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TO ASSESS OCULAR BIOMETRIC AND FUNDOSCOPIC CHANGES IN BETA-THALASSEMIA MAJOR PATIENT

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ABSTRACT

Introduction: Thalassemia are the most common single gene disorder worldwide. Mutations involving the beta globin gene in beta-thalassemia cause disruption in red blood cell maturation leading to ineffective erythropoiesis and multi-system involvement, including eye. In beta-thalassemia patient abnormal erythropoiesis leads to severe anemia, due to which repeated blood transfusions are required to maintain hemoglobin level at or above 10mg/dl. Multiple blood transfusions and ineffective erythropoiesis.

Aims: To study the prevalence of ocular abnormalities in beta thalassemia major patients.

Materials and Methods: The present study was a Institution based descriptive, cross-sectional study. This Study was conducted from one and half year (February 2020 -August 2021) at Department of Ophthalmology North Bengal Medical College and Hospital.

Result: The present study showed that among 75 study subjects 93.3% had refractive errors in either eye and 6.7 % were emmetropic. The present study also showed that among 150 eyes 6% eyes had emmetropia, 69.66% had hypermetropia, 38.66 % eyes had myopia and 45.33% eyes had astigmatism. The mean axial length in our study was 21.78 + 0.73 mm, The mean anterior chamber depth (ACD) in our study was 3.00 + 0.48 mm, The mean (SD) lens thickness in right eye was 4.05 (±0.58) mm and in left eye were 3.90 ((±0.68) mm. In our study the mean (SD) K1 in right eye was 44.61 (±1.49) Diopter and in left eye were 44.87 ((±1.68) Diopter, whereas the mean (SD) K2 in right eye was 44.84 (±1.62) Diopter and in left eye were 45.07 ((±1.43) Diopter.

Conclusion: We included 75 patients of Beta Thalassemia Major patients. The male population was 56% and female were 44%. The mean age of the study subjects was 9.53 + 3.36 years (range 6 to 18 years).

Keywords: Beta thalassemia, Ocular Biometric and Fundoscopic Changes.

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INTRODUCTION

Thalassemia are the most common single gene disorder worldwide. Mutations involving the beta globin gene in beta-thalassemia cause disruption in red blood cell maturation leading to ineffective erythropoiesis and multi-system involvement, including eye.

The World Health Organization (WHO) has suggested that around 5% of the world population are carrier for different inherited disorders of hemoglobin[1]. About 1.5% of world's population carries the beta thalassemia gene. Worldwide, hemoglobin E beta Thalassemia patients comprise of approximately 50 per cent of those affected with severe beta thalassemia[2]. The average prevalence of beta thalassemia is 35 to 45 million carriers in a population of 1.21 billion people according the Census of India 2011. According to 2018 census India has a burden of 100000 patients with Thalassemia syndrome.

Thalassemia along with other haemoglobinopathies constitute the most common non-communicable genetic disease in India. It causes high morbidity and moderate to severe hemolytic anemia among vulnerable segments of the society like infants, children, adolescent girls, pregnant women.

The occurrence of thalassemia trait and sickle cell hemoglobinopathies in India varies between 3-17% and 1-44% respectively. Among Hb varriants, Hb D is more common in northern part of India (particularly Punjab) and Hb S in tribal areas. Hb E (comprising of Hb E homozygous state, Hb E heterozygous state or Hb E trait and other double heterozygous state with Hb E) is the commonest hemoglobin variant in the northeastern region of India with a prevalence of 7-50%. Hemoglobin E has a prevalence of 3-10% in West Bengal [3] and is believed to be harbored mostly by Rajbanshi community, who form the majority of the local population living in the northern part of the state, commonly known as 'North Bengal'.

In beta-thalassemia patient abnormal erythropoiesis leads to severe anemia, due to which repeated blood transfusions are required to maintain hemoglobin level at or above 10mg/dl. Multiple blood transfusions and ineffective erythropoiesis. lead to increased intraocular iron load. Although iron is a crucial element for synthesis of neurotransmitter, Optic nerve myelination and visual phototransduction cascade, excessive iron has toxic effect. It has been found to cause oxidative injury to the retina. It has shown when intravenous iron sulfate is administered to adult mice (C57BL/6), resulting to increase in superoxide radicals in photoreceptor, lipid peroxidation of the photoreceptors and retinal degeneration. Secondary hemochromatosis or acquired hemochromatosis, results from iron intake during the multiple blood transfusion to the patients of beta thalassemia. Defects in Bruch's Membrane underlying the RPE, called ANGIOID STREAKS, can also be observed in these patients. Beside ocular Biometric changes, other ophthalmological changes are decrease in visual acuity, decrease in contrast sensitivity, ocular surface disorder, retinal venous tortuosity, lens opacity, Retinal Pigment Epithelial (RPE) degeneration, retinal mottling and Optic Neuropathy[4].

Thalassemia patients have characteristic expansion of bone marrow, which cause long bone deformities and typical craniofacial changes. Frontal Bossing of skull, prominent malar

eminence, depression of the bridge of the nose, tendency to mongoloid slant of the eye and hypertrophy of the maxillae are seen I beta Thalassemia patients[5].

Ocular growth is intimately related to the growth of the growth of the adjacent bony orbit. As Thalassemia patients has characteristic craniofacial bony changes, causing abnormal bony orbit, which subsequently can cause distinctive ocular biometry[6].

MATERIALS AND METHODS

STUDY DESIGN: Institution based descriptive, cross-sectional study.

STUDY SETTING: Department of OPHTHALMOLOGY, North Bengal Medical College & Hospital, Darjeeling, West Bengal.

PLACE OF STUDY: Department of Ophthalmology North Bengal Medical College and Hospital.

PERIOD OF STUDY: One and half year (February 2020 -August 2021).

STUDY POPULATION: Patients presenting at Eye Department and Paediatrics Department North Bengal Medical College and Hospital which is located at sub-Himalayan region of West Bengal.

SAMPLE SIZE: 75 patients of beta-thalassemia major.

SAMPLING TECHNIQUE: By simple random sampling method, patients fulfilling the inclusion criteria.

INCLUSION CRITERIA:

- Beta-Thalassemia major patients who tested positive for haemoglobin electrophoresis by HPLC and dependent on blood transfusion, in hemodynamically stable condition.
- Patients 5 years of age or older.

EXCLUSION CRITERIA

- Presence of other hemoglobinopathies.
- Anaemia due to other causes.
- Congenital ocular anomalies.
- Previous ocular trauma, or ocular surgery,
- Any systemic disease like Diabetes, Hypertension.
- Uncooperative patients.
- Acute ocular infections.

RESULT AND DISCUSSION

The present study was a Institution based descriptive, cross-sectional study. This Study was conducted from one and half year (February 2020 to August 2021) at Department of Ophthalmology North Bengal Medical College and Hospital.

Beta-thalassemia major is one of the common hemoglobinopathies in Indian subcontinent with incidence being 11,316 per year. As stem cell transplant is out of reach for majority, these children are managed by multiple transfusions. One of the important complications of regular transfusion regime is iron overload. Iron overload affects almost all organs including eye.

In this study from 2019-2021, 75 children diagnosed with Beta-thalassemia major on regular transfusion were examined for ocular changes. The present study was conducted to investigate

ocular biometric and fundoscopic characteristic changes of the eyes of patients with beta thalassemia major and find any association between these parameters and other factors.

In this present study, the sample size was 75 which is comparable to the study conducted by Similarly other studies also had comparable sample size Adnan A et al [7] included 43 children with thalassemia major. Gartganis S et al studied ocular findings among 29 patents of thalassemia major[8].

Mean age for children for this study is 9.53 years, similar to works of earlier Indian authors. Ocular changes are seen more in children above 10 years and rarely in children less than 7 years, suggestion the association of duration pf disease with ocular complications. This has reported by <similar Indian studies [9].

In present study mean visual acuity in logMAR was 0.4+ 0.15. Adnan A et al reported in their study the mean best corrected visual acuity was 1.34 + 0.75 in Thalassemia major and 1.08 + 0.28 in controls. It was lower than 0.1logMAR unit in 10 (23.2%) children with Thalassemia major and 2 (4.2%) in controls, and the difference was statistically significant. ($p<0.05$). The study reported that thalassemia major patients may be affected by visual acuity[7]. Ali T et al[10] found that among 84 Thalassemia patients visual acuity was affected in 13 patients and decrease in visual acuity and decrease in visual acuity was found to be significantly associated with type of thalassemia ($p<0.5$).

Other ocular changes seen in children with beta Thalassemia major are in retina of the eye. Retinal changes in children with beta thalassemia major were note ranging from 78.8%[10] to 16.6 %(96). In this study, retinal changes were seen in 49.3% of children. However our method of detection was subjective qualitative assessment of the vessels or the RPE, and we could not quantify the RPE degeneration or the vessel tortuosity mathematically. However the assessment was done by a single observer (experienced ophthalmologist). Retinal changes consist of degeneration of RPE, retinal venous tortuosity, and angoid streaks. Incorvaia C et al carried out a retrospective study on 36 thalassemia patients and reported that mean venous length in thalassemia patient group was significantly greater than in the control group ($p< 0.001$)[11]. Deewan P et al conducted a study to determine the presence of ocular abnormalities in multi-transfused children with beta Thalassemia major receiving Desferrioxamine and found that dilated and tortous vessels was found in 8%(2 out of 25 patients)[12]. This has been observed in this study too. Retinal changes correlate with higher serum ferritin levels, increasing number of transfusions and age of child.

The present study showed that among 75 study subjects 93.3% had refractive errors in either eye and 6.7 % were emmetropic.

The present study also showed that among 150 eyes 6% eyes had emmetropia, 69.66% had hypermetropia, 38.66 % eyes had myopia and 45.33% eyes had astigmatism.

The present study also determined the mean biometric parameters of 150 eyes of our study subjects. The mean axial length in our study was 21.78 + 0.73 mm, while Nowroozzadeh M H et al reported it as 23.01 + 0.12 mm in their study[6]. The accepted values of average axial length is

24.2 mm (range 22.9 to 26.4) in an emmetropic eye[13]. Thus the mean axial length calculated in our study was lesser than accepted value as well as that reported in previous studies.

The mean anterior chamber depth (ACD) in our study was 3.00 + 0.48 mm, while Nowroozzadeh M Het al reported the mean as 3.53 + 0.06 m in their study[6]. The accepted values of average central anterior chamber depth is about 3.15 mm (range 2.6 to 4.4 mm)[14]. Thus the mean anterior chamber depth in our study was lesser than the average accepted value as well as that reported in previous studies.

The mean (SD) lens thickness in right eye was 4.05 (±0.58) mm and in left eye were 3.90 ((±0.68) mm in our study while Nowroozzadeh M H et al reported the means as 4.01 + 0.11 mm in their study[6]. The accepted value of average lens thickness is around 4 mm in our study age group (5 to 18 years)[13]. Thus the mean lens thickness in our study was more than the average accepted value as well as previous reported values.

In our study the mean (SD) K1 in right eye was 44.61 (±1.49) Diopter and in left eye were 44.87 ((±1.68) Diopter, whereas the mean (SD) K2 in right eye was 44.84 (±1.62) Diopter and in left eye were 45.07 ((±1.43) Diopter. Similar observations were made by Nowroozzadeh M H et al in their case control study, where they reported the average keratometry as 44.02 + 0.24 Diopter[6] .

Nowroozzadeh M H et al[6] also reported in their study that , compared with controls, thalassemia patients had a shorter axial length (23.01 + 0.12 mm versus 23.46 + 0.12 mm p= 0.035), thicker crystalline lens (4.01 + 0.11 mm versus 3.87 + 0.1 mm p=0.046) and steeper average Keratometry value (44.02 + 0.24 Diopter) Thus in our study eyes mean axial length (21.78 + 0.73 mm) was shorter than previous study as well as accepted value, anterior chamber depth (3.00 + 0.48 mm) was less than previous study and in the lower normal range of accepted value for our age group and lens thickness (4.05 + 0.58 mm) was greater than previous study.

CONCLUSION

We included 75 patients of Beta Thalassemia Major patients. The male population was 56% and female were 44%. The mean age of the study subjects was 9.53 + 3.36 years (range 6 to 18 years).

We studied ocular biometric parameters and fundoscopy of these patients. We observed that the mean axial length was 21.87 + 0.73 mm, mean anterior chamber depth was 3.03 + 0.47 mm and mean lens thickness was 4.27 + 1.09 mm. Compared to accepted values in this age group, the eyes in beta thalassemia major, has shorter axial length. Anterior chamber depth was in the lower normal range. Lens thickness was more, compared to the normal accepted value for this age group. In our study, study the mean (SD) K1 in right eye was 44.61 (±1.49) Diopter and in left eye were 44.87 ((±1.68) Diopter, whereas the mean (SD) K2 in right eye was 44.84 (±1.62) Diopter and in left eye were 45.07 ((±1.43) Diopter. Ocular Biometric parameters demonstrated no correlation either with age or serum ferritin level.

The refractive status of these patients were determined. Among the study eyes (n=150) majority were hypermetropic (55.33%), followed by emmetropic (6 %), and the least were myopic (38.67%).

Retinal changes are seen in 34% of cases, with majority being early adolescents and serum ferritin level > 2500ng/ml, thus contributing to decrease visual acuity.

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Table: Distribution of study subjects according to refractive error of right and left eye

		Frequency	Percentage
Refractive error of right eye	**Emmetropic**	05	6.7
	Myopic	30	40.0
	Hypermetropic	40	53.3
	Total	75	100.0
Refractive error of left eye	**Emmetropic**	04	5.4
	Myopic	28	37.3
	Hypermetropic	43	57.3
	Total	75	100.0

Table: Distribution of study subjects according to Axial length, Anterior chamber depth, Lens thickness (mm), K1 (Diopter) and K2 (Diopter)

		Mean	Standard deviation
Axial length (mm)	**Right eye**	21.78	0.73
	Left eye	21.81	0.72
Anterior chamber depth (mm)	**Right eye**	3.00	0.48
	Left eye	3.03	0.48
Lens thickness (mm)	**Right eye**	4.05	0.58
	Left eye	3.90	0.68
K1 (Diopter)	**Right eye**	44.61	1.49
	Left eye	44.87	1.68
K2 (Diopter)	**Right eye**	44.84	1.62
	Left eye	45.07	1.43

Table: Distribution and association between serum ferritin and fundus changes of right and left eye

		Serum ferritin			χ2value, df, p value
		0-1499	**1500-2499**	**>2500**	
Fundus changes (Right eye)	Absent	13 (36.1)	16 (44.4)	07 (19.4)	0.288, 2, 0.866
	Present	12 (30.8)	18 (46.2)	09 (23.1)	
Fundus changes (Left eye)	Absent	15 (39.5)	17 (44.7)	06 (15.8)	1.987, 2, 0.370
	Present	10 (27)	17 (45.9)	10 (27.1)	

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		Frequency	Percentage
Refractive error of right eye	**Emmetropic**	05	6.7
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	Hypermetropic	40	53.3
	Total	75	100.0
Refractive error of left eye	**Emmetropic**	04	5.4
	Myopic	28	37.3
	Hypermetropic	43	57.3
	Total	75	100.0