BMJ Open Ophthalmology

Burden of ocular abnormalities in patients with beta thalassaemia: a cross-sectional study

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To cite: Baig R, Zahid N, Kausar F, *et al*. Burden of ocular abnormalities in patients with beta thalassaemia: a cross-sectional study. *BMJ Open Ophthalmology* 2023;**8**:e001293. doi:10.1136/bmjophth-2023-001293

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjophth-2023-001293).

Received 16 March 2023
Accepted 21 June 2023

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ABSTRACT

Introduction In Pakistan, the reported carrier rate of thalassaemia is estimated to be 5%–8% with 5000 new patients diagnosed every year. Several known systemic complications of beta thalassaemia major have been studied, but no studies are conducted to assess ocular complications among these patients from our population.

Methods It was a cross-sectional study design conducted at three private and public sector centres in Pakistan. We recruited 203, 11–17 years old children with beta thalassaemia major in our study. Frequency of overall ocular complications such as retinal pigment epithelium degeneration, visual field defects, increased retinal vascular tortuosity, lenticular opacities, anterior segment abnormality, etc among beta thalassaemia patients were verified by an ophthalmologist.

Results On univariate analysis male gender (prevalence ratio (PR): 1.023 (0.903 to 1.160), OGTT levels (PR: 0.99 (0.978 to 1.003) and serum calcium levels (PR: 0.716 (0.616 to 0.936)) were significantly associated with ocular complications. However, on multivariable analysis after adjusting for covariates we observed that the prevalence of ocular complications was 88% higher in males as compared with females. Moreover, with every one unit increase in serum calcium levels the prevalence of ocular complications were decreased by 24%.

Conclusion Our study results showed that the frequency of ocular complications in beta thalassaemia children was 22.7%. Male gender was a risk factor for ocular complications among children with beta thalassaemia. However, high calcium levels among these patients were found to be protective for ocular complications.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Ocular manifestations are seen in patients suffering from thalassaemia. They range from decreased visual acuity, colour vision anomalies, night blindness due to cataract, visual field defects and optic neuropathy. Western studies have reported ocular changes in figures of 41.3% and 71%. Scientific knowledge on ocular complications in thalassaemia major (TM) children exists, however, conducting a study in Pakistan is essential to understand the unique characteristics and burden of these complications in the local population. The study can provide insights into risk factors, impact on visual health and inform targeted interventions for better management and care.

WHAT THIS STUDY ADDS

⇒ This study has provided population-specific data on the prevalence and characteristics of ocular complications in TM children within the Pakistani population. This data is valuable for healthcare providers and policymakers to understand the burden of ocular complications and develop targeted interventions. Through this study, we have identified local risk factors of ocular complications.

INTRODUCTION

Background

Thalassaemia

Thalassaemia is among the most common single gene diseases in the world.[1] Beta thalassaemia is an array of hereditary blood disorders which are characterised by abnormalities beta globin chain synthesis of haemoglobin resulting in variable phenotypical outcomes which can range from clinically asymptomatic individuals to severe anaemia. The worldwide incidence of symptomatic beta thalassaemia patients is estimated to be at 1 in 100 000 per year and every 1 in 10 000 people in the European Union. There have been three main types described so far: thalassaemia major (TM), thalassaemia minor and thalassaemia intermedia.[2] The prevalence of beta thalassaemia is increasingly high in developing parts of the world and in those multiethnic cities of the west that host a large immigrant population.[3] Approximately 1.1% of couples all over the world face the risk of having a child with a haemoglobin disorder, which on the whole results in 2.7 per 1000 births being affected. Therefore, approximately 5.3%

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There will be several implications of this study; the study can help healthcare providers better understand the needs of these patients and develop tailored care strategies to improve their ocular health outcomes. By identifying the prevalence and types of complications in the Pakistani population, healthcare professionals can implement targeted screening programmes to detect and manage ocular issues at an early stage among children with thalassaemia major (TM). This study can also guide healthcare providers in making informed decisions regarding interventions, follow-up protocols and referral pathways to ensure optimal care for affected individuals. The study findings can support policymakers and healthcare administrators in identifying areas of need, such as specialised eye care facilities, trained personnel and equipment, to address the ocular health requirements of this specific population. Moreover, the study's results can also contribute to public health interventions aimed at preventing and reducing the burden of ocular complications in TM children. This can involve educational campaigns to raise awareness about the importance of regular eye examinations, the risks of complications and the benefits of early intervention and management.

of the world's population currently is a carrier of a significant haemoglobin variant.[4] These haemoglobin disorders are highly prevalent in South Asia. The large population sizes of south Asian countries (India, Pakistan and Bangladesh, Sri Lanka) and high levels of haemoglobinopathies in these countries makes it a significant public health concern. On an estimate, 17 million beta thalassaemia carriers are reported in India and a figure of 8 million thalassaemia carriers has been pitched in Pakistan. These numbers are thought to be 3 million in Bangladesh and 0.5 million in Sri Lanka.[4] In Pakistan (Sindh) the frequency of mutation in IVS I-5 (G>C) allele was reported to be 31% and 28.6% for 619-bp deletion. Moreover, in Baluchistan, 78.9% of alleles were found out to be IVS I-5 (G>C). However, in Codon 8/9 (+G) was the most common beta thalassaemia allele in both Punjab (38.6%) and neighbouring Khyber Pakhtunkhwa (47.7%).[5] Pakistan shows a carrier rate of 5%–8% approximately, with 5000 new patients diagnosed with TM each year.[6]

Thalassaemia and systemic diseases

TM is identified as a serious medical and psycho-social dilemma. The series of events in this illness largely depends on adequate blood transfusions along with other therapeutic facilities. The life expectancy of these patients is generally thought to be lower than the normal population, but, many patients in developed countries have managed to survive upto their fifth decade of life. Certain systemic diseases are associated with TM such as growth retardation, delay in sexual maturity, hormonal issues such as thyroid, parathyroid and sex hormone deficiencies, diabetes, cardiovascular and heart function disorders. The cause of systemic disorders associated with TM is multifactorial which includes: chronic hypoxia and anaemia, iron overload, decreased somatomedin activity, multiple endocrinopathies, poor socioeconomic status, and ethnic or racial factors.[6]

Thalassaemia and ocular involvement

In order to prevent systemic complications secondary to siderosis, desferrioxamine and deferriprone are commonly used iron chelating agents. This leads to chelation of metals such as iron, zinc, copper, cobalt and nickel in the retina. Nickel and cobalt are the most essential metals for normal functioning of the retina and lack of these metals causes several ocular abnormalities.[6] The disease itself can lead to several adverse changes in the apart from iron overload, or iron chelators. These can range from reduced visual acuity, colour vision abnormalities and nyctalopia, to cataract formation, retinopathy,optic neuropathy and visual field defects.[6 7] The frequency of ocular involvement in beta thalassaemia varies between 41.3% and 85% across different studies.[8–11] Ocular manifestations in beta thalassaemia can be attributed to the disease itself, iron overload or the use of chelating agents. Common ocular findings from different studies include ocular surface disease indicated by tear function parameters and lens opacities reported in 9.3%–44% of cases. Lenticular opacities and retinal pigment epithelium (RPE) degeneration are positively associated with the use of desferrioxamine and deferriprone, respectively. Ocular fundus abnormalities consistent with pseudoxanthoma elasticum (PXE), such as peau d'orange, angioid streaks, pattern dystrophy-like changes and optic disc drusen, have been observed in seven studies. Patients with PXE-like fundus changes tend to be older, and age and splenectomy are strongly associated with the presence of these changes. Retinal vascular tortuosity, independent of PXE-like fundus changes, has been detected in 11%–17.9% of cases and is correlated with aspartate aminotransferase, haemoglobin and ferritin levels. In addition to fundus examination, other techniques like fundus autofluorescence and electrophysiological testing (electroretinogram and electro-oculogram) can provide insights into the early stages or more extensive damage in the eyes of individuals with beta thalassaemia.[7]

In Pakistan, the reported carrier rate of thalassaemia is estimated to be 5%–8% with 5000 new patients diagnosed every year.[5] Several known systemic complications of beta TM have been studied. Scientific knowledge on ocular complications in TM children exists, however, conducting a study in Pakistan is essential to understand the unique characteristics and burden of these complications in the local population. The study can provide insights into risk factors, impact on visual health and inform targeted interventions for better management and care.

Therefore, this study was planned with the following objectives.

Objectives

1. To determine the overall frequency of ocular complications such as (RPE degeneration, visual field defects, lenticular opacities, anterior segment abnormality) in patients with beta thalassaemia.
2. To identify factors associated (sociodemographic factors, use of iron chelating agents, no of transfusions, spleenectomy) with ocular complications in patients with beta thalassaemia.

METHODOLOGY

Study design

This cross-sectional study was conducted in accordance to the principles of good clinical practice as laid by Declaration of Helsinki.

Study participants and site

The study participants were recruited from Fatimid Foundation, Garden East, Karachi which is the pioneer non-for profit, voluntary blood transfusion service in Pakistan. It provides free of cost blood transfusion and medical services to patients with thalassaemia and haemophilia. The ophthalmological consultation and examination was done at Aga Khan Hospital and Patel Hospital, Karachi with the study duration of 6–12 months after the ERC approval.

Eligibility criteria

Individuals of adolescent age group (11–17 years) consenting/assenting to study participation of either gender with the diagnosis of transfusion dependent thalassaemia including all sickle beta thalassaemia, hbE/thal, HbD/thalassaemia intermedia, registered with Fatimid Foundation for transfusion and medical services were included.

Patients with any congenital ocular abnormalities such as aniridia (partial or complete absence of the iris in one or both eyes), anophthalmia (absence of one or both eyes), coloboma (optic fissure that did not close in one of the structures of the eye—iris, retina, lens or choroid, microphthalmia (one or both eyes are smaller than average) and optic nerve hypoplasia were excluded from the study as these could result in overestimation of the results.

Sample size

We required a minimum sample size of 203 patients with beta thalessaemia based on the anticipated frequency of ocular complications among such patients ranging from 3.7% to 58%,[9–13] with a precision of 5%, a level of significance of 5% while also taking into account a 10% non-response rate.

Sampling technique

This study used purposive sampling for selection of the participants. The key objective of purposive sampling was to focus on population features that were of interest to the researcher, who can answer the study questions. Our target population, that is, patients with beta TM was approached and screened using our eligibility criteria. Those who fulfilled our eligibility criteria and gave informed consent were enrolled in the study (online supplemental figure 1).

Data collection

Clinical and haematological reports were evaluated by our trained data collector and the diagnosis of beta thalassaemia was made based on these. The ocular complications were evaluated by an ophthalmologist by ocular examination including Snellens chart—visual acuity, Ishihara—colour vision testing, slit lamp examination with examining anterior segment (cornea, lens, iris) and fundus examination (posterior segment, that is, retina, optic disc, macula). Optical coherence tomography (OCT) to look for layers of the retina, optic nerve, peripapillary retinal nerve fibre layer thickness and macular volume, visual field test for central and peripheral vision or to diagnose glaucoma or fundus fluorescein angiography for evaluating tiny blood vessels in the eye were undertaken when necessary as per the examining ophthalmologist.

Outcome of interest

Frequency of overall ocular complications such as RPE degeneration, visual field defects, increased retinal vascular tortuosity, lenticular opacities, anterior segment abnormality and refractive error among beta thalassaemia patients were verified by an ophthalmologist.

Independent variables

The information on socio demographics such as; age, gender, ethnicity, education, per capita family income. Serum ferritin levels, Hb levels, SGPT levels, frequency of transfusion, frequency of iron chelation, type of iron chelation, splenectomy will be evaluated from the medical records. History on comorbids such as heart disease, liver disease, endocrinopathies (thyroid disease and parathyroid disease). Diabetes, hepatitis C, HIV and family history ocular diseases was collected by a trained data collector.

Plan of analysis

Data were analysed by SPSS V.12. The descriptive for quantitative variables were reported as mean±SD/median (IQR) depending on the normality of the data. The relationship of these variables with the outcome (ocular complications) was assessed by independent t-test or Mann-Whitney U test as appropriate. The categorical variables were reported as frequency and percentages and were assessed by χ^2 test of independence or Fisher exact test. Unadjusted and adjusted PR with their 95% CI were reported to determine the association of independent variables with ocular complications by Cox regression algorithm. A p value of <0.05 was considered significant throughout the study.

Table 1 Overall sociodemographic characteristics of beta thalassaemia patients

Variables	Frequency	Per cent
Gender		
Male	109	53.7
Female	94	46.3
Age of patient		
Median (IQR)	14 (12–17)	
Education status		
No education	111	54.7
Primary	75	36.9
Secondary	17	8.4
Language		
Sindhi	50	24.6
Urdu	27	13.3
Pashto	32	15.8
Punjabi	8	3.9
Balochi	42	20.7
Saraiki	25	12.3
Hindko	6	3
Memoni	9	4.4
Bengali	4	2
Household monthly income median (IQR)		
PKR/USD	PKR 17 000 (15 000–20 000)/US$75 (66–88)	
Family history of ocular complications		
Yes	68	33.5
Parents	11	
Siblings	44	
Maternal/paternal uncle	3	
Maternal/paternal aunt	2	
Grand parents	6	
Paternal cousin	2	

Table 2 Types of treatment

Variables	Frequency	Per cent
Frequency of transfusion		
Weekly	10	4.9
Every 15 day	189	93.1
Every month	4	2.0
Type of iron chelation		
Deferasirox	68	33.5
Deferiprone	121	59.6
Desferrioxamine	11	5.4
Splenectomy		
Yes	16	7.9
No	187	92.1
Total	203	100.0

RESULTS

Table 1 shows the overall sociodemographic factors of the study participants. We recruited 203 participants about 109 (53.7%) were males and 94 (46.3%) were females. Their age ranged from 12 to 17 years, that is, median 14, 36.9% had acquired primary education, 8.4% had acquired secondary education while 54.7% had no education. A higher proportion of the participants mother tongue was Sindhi, that is, 24.6%. PKR 17 000 (15 000–20 000)/US$75 (66–88). 1.5% of the participants had their own business. Out of 203 about 68 participants had a first-degree family history of ocular complications.

Table 2 shows the type of treatment that the participants received. A higher proportion of participants received blood transfusion every 15 days (93.1%). More than half of the participants received deferiprone for iron chelation. About 7.9% of the participants had splenectomy.

Table 3 depicts the frequency of ocular complications in beta thalassaemia patients. Overall 22.7% of the patients with beta thalassaemia had ocular complications. Among these 11.8% had optic nerve abnormality; 10.3% had retinal macula abnormality; 5.9% had decreased colour vision; 7.9% had retinal periphery abnormality; 4.9% had lens opacity; 1% had corneal opacity and disc hyperaemia, respectively and 0.5% had iris abnormality. The refractive error was found in 5 (2.3%) patients. Amblyopia was in three patients, anisometropia in one patient and myopia in one patient.

Table 4 shows the relationship of sociodemographic, biochemistry and treatment related factors with ocular complications among patients with beta thalassaemia patients. It was observed that a significantly higher proportion of males (70%) had ocular complications vs females (30%). A significantly high median serum ferritin levels 5113 (3140–6477) were observed in patients with ocular complications vs those with no ocular complications 3857 (2495–4950). While a significantly low median calcium levels were seen in patients with ocular complications 8.75 (7.87–9.29) versus those with no complications 9.01 (8.51–9.46). However, there was no significant difference in age, household monthly income, educational status, ethnicity, family history of ocular complications, biochemistry and treatment related factor among patients with and without ocular complications.

Table 5 depicts univariate and multivariable analysis to assess the association of various demographic, disease and treatment related factors with ocular complications in beta thalassaemia patients. On univariate analysis male gender (prevalence ratio (PR): 1.023 (0.903 to 1.160), OGTT levels (PR: 0.99 (0.978 to 1.003) and serum calcium levels (PR: 0.716 (0.616 to 0.936)) were significantly associated with ocular complications. However on multivariable analysis after adjusting for covariates we observed that the prevalence of ocular complications was

Table 3 Frequency of ocular complications in beta thalassaemia patients

Ocular complications	Frequency	Per cent
Overall ocular complications		
Yes	46	22.7
No	157	77.3
Colour vision decreased		
Yes	12	5.9
No	191	94.1
Cornea opacity		
Yes	2	1.0
No	201	99.0
Lens opacity		
Yes	10	4.9
No	193	95.1
Iris abnormality		
Yes	1	0.5
No	202	99.5
Disc hyperaemia		
Yes	2	1.0
No	201	99.0
Retinal periphery abnormality		
Yes	16	7.9
No	187	92.1
Total	203	100.0
Optic nerve abnormality		
Yes	4	11.8
No	30	88.2
Total	34	100.0
Retinal macula abnormality		
Yes	21	10.3
No	182	89.7
Total	203	100.0

88% higher in males as compared with females. Moreover, with every one unit increase in serum calcium levels the prevalence of ocular complications were decreased by 24%.

DISCUSSION

Overall, we report lower frequency of ocular findings in our patients, that is, 22.7%, both in anterior and posterior segment examinations than in other parts of the world. Gartaganis *et al*[8] reported percentages of 41.3%, Jafari *et al* reported it to be 68.5%,[11] Taneja *et al*[9] put forward a figure of 58%, while Abdel-Malak *et al*,[10] found it out to be 85% (online supplemental figure 2). A lower frequency of ocular problems in our subjects might indicate successful transfusion and chelation therapy in our study population however this protective affect was not statistically significant in our study, This can be explained by relatively lower number of transfusion independent patients in our study which is in line with the study findings of Haghpanah *et al* reported in 2020.[14]

The unaided visual acuity was found normal in 49.5% of participants in our study. Taneja *et al* reported normal visual acuity in 67% of their subjects with the view point that the whatsoever iron-chelating agent was used, it had no influence on the decreased visual acuity, our study's findings were also consistent. Another study on Iranian patients also reported visual acuity of no less than 20/40 in all participants.[14]

In our study males the prevalence of ocular complications were higher in males as compared with females. This is in line with certain relevant studies in literature which have reported slight male preponderance.[8–10] Taneja *et al* report a ratio of 1.25:over females. This is consistent with the studies of Gartaganis *et al*[8] and Gaba *et al*[15] where ratios of 1.07:1 and 1.33:1 were observed, respectively.

Seven out of 203 (6.9%) subjects in our study were found to have lenticular opacities. This value was lower than that reported in the literature. No significant correlation between the occurrence of lens opacity and raised serum ferritin levels or iron chelation therapy was noted. This is in contrast with the results reported by Taneja *et al* which showed a significant level of correlation between occurrence of lens opacities and higher average levels of iron in the serum, along with serum ferritin levels and number of blood transfusions received. Results of relevant studies show this involvement to be as high 9.3% by Aksoy *et al*,[13] 44% by Taneja *et al*,[9] 10% by Abdel-Malak *et al*[10] and 10.2% by Jafari *et al*.[11]

Thirty-one percentage of our patients had retinal abnormalities resembling non-PXE-like manifestations. The frequency of retinal abnormalities in our patients was lower than what was reported in previous studies.[9–11] One important finding of them was of foveal thinning identified on spectral domain-OCT which was found in five of our patients. Similar findings of foveal thinning were also reported by El-Shazly *et al* in 2016 in patients treated with subcutaneous deferoxamine.[16] No significant association between the type of iron chelation used and the detection of foveal thinning was seen in our study. Mentioning the fundus finding, RPE degeneration was detected in only one of our female patient. Other studies have reported up to 17.5%.[10] Taneja *et al* study had postulated RPE changes are somehow related to the type of chelation used, based on their observation that patients who had RPE degeneration had received lesser doses of desferrioxamine as compared with doses of deferriprone suggesting that desferrioxamine might have a protective effect while deferriprone use might be a contributory factor to RPE degeneration. Based on our results, no significant relationship was detected between retinal abnormalities and type of iron chelating therapy used. There are some disputes in the literature regarding the relationship between iron chelation and the frequency of ocular manifestations.[9 17] For accurate

Table 4 Relationship of sociodemographic, biochemistry and treatment related factors with ocular complications among patients with beta thalassaemia patients

	Ocular complication				
	No (n=157)		Yes (n=46)		
	Count	Column N %	Count	Column N %	P value
Sociodemographic factors					
Gender					
Male	77	49	32	70	0.014*
Female	80	51	14	30	
Age of patient					
Median (IQR)	14 (12–17)		14.50 (12–17)		0.652
Educational status					
No education	83	53	28	61	0.355
Primary completed	62	40	13	28	
Secondary completed	12	8	5	11	
Higher secondary or above completed	0	0	0	0	
Household monthly income median (IQR)					
PKR/USD	PKR 18 000 (15 000–20 000)/US$79 (66–88)		PKR 15 000 (15 000–20 000/US$66 (66–88)		0.288
Mother tongue					
Sindhi	38	24	12	26	0.156
Urdu	18	12	9	20	
Pushto	20	13	12	26	
Punjabi	6	4	2	4	
Balochi	36	23	6	13	
Saraiki	23	15	2	4	
Hindko	5	3	1	2	
Memon	7	5	2	4	
Bengali	4	3	0	0	
Family history of ocular complications					
Yes	53	34	15	33	0.855
No	104	66	31	67	
Biochemistry					
Serum ferritin					
Median (IQR)	3857 (2495–4950)		5113 (3140–6477)		0.01†
Haemoglobin levels					
Median (IQR)	8.60 (7.80–9.18)		8.20 (7.65–9.45)		0.713
SGPT					
Median (IQR)	45 (26–68)		47 (30.5–62.5)		0.934
OGTT					
Median (IQR)	99 (93–110)		98 (89.25–110)		0.522
Calcium levels					
Median (IQR)	9.01 (8.51–9.46)		8.75 (7.87–9.29)		0.034†
Treatment					
Frequency of transfusion					
Weekly	9	6	1	2	0.616
Every 15 days	145	92	44	96	
Every month	3	2	1	2	

Continued

Table 4 Continued

	Ocular complication				
	No (n=157)		Yes (n=46)		
	Count	Column N %	Count	Column N %	P value
Type of iron chelation					
Deferasirox	49	32	19	41	0.483
Deferiprone	96	62	25	54	
Defroxamine	9	6	2	4	
Frequency of iron chelation					
Median (IQR)	1000 (500–1000)		1000 (500–1125)		0.359
Splencectomy					
Yes	14	9	2	4	0.312
No	143	91	44	96	

*Significant at p value <0.05 by using chisquare test of independence.
†Significant at p value <0.05 by using Mann-Whitney U test.
OGTT, Oral Glucose Tolerance Test ; SGPT, Serum Glutamic Pyruvic transaminase .

assessment of iron chelating agents' effect on the occurrence of ocular manifestations, a multicentre clinical trial study should be designed. However, researchers are bound by certain ethical considerations such as it is not possible and morally justifiable to stop chelation therapy in one group to compare responses.

Table 5 Univariate and multivariable analysis for assessing factors associated with ocular complications in children with beta thalassaemia patients

	Unadjusted prevalence ratio (PR)	95% CI for exp(B)		Adjusted prevalence ratio	95% CI for PR	
		Lower	Upper		Lower	Upper
Age	1.023	0.903	1.160	NS		
Gender (Male)	1.97*	1.052	3.694	1.88†	1.005	3.552
Educational status				NS		
No education	0.858	0.331	2.221			
Primary education	0.589	0.210	1.653			
Household monthly income	1.000	1.000	1.000	NS		
Family history of ocular complication—Yes	0.961	0.519	1.779	NS		
Serum ferritin	1.000	1.000	1.000	NS		
Haemoglobin	1.029	0.919	1.151	NS		
SGPT	0.997	0.989	1.005	NS		
OGTT	0.99*	0.978	1.003	NS		
Hepatitis C	1.344	0.626	2.885	NS		
Serum calcium	0.76*	0.616	0.936	0.76†	0.613	0.938
Frequency of transfusion				NS		
Every 15 days	2.328	0.321	16.897			
Every 1 month	2.500	0.156	39.969			
Frequency of chelation	1.000	1.000	1.001	NS		
Type of iron chelation				NS		
Deferiproone	1.537	0.358	6.598			
Desferrioxamine	1.136	0.269	4.798			
Splenectomy	0.531	0.129	2.191	NS		

*Significant at p value <0.25 by univariate linear regression.
†Significant at p value <0.05 by multivariable linear regression.
NS, non significant.

Studies in the recent past have established higher incidence of hypercalcuria and lower levels of calcium in patients affected with beta thalassaemia.[18 19] One interesting and relatively new finding of elevated serum calcium levels was seen in our study. In patients with ocular abnormalities, serum calcium was found to be significantly lower when compared with patients who did not show any ocular abnormality. This association was found to be statistically significant. This significant association has turned out to be unique finding which has not been previously reported in other studies. It was observed that for every one unit increase in serum calcium led to 24% decrease in the frequency of ocular complications. Could higher levels of calcium confer a protective element to patients affected with thalassaemia remains an unanswered question. Further studies can be done in the future to well establish this relationship.

To the best of our knowledge, this is the first study in Pakistan to evaluate the ocular complications among beta TM patients and is adequately sized. Robust measures were taken for evaluating both ocular lesions by an experienced ophthalmologist and beta TM by clinical expertise and lab reports.

Limitations

There might be certain limitations to this study. One such limitation was of the age group enrolled. We could only assessed patients from 11 to 17 years of age which might have affected the results. Although it was a single centred study but our results are generalisable to all those beta thalassaemia patients who present to other settings as patients presenting to Fatimid foundation presented from different ethnic and socioeconomic classes where free of cost blood transfusion and medical services are provided to the patients. Temporality of the disease cannot be established due to the limitation of the study design. However, in the future we plan to conduct a longitudinal study (cohort study) so that temporality between beta TM and ocular complications can be established.

CONCLUSION

Our study results showed that the frequency of ocular complications in beta thalassaemia children was 22.7%. Male gender was a risk factor for ocular complications among children with beta thalassaemia. However, high calcium levels among these patients were found to be protective for ocular complications. Regular eye examination are essential in managing ocular complications in children with TM. They aid in early detection of conditions, monitoring retinal health, assessing visual acuity, detecting cataracts and managing eye infections. These examinations would enable healthcare professionals to provide appropriate interventions and improve the overall ocular health and well-being of TM children. Moreover, in future follow-up studies can be conducted to establish temporality of beta TM and ocular complications.

Acknowledgements The authors would like to acknowledge the research associate Aneesa Hassan.

Contributors RB conceived the study, NZ conceived the study, analysed the data and critically reviewed the manuscript. FK analysed the data, drafted and critically reviewed the manuscript. HIAQ drafted and critically reviewed the manuscript. BM, SH, AHK, FA, KA were the subject experts and contributed to the design of the study. All authors have contributed intellectually to this manuscript and have read and approved the final manuscript. NZ is the guarantor.

Funding The work is funded by Aga Khan University's SEED Money grant Award Number PF 130/0319 and the funders had no role in the study design and development of the proposal.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained from parent(s)/guardian(s).

Ethics approval This study involves human participants and ethics approval was sorted from Aga University Ethical Review Committee ERC # 2020-2199-7326. Permission was taken from Fatimid foundation for recruitment of beta thalassaemia patients and from Patel Hospital for performing ophthalmological examination. Written informed consent from parents and child's assent in English or Urdu depending on the understanding of the participant was taken by a trained data collector. Participation was voluntary. The study procedures were explained in detail to the study participants along with the risks and benefits associated with being a participant. In this particular study, possible risks will be minimal. However, ocular complications were evaluated by an ophthalmologist by certain instrument which may have caused some discomfort. If any complication was diagnosed by the ophthalmologist the patient were advised treatment and were given referral. All information was kept confidential. Strict privacy rules were followed and interviews were conducted in privacy. All study materials containing personal identifiers were kept in a locked file cabinet and the electronic data base was password protected. A unique study identification number were assigned to each participant.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

ORCID iDs

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