	Haemoglobin 'SS' patients (%)	Haemoglobin 'SA' patients (%)
1	Vaso-occlusive	102(85%)	64(76.19%)
2	Sequestrtion	14(11.66%)	0(0%)
3	Haemolytic	36(30%)	2(2.38%)
4	Aplastic	0(0%)	0(0%)

Above table shows that the most common type of crisis in both Haemoglobin 'SS" and Haemoglobin 'AS' patients was Vasoocclusive crisis followed by haemolytic and sequestration crisis. No patient had Aplastic crisis in the present study. (Table 3)

Table 4: General Examination

Sr. No.	Findings	No of patients	Percentage (%)
1.	Pallor	166	81.37
2.	Icterus	83	40.68
3.	Splenomegaly	94	46.07
4.	Hepatomegaly	88	43.13

In the present study 166 patients (81.37%) were pale, 83 patients (40.68%) had icterus, 94 patients (46.07%) had splenomegaly and 88 (43.13%) patients had hepatomegaly. (table 4)

Table 5: Eye symptoms **a):** Table showing number of patients having eye symptoms in the present study

Sr. No	Haemoglobin pattern	No of patients	Percentage (%)
1.	Haemoglobin'SS'	49	40.83
2.	Haemoglobin'AS'	15	17.85

b): Table showing various eye symptoms in the present study

Sr. No.	Eye symptoms	Haemoglobin'SS'	Haemoglobin'AS'
1.	Diminition of vision	3	2
2.	Pain in eyes	20	2
3.	Headache	35	12
4.	Watering of eyes	0	0

Table 5a shows that 49(40.83%) patients out of Haemoglobin SS were having eye symptoms and 15 (17.85%) patients out of 84 patients of haemoglobin AS were symptomatic for eye. Table 5b shows that headache was present in 35 patients of symptomatic 49 patients Haemoglobin SS and 12 patients of symptomatic 15 patients of Haemoglobin AS. Diminision of Vision in 3 patients of Haemoglobin SS and 2 patients of Haemoglobin AS. Pain in eyes in 20 patients of Haemoglobin SS and 2 patients of Haemoglobin AS.

Table 6: Ocular findings a) Acuity of Visions:

Sr. No	Acuity of visions	No of patients	Percentage (%)
1.	Normal	168	82.35
2.	Decrease of one eye	1	0.49
3.	Decrease of both eye	22	10.78
4.	Not cooperative	13	6.37

In the present study, 168 patients had normal vision in both eyes, 22 patients had refractive error, 1 patient had central retinal occlusion with complicated cataract and 13 patients were not cooperative. (Table 6a)

b) Conjunctival sign

i) Conjuctival sickling sign

Sr. No	Haemoglobin pattern	No of Patients	Percentage
1.	Haemoglobin "SS"	36	30
2.	Haemoglobin "AS"	2	2.38

Table 6b(i) shows that 36 patients (30%) out of 120 patients with homozygous sickle cell amaemia had conjuctival sickling sign. 2 patients (2.38%) out of 84 patients with heterozygous sickle cell trait had conjuctival sign,

ii) Other conjunctival signs

Pallor present in 166 patients (81.37%), icterus in 83 patients (40.68%). Bitot spots was present in 3 patients and conjuctival xerosis in 1 patient.

Intraocular tension: Intraocular tension was raised in 1 patients

Nasolacrimal passage: 5 patients had regurgitation from nasolacrimal passage.

Lens:Complicated cataract was found in 1 patient.

Fundus findings:

Fundus changes	No of patients
Pallor of disc	1
Papilloedema	3
Macular exudates	0
Macular microaneurysm	1
Venous Tortusity	0
Venous fullness	0
Salmon patch	0
Black sunburst	0
Whitening of retina	0
Mottled brown area	0
Peripheral retinal remodeling	0
Neovascularization	0
Retinal detachement	0
Angioid Streaks	0
Retinal hemorrhage	1
Retinal vein thrombosis	0
Negative fundus	200

Fluorescein Angiography: Fluorescein Angiography was done in 7 patients, out of which 6 patients were normal and 1 patient had left central artery occlusion.

Ocular manifestation due to sickling phenomenon

Sr. No	Ocular manifestation	Haemoglobin SS	Haemoglobin AS	Total (n=204)
1.	Conjuctival sickling sign	36	2	38(18.62%)
2.	Glaucoma	1	0	1(0.49%)
3.	Central retinal artery occlusion	0	1	1(0.49%)
4.	Fundus findings	0	1	1(0.49%)

In the present study 39 (19.11%) patients out of 204 had ocular findings due to sickle cell disease. 38(18.62%) of patients had conjuctival sickling sign. 1 patient had glaucoma and 1 patient had central retinal artery occlusion of one eye.

DISCUSSION

A total of 204 cases of SCD who were electrophoretically confirmed for diagnosis of sickle cell haemoglobinopathy were enrolled during study period. 49 patients out 120 patients of Haemoglobin SS were having eye symptoms and 15 patients out of 84 patients of haemoglobin AS were symptomatic for eye. Thus the **Prevalence** of ocular manifestation for Homozygous 'SS' and Heterozygous 'AS' found in our study are 40.83% and 17.85% respectively. In present study 58 patients (28.43%) were in age group of 2-5 years, out of which 32 were male and 36 females. 51 patients (25%) were in age group of 6-8

years, out of which 26 were males and 25 females. 95 patients (46.56%) were in age group of 9-12 years, out of which 61 were males and 34 females.

Sickle cell trait "AS" and Ocular changes in different studies:

Sr. No.	Authors	Years	Ocular changes
1.	Kabakow[9]	1955	Central retinal artery occlusion
2.	Shapiro and Baum[10]	1964	Gluacoma
3.	Welch and Goldberg[11]	1966	Sunburst, optic atrophy, papilloedema
4.	Stein and Gay[12]	1970	Acute chorioretinal infarction

Sickle cell anaemia "SS" and ocular changes in different studies

Sr. No.	Authors	Years	Ocular findings
1.	Cook[13]	1930	Retinal haemorrhages
2.	Paton[7]	1961	Conjunctival sign
3.	Condon and Serjeant[14]	1972	Tortusity and dilatation of retinal vessels

Age and ocular changes in different studies

Sr. No.	Authors	Years	Comment
1.	Levine and Kaplan[15]	1965	Peripheral fundus changes at age of 5 years
2.	Welch and Goldberg[11]	1966	Fundus changes in agr group of 21-27 years
3.	Stein and Gray[12]	1970	Acute chorioretinal infarction in infants

Ocular Manifestation in present study with respect to other studies

Conjunctival sign: In present study 36(30%) patients out of 120 patients with homozyous Sickle cell anaemia and 2(2.38%) out of 84 patients had conjuctival sign. Comer *et al*[16] (1964) observed conjuctival sickling sign in 30 of 33 patients with homozygous sickle cell anaemia and in none of 50 patients with with either sickle cell trait or normal haemoglobin. Mansour F. Armoly *et al* [4](1974) proposed that conjuctival sign in SCD was proportional to percentage of sickled cells. Nagpal *et al* [17](1977) observed a statistically significant positive correlation between severity of conjunctival sickling sign and the counts of irreversibly sickled cells. In the study of Al-salem *et al*[18] (1990) 7 patients (15.2%) with homozygous sickle cell anaemia had conjunctival sign. In study done by Kaimbo Wa Kaimbo D *et al* [19](2000) conjunctival sign was seen in 32 % patients with homozygous sickle cell disease and in study of Al-hazzaa S *et al*[20] (2001), 5(24%) with sickle cell trait had conjunctival sign which correlate with our study. The Possible explanation for low incidence of conjunctival sickling sign in sickle cell trait "AS" compared to sickle cell anaemia "SS" may be presence may be this low quantity of haemoglobin 'S' and secondly associated haemoglobin with haemoglobin S in sickle cell trait, which affects the gelation process of haemoglobin. Visual acuity: In the present study, 168(82.35%) patients had normal vision in both eyes, 22(10.78%) patients had refractive error and 13(6.37%) patients were not cooperative. In the study of J. F Talbot *et al* [21] (1982), decreased visual acuity seen in 88 childrens, while in 8 patients visual acuity could not be elicited. Similarly in the study of Al Salem *et al*[18] (1990) visual acuity was decreased in 93.7% of patients. Our present study correlates with above two studies. Gluacoma: In the present study, 1 patient with homozygous sickle cell anaemia had gluacoma . In the study of Abiose A[22] (1978), al- saleem5 (1990), Kaimbo Wa D[19] (2000), no case of gluacoma was observed. However Goldberg[23] (1979) reported gluacoma in 3 patients with sickle cell trait. It is because the red cells after deoxygenation get converted into the sickled cells which block trabeculae and cause gluacoma. **Central Retinal artery occlusion:** In present study 1 patient of sickle cell trait had sudden loss of vision of left eye, which shows left central artery occlusion on flurescein angiography. Stein and Gray[12] (1970) reported a case of a 6 month old Negro male infant with sickle cell trait, who presented with extreme dehydration, pneumonia, acute renal failure and bilateral central retinal artery occlusion. Similarly Conrad and Major[24] (1996) reported a case of central artery occlusion in 32 years old Negro with sickle cell trait. Occlusion of small artery by deformed sickled cell is explainable but occlusion of large artery by sickling phenomenon only, is not explainable. The exact mechanism of occlusion of central retinal artery is not known. Lens: In the present study 1 patient had cataract of left lens. Fundus examination: In present study 6 patients had abnormal fundus, with pallor of disc in 1 patient, papillodema in 3 patients, macular micro aneurysm in 1 patient and retinal hemorrhages in 1 patient.

Fundus findings in different study

Sr. No	Authors	Years	Changes in the fundus
1.	Cook[13]	1930	Peripheral fundus changes
2.	Harden[25]	1937	Tortuosity and dilatation of retinal veins
3.	Klinfelter[26]	1942	Tortuosity and dilatation of retinal veins
4.	Ray and cecil[27]	1944	Tortuosity and dilatation of retinal veins
5.	Edington[28]	1952	Sickle cell Retinopathy
6.	Goodman[29]	1957	Angioids Streaks
7.	Welch and Goldberg[11]	1966	Neovascular patches

8.	Goldberg[30]	1971	Arteriovenous anastomosis
9.	Condon and Serjeant[14]	1972	Black sunburst
10.	Stevens[31]	1974	Macular vessels abnormalities
11.	Asdousiam[32]	1975	Black sunburst

Retina: In present study no patient had retinopathy associated with SCD. Similarly findings were observed in Al salem M *et al*[18] (1990) and Kaimbo *et al* [19](2000) studies.

CONCLUSION

The prevalence of ocular manifestation was more in Homozygous "SS" patients compared to Heterozygous "AS" patients. The most common age group was 9-12 years with male to female distribution of 1.4:1. Among Community, Buddhist was most commonly affected and vasoocclusive crisis was most common presentation. Headache was most common symptom and Conjunctival sickling sign was found to be most common sign in ocular manifestation in SCD in childrens.

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