

Original Research Article

Ocular abnormalities in patients with beta-thalassemia: a prospective study

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ABSTRACT

Background: Beta thalassemia is severe genetic blood disorder caused by mutation in the gene encoding for the beta chains of haemoglobin and individuals with beta thalassemia require life-long red blood cell transfusions to survive which leads to hemosiderosis and affects all the organs in the body including eyes. The study aims to study ocular manifestations in these children and its correlation with age and serum ferritin levels.

Methods: A descriptive cross-sectional study was done in government medical college Jammu in 2014-2015 on 67 BTM children. Children below 3 years of age and with pre-existing ocular abnormalities, infections were excluded from the study. Ocular examination was done for any major eye abnormality, congenital malformations or trauma. Retinal examination was done using direct and indirect ophthalmoscope, changes were recorded.

Results: 47.76% of children belonging to the group: 5-10 years, while only 5.97%, i.e., 4 in number pertained to the age group: >15 years. Lens opacity was seen in 29.85% of children. 31 children showed changes in retinal activity, while decreased visual acuity was also observed in 17 children. Iris was significantly affected in children with serum ferritin >2500 ng/ml. Even greater lenticular changes and opacities were observed in children with higher serum ferritin levels (>4500 ng/ml).

Conclusions: As life expectancy for beta-thalassemia patients extends, regular monitoring of the progression of disease and symptoms to detect early changes in their ocular system is recommended, to achieve a better quality of life for this patient group.

Keywords: Beta-thalassemia, Ocular Abnormality, Blood Transfusion, Ferritin

INTRODUCTION

Thalassemia is severe genetic blood disorder caused by a mutation in the globin gene. Abnormal globin chains lead to the excessive destruction of red blood cells.¹ The phenotypes of homozygous or genetic heterozygous compound beta-thalassemia include thalassemia major (TM) and thalassemia inter-media (TI). Individuals with thalassemia major usually come to medical attention with in the first two years of life. These patients require lifelong RBC transfusion at regular intervals to survive. Thalassemia inter-media includes patients with milder symptoms, who present at an older age and do not require regular transfusions.² More than 42,000 new-borns are affected by beta-thalassemia every year, world-wide.

Without blood transfusion, beta thalassemia major (TM) cause death amongst infected children before the age of three.³ Although transfusions can prevent death and decrease mortality, iron accumulated from transfused red blood cells can lead to organ failure.⁴ Iron chelation treatment, to reduce iron store in the body and improve the long-term survival rate of the patients with TM, is considered a mandatory adjuvant therapy.

Repeated blood transfusions lead to siderosis. Increase in intraocular iron has been shown to cause oxidative injury to the retina particularly retinal pigment epithelium (RPE). RPE is the chief site of iron deposition. Angioid streaks due to the defects in Bruch membrane underlying the RPE can be observed in these patients. But it is

difficult to differentiate the effects of iron overload, intraocular haemorrhages and chelation therapy on the retina. It is possible that these patients have retinal overload.⁵

Ocular manifestations are seen in patients suffering from thalassemia. They range from decreased visual acuity, colour vision anomalies, night blindness due to cataract, visual field defects and optic neuropathy. Western studies reported ocular changes in figures of 41.3 and 71%.⁶ Indian studies have shown figures of 40% of lenticular opacities and 33% of decreased visual acuity. Electroretinographic and visual evoked potentials are also affected in children with thalassemia which are very similar to early forms of siderosis bulbi. There is a relative low awareness of these ophthalmic manifestations due to very few studies in Indian populations. Hence the need for the study was felt.⁷

The objective of this study is thus, to evaluate visual acuity, anterior segment fundus and retina, and to correlate these findings with age and serum ferritin in these children.

METHODS

There is a descriptive cross-sectional study done in government medical college Jammu between the years: 2014-2015. Children diagnosed with beta thalassemia major, confirmed by clinical, haematological and electrophoretic studies were included in the study. Children with pre-existing ocular abnormalities, ocular trauma, infections; children below 3 years were excluded from the study. The study was approved by institutional ethical committee. After obtaining informed consent from the patients and or parents' relevant history i.e., age of diagnosis, number of transfusions received annually, serum ferritin levels, chelation therapy, were recorded. Enrolled children were asked about any difficulty in vision, presence of any floaters, grittiness, blurring of vision or any problem if any. Ocular examination was done for any major eye abnormality, congenital malformations or trauma. Visual acuity was tested by Snellen's chart and expressed as fraction. Slit lamp examination was done to see corneal surface changes, anterior chamber and lens. Tear film was examined for break up time (BUT). BUT<10 seconds was taken significant. Fluorescence dye was instilled to see for any erosions and ulcers. Corneal thickness was determined by patchy meter. Retinal examination was done using direct and indirect ophthalmoscope, changes were recorded. Statistical analysis was done using SPSS version 26.0.

RESULTS

67 children diagnosed for BTM were enrolled for the study. The overall age ranged from 3 to 17 years, with maximum number of children belonging to the group: 5-10 years, i.e., 32 NOS or 47.76%, while only 5.97%, i.e.,

4 in number pertained to the age group: >15 years. Only 16 (23.88%) out of total 67 were females (Figure 1).

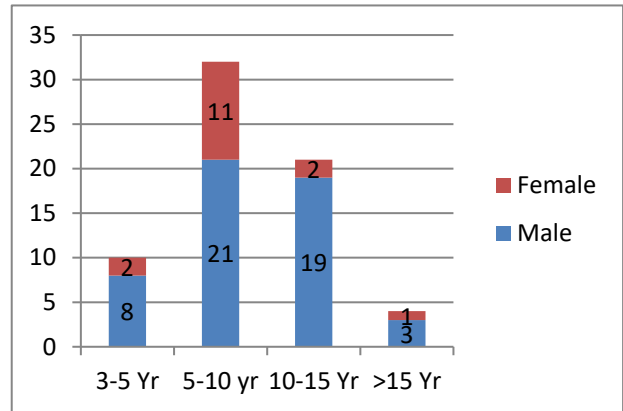


Figure 1: Age-wise and gender-wise comparative distribution.

All the children had irregular chelation treatment and poor compliance. Corneal dryness with break up time less than 10 sec was reported for 17.91% of cases. However, no ulcerations were discovered. Corneal thickness was 530±8.665 um on the average. Lens opacity was seen in 29.85% of children. None of the opacities were visually significant. Heterochromia and mottling were observed in 23.88% of children. However, retinal changes were the most common among the changes in eye part of the subjects, with thinning of disc (n=9), retinal venous engorgement (n=7) vessel tortuosity (n=6) seen significantly. In total 31 children showed changes in Retinal activity. Decreased visual acuity was also observed in as many as 17 children (Table 1).

Table 1: Eye changes seen among study subjects.

Changes seen in the part of the eye	Number of children (%) n=67
Cornea	12 (17.91)
Lens	20 (29.85)
Iris	16 (23.88)
Retina	31 (46.27)
Anterior chamber	2 (2.98)
Visual acuity	17 (25.37)

Majority of subjects had a raised ferritin levels with 37.31% having s. ferritin level 2501 ng/ml or above. (Table 2) It was observed that a significant no of children showed even higher s. ferritin levels of 4501 ng/ml and above with associated complications and eye changes.

Average age for the children with corneal changes was observed to be: 13.98 years, while average age for children with lenticular abnormality was: 11.32 years. The correlation study between various eye changes and Serum Ferritin levels showed insignificant results, however some relation could not be ruled out (Table 3).

Table 2: Serum ferritin levels among study subjects.

Ferritin levels (ng/ml)	Number (%)
0-1500	16 (23.88)
1501-2500	26 (38.8)
2501 and above	25 (37.31)

Table 3: Correlation between serum ferritin levels and certain eye changes.

S. ferritin levels (ng/ml)	Number			
	Corneal Changes	Lenticular opacity	Iris changes	No changes
0-1500	2	2	4	5
1501-2500	4	7	4	1
2501-4500	5	8	6	0
4501 and above	1	3	2	0
P	0.032	0.165	0.061	

Iris changes were seen in 11 males and 5 females. (However, study size with regards to the female children is not sufficient) On comparing with that of lower levels, it is seen that iris was significantly affected in children with serum ferritin >2500 ng/ml. Even greater lenticular changes and opacities were observed in children with higher serum ferritin levels (>4500 ng/ml) (Table 3).

DISCUSSION

Patients with beta thalassemia tend to present different ocular signs: both structural and functional. Jafari et al reported 68.5% of subjects with ocular involvements, while Gartaganis et al reported 41.3% for the same.^{8,9} Although, such frequencies differ among studies worldwide, but correlate to the disease itself, iron overload or the chelating agents used.

During the course of BTM, patients subjected to regular blood transfusions and chelation therapy, do show spectrum of systemic symptoms.¹⁰ Defects in colour vision, night blindness or abnormal dark adaptations are reported in patients receiving daily doses of iron-chelating agents like desferrioxamine for a prolonged period.¹¹ Although iron-chelating agents are reported to be the cause of many ocular changes, most of them in BTM patients can be attributed to the course of disease or severity thereof. This suggests reductions in iron and ferritin levels by iron-chelating agents forming the mainstay of current treatment of BTM. These side-effects can be prevented or controlled by regular examination.

Definitive therapy, like stem cell therapy is generally beyond the reach of the majority in India, therefore, multiple blood transfusions is the only way currently forward. Ocular changes to the children with BTM

correlates to the iron over load due to disease progression and treatment. This presents as a major reason for the higher incidence among children above 10 years of age. Retinal changes, vessel tortuosity and decreased visual acuity observed in our study correspond well to the other similar studies carried out by Taher, Sorcinelli and Gartaganis et al however showed that correlation of eye changes with serum ferritin level was not significant, which is similar to the findings of this as well.¹²⁻¹⁴ About 25.37% of BTM patients had decreased visual acuity, having refractive error, and consistent with other such findings Taneja and Gibson et al.^{15,16}

The limitation of this study is that it was carried out on a relatively small set of patients and that too from lower economic strata. Besides, some results and analysis are based upon limited number of prior studies to bank upon. It can be a foregone assumption that age, diversity of characteristics and physical conditions and differences in beta thalassemia treatment protocols in the past may have confounded the results to some extent. Besides, this study is not in a position to appropriate any type of chelation regimen.

CONCLUSIONS

Except for lenticular opacities, there exist suitable methods for the assessment and monitoring of fundus changes during BTM, and there can be further investigations on the efficacy of iron chelators as well. The association between ocular abnormality and chelator type was beyond the scope of the present study. Hence further prospective investigation with a large sample of thalassemia patients based on the type of chelator they received is recommended. Advances in imaging devices, with increase in resolution, differentiation of variability and reliability, are likely to affect future investigations and estimations for precise individual monitoring for now but, awareness and identification of systemic factors among patients will always play significant part in the disease management. As life expectancy for beta-thalassemia patients extends, regular monitoring of the progression of disease and symptoms to detect early changes in their ocular system is recommended, to achieve a better quality of life for this patient group.

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