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Ocular Manifestations in Multi-Transfused Beta-Thalassemia Patients

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Abstract
Introduction: *Ocular abnormalities are unseen morbidity due to iron overload in thalassemia patients which is being brought into light by our study.*
Aim & objectives: To study the ocular manifestations in transfusion dependent beta-thalassemia major patients and correlate serum ferritin levels and oral chelation therapy with ocular manifestations.
Study Design: *Cross sectional observational study.*
Methods: 52 thalassemia major patients of 5 to 14 years were selected as case group and 30 age matched anaemic patients were taken as a control group. Full medical history, physical and ophthalmological examination including visual acuity, slit lamp examination, fundoscopy. We computed ocular findings with mean serum ferritin level and duration of iron chelating agent. Minitab version 17 was used for computation of statistics.
Results: *Out of 52 thalassemia patients ocular involvement was seen in 31(59.6%) of cases in the form of decreased visual acuity(42.3%), hyperemic disc(34.6%), cup obliteration (23.7%), anterior segment involvement(17.3%) and venous tortuosity (7.6%). The prevalence of ocular abnormalities in control group was 19.4%, which was significantly lower than that in thalassemia patients. High serum ferritin was significantly associated with anterior segment involvement and hyperemic disc.*
Conclusion: *Ocular abnormalities present in thalassemia patients were significantly higher as in control group. So reduction in serum ferritin level by chelation and regular ocular examination is recommended to prevent or delay ocular abnormalities .*
Keywords: *Chelation Therapy, Ferritin, Thalassemia, ocular abnormalities.*

I. Introduction

Beta thalassemia is a genetic disorder and one of the most common hemoglobinopathies. Mutations involving the beta globin gene in β Thalassemia cause disruption in red cell maturation leading to ineffective erythropoiesis and was associated with erythrocyte dysplasia and destruction. As chronic anaemia adversely affects the growth and development of the children, iron accumulation in the tissues due to destruction of the red blood cells, excessive blood transfusion create a negative impact on the organs functions[1].One of the tissues affected by thalassemia major is eyes. Thalassemia patients are taking regular blood transfusion therapy which causes iron overload. Adverse ocular changes may occur as a result of the disease and includes visual defect, cataract, retinal pigment epithelial degeneration, retinal pigment epithelial mottling, retinal venous tortuosity, vitreoretinal haemorrhage, disc changes etc[2].

II. Material And Methods

It was a cross sectional observational study. The study was carried out in the department of Paediatrics and the department of Ophthalmology Gandhi Medical College, Bhopal for duration of 10 months. 52 children diagnosed as beta Thalassemia major patients were enrolled in the study. All children enrolled have been receiving treatment in the form of packed red cell transfusion at a dose of 10 ml/kg body weight in order to maintain their haemoglobin concentration between 9 –11 gm/dl and iron chelating agents were started if the serum Ferritin level was above 1000 µg/dl. To compare the results 30 age matched controls with anaemia were recruited. An informed consent for participation was obtained. Patients with haemoglobin disorders other than beta thalassemia major ,congenital ocular abnormalities and ocular trauma were excluded.

All Thalassemia Major And Control Patients In This Study Were Subjected To The Following:

Full medical history including onset and duration of the disease, frequency of blood transfusions per month, Iron chelating agents dose, duration and compliance. Thorough physical examination performed
Each patient underwent a complete eye examination Bhopal which includes visual acuity, slit lamp examination, fundoscopy. Uncorrected visual acuity was determined monocularly, at 6 meter using snellen's chart, illuminated with luminance of 100 cd/m2. Anterior segment examination was carried out with a (SI.No.SLPS-H1301321 Appasamy associate's-Chennai, India)slit lamp bio microscope. Posterior segment was assessed as follows: both pupils were dilated with 0.5% tropicamide eye drops to view the fundus. Examination of the fundus was then

performed with an indirect ophthalmoscope using a Volk 20 dioptre lens (Indirect Ophthalmoscope, Appasamy associate's-Chennai, India) and direct ophthalmoscope (Neitz halogen ophthalmoscope, Japan). For the purpose of study,we computed ocular findings with mean serum ferritin level, duration and complianceof chelation therapy in thalassemia major patients.

III. Results

Fifty two thalassemia subjects aged 5-14 years and 30 healthy controls aged 5-14 years were evaluated for ocular abnormalities. Among thalassemia major patients 37 subjects (71.1%) were male and 15 subjects (28.8%) were female. The mean age ± standard deviation (SD) of thalassemia patients was 8.40+2.61 SD years. The mean serum ferritin level of thalassemic patients was 2519.96ng/ml, and the mean level of hemoglobin in them was 6.35 ± 0.96 SD g/dl(table no.1)

Table 1-: General profile

Group	Mean Age (Years)	Mean age of diagnosis(years)	Mean Hemoglobin (g/dl)	Mean Serrum ferritin(ng/ml)
Thalassemia major	8.40+2.61SD	3.06+3.29SD	6.35+0.96SD	2519.96
Control	7.80+2.20SD	7.8+2.2SD	7.4+0.62SD	12.07

Table2 -: Ocular manifestation in thalassemia and control group

Manifestations	Thalassemia	Control
No. of patients with ocular involvement	31(59.6%)	6
Decreased visual acuity	22(42.3%)	0
Anterior segment involvement	9(17.3%)	0
Hyperemic Disc	18(34.6%)	0
Cup Obliteration	12(23.07%)	0
Vitreous Opacities	1(1.9%)	0
Macular Edema	2(3.8%)	0
Choroidal Tesselation	2(3.8%)	0
Venous Tortuosity	4(7.6%)	2(6.6%)
Sun Burst Appearance	0	0
Rp Attenuation	0	0
Pale Disc	0	1(3.3%)
Cotton Wool Appearance	0	1(3.3%)
Cup: Disc -0.5	1(1.9%)	0

In our study among fifty two patients ocular involvements were detected in 31 cases (59.6%) in the form of decreased visual acuity(42.3%) which is a most common finding followed hyperemic disc(34.6%), cup obliteration (23.7%),anterior segment involvement(17.3%) and venous tortuosity (7.6%)in descending order. The prevalence of ocular abnormalities in control group was 19.4%.

Table3 -: Ocular Manifestations of Thalassemia major with mean serum ferritin

Ocular Manifestations	No. of Subjects	Mean serum ferritin (ng/ml)	P value
Total no. Cases with Ocular involvement			
Yes	31 (59.62%)	2580.94+1194.76	0.23
No	21 (40.38%)	2294.26+945.60	
Anterior segment involvement			
Yes	9 (17.31%)	3305.43 + 1395.04	0.03
No	43 (82.69%)	2381.72 + 946.43	
Visual Acuity			
Decreased	22 (42.31%)	2602.39 + 1160.85	0.43
Normal	30 (57.69%)	2351.04 + 920	
Venous Tortuosity			
Present	4 (7.69%)	2748.25 + 510.03	0.65
Absent	48 (92.31%)	2498.72 + 1088.71	
Disc Hyperemia			
Present	18 (34.69%)	3056.06 + 1136.84	0.01
Absent	35 (67.31%)	2276.27 + 898.63	
Increased Cup/disc ratio			
Present	1 (1.92%)	4511	-
Absent	51 (98.08 %)	2476.67 +1008.01	
Cup Obliteration			
Present	12 (23.07 %)	2911 + 818.86	0.160
Absent	40 (76.9 %)	2400.47 + 1094	

In the study 31 (59.62%) patients had ocular manifestations with high serum ferritin(table no.3)There was statistically significant difference for mean ferrtin levels in patients with anterior segment involvement and Disc hyperemia.

Table 4 -: Duration of Regular Chelation Therapy of Desirox

Duration	No. of patients on chelation Therapy	Patient on regular Desirox	Patient with ocular findings with Desirox	Odds ratio	P Value
< 2 Years	2 (3.85%)	2 (3.85%)	1 (1.92%)	0.19 (95 % CI: 0.0099 to 3.4734	0.2595
2 – 5 Years	25 (48.08%)	18 (34.62%)	13 (25%)	0.1733 (95 % CI: 0.0179 to 1.6810	0.1305
> 5 Years	20 (38.46%)	14 (26.92%)	14 (26.92%)	13 (95 % CI: 0.6688 to 252.6786	0.0902
Total	47 (90.38%)*	34 (65.38%)	28 (53.85%)*	3.11 (95 % CI: 0.4233 to 22.8665)	0.2647

Odds ratio of patients on Desirox developing ocular manifestations is 3.11. (with 95 % CI: 0.4233 to 22.8665) and p value was 0.2647 . We observed that with increase in duration of chelation therapy there was increase in ocular manifestation but this was not statistically significant(table no. 4)

IV. Discussion

In our study the mean age ± standard deviation (SD) of thalassemia major patients was 8.4+2.61years,this was similar to Adnan Aksoy et al[1] were mean age of study population was 9.31 years.
In our study the mean serum ferritin level of thalassemia major patients was 2519.96 ± 1050.78ng/ml, this was similar to Pooja Diwan et al[3] were mean serum ferritin level of the thalassemia children was 2995.2 ng/ml.
Frequency of ocular involvement in our study was 59.6%.This was in accordance with studies done by Gaba A et al[4] and Taneja et al[5]who reported ocular involvement in 71.4% and 58% of subjects respectively.

We found visual acuity was affected in 42.3% patients ,which was similar to study done by Dalia S.M. et al [6]where decreased visual acuity was seen in 45% and Taneja et al In our study cataract was found in 3.8% of thalassemia major cases. This finding was not consistent with study done by Pooja Diwan et al[3]and Taneja et al[5] where they found cataract in 33% and 44% of thalassemia major cases respectively. This difference was probably due to the reason that other two studies included cases with wide range of age group. In our study Correlation of mean serum Ferritin levels and hyperemic disc was statistically significant (P=0.01).Similar correlation was done by Dalia S.M.et al[6] but no significant correlation was found in their study. Also we found correlation of mean serum Ferritin levels and anterior segment involvement to be statistically significant (P=0.03). Retinal venous tortuosity was observed in 7.6%, this was similar to study done by Pooja Diwan et al[3]and Taneja et al[5]were venous tortuosity was seen in 8% and 11% respectively. In our study we found odds ratio of patients on desirox developing ocular manifestation is 3.1.We observed that with increase in duration of chelation therapy there is increase in ocular manifestations but this was not statistically significant. This was similar to study done by Gosai DK et al[7]in 2014 who reported that duration of deferasirox has no direct relation with ocular anomalies in thalassemia major patients.The increased possibility of ocular manifestations in children with prolonged chelation therapy could be paradox as these children have high duration of disease which can probably explain ocular manifestation.

V. Conclusion

Although all of our thalassemia patients were asymptomatic but large number of ocular abnormalities were detected. Decrease in serum ferritin levels by iron- chelating agents is useful for preventing adverse effects associated with iron overload and regular ophthalmological evaluation to detect early changes in their ocular system due to disease and chelating agentis is recommended, in order to achieve a better life quality for this patient group.

VI. Limitation

The direct effect of chelation therapy on eyes could not ne analayed as all the patients of high age were being on chelation therapy.

Conflit of interest
There are no conflicts of interest.

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