

Comparison of Ocular Characteristic Between Major Thalassemia and Healthy Group

Leili Koochakzadeh¹, Hassan Hashemi², Reza Pakzad³, Zahra Hemmatian Rabbani⁴, Samira Heydarian⁵, Abbasali Yekta⁴, Fahimeh Khoshhal⁶, Hadi Ostadimoghaddam⁷, Parastoo Tajzadeh⁸, Sara Sardari², Mehdi Khabazkhoob⁹

¹ Department of Pediatrics, Children's Medical Center Hospital, Tehran University of Medical Sciences, Tehran, Iran

² Noor Research Center for Ophthalmic Epidemiology, Noor Eye Hospital, Tehran, Iran

³ Department of Epidemiology, Faculty of Health, Ilam University of Medical Sciences, Ilam, Iran

⁴ Department of Optometry, School of Paramedical Sciences, Mashhad University of Medical Sciences, Mashhad, Iran

⁵ Department of Rehabilitation Sciences, School of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran

⁶ Department of Pediatrics, Dezfoul University of Medical Sciences, Dezfoul, Iran

⁷ Refractive Errors Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

⁸ Higher Health Education, Complex of Kashmar, Mashhad University of Medical Sciences, Mashhad, Iran

⁹ Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 02 Feb. 2021; Accepted: 26 Sep. 2021

Abstract- To determine and compare ocular characteristics and refractive errors between major thalassemia patients and normal subjects. In this study, 71 thalassemia major patients and 79 age and sex-matched healthy subjects that were selected in an ongoing manner underwent complete optometric and ophthalmic examinations, including autorefraction, subjective refraction, fluorescein tear break-up time, and pachymetry after anthropometric measurements. The results showed that the mean UCVA was better in the control group versus the thalassemia group ($P<0.001$), while there was no difference in BCVA between the two groups ($P=0.416$). Moreover, the mean spherical equivalent was 0.38 ± 0.13 D less in the thalassemia group compared to the control group ($P=0.007$), while corneal power ($P<0.001$) and cylinder power ($P=0.001$) were larger in thalassemia patients. The most common type of astigmatism was against the rule pattern in thalassemia patients and with the rule pattern in the control group ($P<0.001$). The mean tear break-up time was 11.35 ± 6.43 in the thalassemia group and 14.63 ± 5.79 in the control group ($P=0.001$), and the mean near the point of accommodation (NPA) ($P=0.009$) and near the point of convergence (NPC). ($P=0.003$) were significantly smaller in the thalassemia group compared to the control group. These patients suffer from a myopic shift due to exaggerated responses to changes in ocular growth, dry eye secondary to goblet cell loss, and a higher prevalence of vertical astigmatism due to eyelid laxity and pressure on the cornea. Therefore, regular ophthalmological evaluations are highly recommended in these patients.

© 2021 Tehran University of Medical Sciences. All rights reserved.

Acta Med Iran 2021;59(10):603-609.

Keywords: Beta-thalassemia; Ocular characteristic; Refractive errors; Cohort study

Introduction

Thalassemia major is a genetic disease caused by insufficient or lack of beta chains in the hemoglobin that usually manifests during childhood (1). The patients need a lifelong blood transfusion to prevent disease complications, including compensatory bone marrow

expansion and hypochromic microcytic anemia (2,3). Although this treatment method reduces the symptoms of anemia, the patients require chelation therapy due to iron accumulation in different tissues as a result of the destruction of red blood cells. Although this treatment combination increases the patients' survival, it impairs physical growth and mental development and causes

Corresponding Author: H. Ostadimoghaddam

Refractive Errors Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
Tel: +98 9153114403, Fax: + 98 2142910703, E-mail address: ostadih@mums.ac.ir

Copyright © 2021 Tehran University of Medical Sciences. Published by Tehran University of Medical Sciences

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (<https://creativecommons.org/licenses/by-nc/4.0/>). Non-commercial uses of the work are permitted, provided the original work is properly cited

general weakness and systemic dehydration (2-5).

Despite regular blood transfusion, major thalassemia patients develop a dramatic bone marrow expansion, resulting in enlargement, deformity, and brittleness of bony structures (6,7). Deformity of flat bones, especially the skull, causes craniofacial changes that are associated with bossing of the skull, a depressed nasal bridge, and an abnormal bony orbit (1,6,8). Moreover, systemic iron overload resulting from repeated blood transfusions leads to retardation in the systemic growth (3,9-12) through endocrine and exocrine dysfunction (13) and growth hormone efficiency (12,14,15). Systemic iron overload, on the one hand, and the abnormal bony orbit, on the other hand, disturb the ocular biometry and refraction (3,11). Studies in thalassemia patients have shown marked changes in ophthalmic parameters, including a shorter axial length, a steeper cornea, a thicker lens, a lower visual acuity, and a higher prevalence of refractive errors especially against-the-rule astigmatism (1,3,10,11,16-18). Some studies also found a marked difference in the prevalence of dry eye between normal and thalassemic subjects (3-5,16).

With 13,879 thalassemic patients and a prevalence of 23 in 100,000 populations in 2007, Iran is one of the high-risk areas in the world, and considering its population growth and increased survival of thalassemia patients as a result of improved patient care; it is expected that its prevalence will increase in large Iranian cities (19). Several studies have evaluated visual disorders in thalassemic patients in Iran and have published inconsistent results (1,11,13,20,21). Comprehensive information about the visual status of thalassemic patients is required for designing relevant health plans. Mashhad is the second largest city of Iran on the one hand, and a large number of immigrants from neighboring countries, on the other hand, seemed to be an appropriate setting for this study; (22) therefore, this study was conducted to investigate ocular characteristics and refractive errors in thalassemic patients in Mashhad, Iran.

Materials and Methods

This Cohort study was conducted in the Thalassemia-Hemophilia Center, Mashhad, Iran, in 2018. The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences.

Considering the mean spherical equivalent (SE) as the main objective of this study and according to a previous study, (3) the mean SE was considered -0.05 ± 0.44 D in the thalassemia and -0.25 ± 0.69 D in the

control group. Then, using a confidence interval of 95% and power of 80%, the sample size was calculated at 65 subjects in each group. Finally, considering a non-response rate of 20%, it was decided to enroll 80 subjects in each group (160 participants in total).

In this study, the exposure group comprised major thalassemia patients aged 15-30 years that presented to Mashhad Thalassemia-Hemophilia Center, and a diagnosis of thalassemia major was confirmed in their medical records by the treating physician. All the selected patients received regular blood transfusions (every 15-30 days) and were on chelation therapy. These patients were selected from Jun to September in an ongoing manner. To match the source population of thalassemia and control groups, control subjects were selected from healthy people who presented to the Center for reasons other than thalassemia. Group matching was done between thalassemia and control groups in terms of age and sex. The exclusion criteria were a history of corneal diseases, contact lens wear, ocular surgery, any ocular trauma in the past, any systemic disease in the eye including glaucoma, keratoconus, uveitis, cataracts or cataract surgery, and use of topical eye drugs. After explaining the study objectives, the selected subjects were introduced to Mashhad Optometry Clinic by issuing an ID card if they were interested in joining the study.

The weight, height, and body mass index (BMI) of all subjects were recorded by a trained assistant. Then, all participants underwent optometric examinations. First, monocular and binocular uncorrected visual acuity as well as visual acuity with previous correction and final prescription were measured by a projector E chart, recorded in decimals, and transformed to LogMAR for statistical analysis. Then, refractive errors were examined objectively using a Nidek auto refractometer and Heine Beta 200 retinoscope and subjectively using a lens box and trial frame first monocularly and then binocularly. Emmetropia, myopia, and hyperopia were defined as a SE of $+0.05$ to -0.50 D, less than -0.50 D, and more than $+0.05$ D, respectively. Type of astigmatism was defined according to its axis as with the rule ($0^\circ \pm 30^\circ$), against the rule ($90^\circ \pm 30^\circ$) and oblique ($30^\circ - 60^\circ$ and $120^\circ - 150^\circ$).

Near the point of accommodation (NPA) and near the point of convergence (NPC) were measured by bringing a target (20/20 letters on the near chart) close to the person until blurring (push-up method) and diplopia occurred, and their values were recorded in cm. A slit-lamp was used to examine the corneal, conjunctival, and lens surfaces and the middle portion of the eye. Tear

break-up time (TBUT) without local anesthesia was used to detect dry eye syndrome. For this test, a strip impregnated with fluorescein was moisturized with a drop of normal saline, and the inferior bulbar conjunctiva was gently touched with the stripped tip. The cornea was examined under a cobalt blue filter on the slit lamp. The patient was instructed to blink several times and then avoid blinking until told otherwise. The time between the last blink and the appearance of a dry spot was measured in seconds using a stopwatch. The Oculus Keratograph 4 (G/70700/0109/en) was used to record corneal parameters.

Statistical method

Data are presented as mean, percentage, and 95% CI (confidence interval). T-test and chi-square tests were used to compare qualitative and quantitative variables between the two groups, respectively. Data normality was checked using the Kolmogorov-Smirnov test, and non-parametric tests were used if data did not have a

normal distribution. The Stata version 14 was used for statistical analysis, and *P* less than 0.05 was considered significant.

Results

Of 160 participants, the data of 71 thalassemia patients and 79 controls were collected. Ten subjects were excluded from analysis due to missing and the data of 150 participants were finally analyzed. The mean age of the subjects was 22.83 ± 5.17 years (range: 15-30 years) in the thalassemia group and 21.97 ± 5.18 years (range: 12-30 years) in the control group, indicating no significant difference ($P=0.317$). Thirty-nine participants (49.4%) in the control group and 34 subjects (47.9%) in the thalassemia group were male ($P=0.856$). The mean height ($P<0.001$) and weight ($P<0.001$) were significantly lower in cases compared to controls. Table 1 presents other baseline characteristics.

Table 1. Baseline characteristics of participants

Variable	Thalassemia (N=71)	Control (N=79)	<i>P</i>
Age (yrs.)	22.83±5.17	21.97 ± 5.18	0.317
Height (cm)	157.88±11.06	164.97 ± 8.70	<0.001
Weight (kg)	50.35±10.46	59.16 ± 9.74	<0.001
BMI (kg/m ²)	20.08±3.17	21.59 ± 1.82	0.001
Sex*	Male	34 (47.9%)	39 (49.4%)
	Female	37 (52.1%)	40 (50.6%)
Ferritin (ng/mL)	3018.35±2895.93	--	--
Hemoglobin (g/dL)	9.50±0.05	--	--

*: Column percent

Table 2 shows the results of the comparison of ocular characteristics between the two groups. According to Table 2, the mean uncorrected visual acuity (UCVA) was better in the control group compared to the thalassemia group ($P<0.001$), while there was no significant difference in best-corrected visual acuity (BCVA) between the two groups ($P=0.416$). Comparison of refractive errors between the two groups showed that the mean sphere was 0.25 ± 0.12 D lower in the thalassemia group versus the control group ($P=0.40$). The mean cylinder power was -0.65 ± 0.58 D in the thalassemia group and -0.39 ± 0.32 D in the control group, indicating a significant difference ($P=0.001$). Moreover, the mean SE was 0.38 ± 0.13 D less in the thalassemia group compared to the control group ($P=0.007$), while the mean corneal power, K_{max} , and K_{min} were significantly higher in the thalassemia

group versus the control group ($P<0.001$ for all).

The mean TBUT was 1.35 ± 6.43 in the thalassemia group and 14.63 ± 5.79 in the control group, indicating a significant difference ($P=0.001$). The mean NPA was 8.68 ± 1.93 in the thalassemia group, which was significantly smaller than the control group (9.44 ± 1.62) ($P=0.009$). The mean NPC was 4.79 ± 1.99 in the thalassemia group and 5.82 ± 2.12 in the control group, suggesting a significant difference ($P=0.003$).

Table 3 shows the prevalence of total astigmatism in the two groups. There was a significant difference in the astigmatism pattern between the two groups ($P<0.001$) as the against the rule pattern had the highest prevalence in the thalassemia group (47.88%; 95% CI: 35.87-60.07) while the rule pattern was the most common type in the control group (72.15%; 95% CI: 60.92-81.65) (Figure 1).

Table 2. Comparison of ocular characteristics between thalassemia and control groups

Variables	Mean±SD		Mean difference±SE	P	
	Thalassemia group (N=71)	Control group (N=79)			
UCVA (LogMAR)	-0.03±0.08	-0.09±0.03	0.06±0.01	<0.001	
BCVA (LogMAR)	0.09±0.25	0.05±0.30	0.04±0.04	0.416	
Refractive index	Sphere (D)	-0.32±0.83	-0.07±0.65	-0.25±0.12	0.040*
	Cylinder (D)	-0.65±0.58	-0.39±0.32	-0.26±0.07	0.001*
Refractive index	SE (D)	-0.65±1.01	-0.26±0.68	-0.38±0.13	0.007*
	CA (D)	1.44±1.40	1.09±0.94	0.35±0.19	0.770
	CP (D)	44.38±1.12	43.43±1.37	0.94±0.20	<0.001
	Kmax (D)	44.81±1.50	43.84±1.38	0.97±0.23	<0.001*
	Kmin (D)	43.96±1.40	43.04±1.61	0.92±0.24	<0.001*
Binocularity index	NPA (Cm)	8.68±1.93	9.44±1.62	-0.76±0.28	0.009*
	NPC (Cm)	4.79±1.99	5.82±2.12	-1.02±0.33	0.003*
	AA (D)	12.21±3.34	10.91±1.99	1.29±0.44	0.005*
TBUT	11.35±6.43	14.63±5.79	-3.28±0.99	0.001*	

TBUT: Tear Breakup Time; SE: Spherical Equivalence; Kmin: Minimum Keratometry; Kmax: Maximum Keratometry; CA: Corneal Astigmatism; CP: Corneal Power; UCVA: Uncorrected Visual Acuity; BCVA: Best Corrected Visual Acuity

Table 3. Prevalence of Different Pattern of Total Astigmatism in Thalassemia and Control Group

Total Astigmatism	Type	Number (Percent; 95% CI)		P
		Thalassemia Group	Control Group	
Total Astigmatism	WTR	27 (38.02%; 26.76 – 50.32)	57 (72.15%; 60.92 – 81.65)	<0.001
	oblique	10 (14.08%; 6.96 – 24.38)	9 (11.39%; 5.34 – 20.52)	
	ATR	34 (47.88%; 35.87 – 60.07)	13 (16.45%; 9.06 – 26.49)	

WTR: with the rule; ATR: against the rule; CI: confidence interval

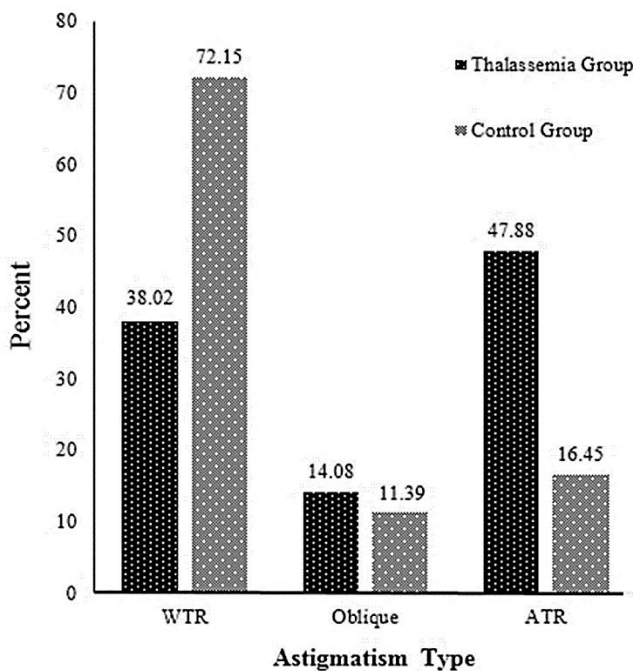


Figure 1. Prevalence of astigmatism type in thalassemia group and control group (WTR: with the rule; ATR: against the rule)

Discussion

Thalassemia major is an important socio-economic problem in many countries that requires lifelong follow-up and regular blood transfusions. In addition to

systemic problems, these patients also suffer from ocular disorders, including decreased visual acuity, astigmatism, and dry eye, which are caused by both the disease itself and the use of iron-chelating agents, such as desferrioxamine and deferiprone. The ophthalmic side

effects of these treatments can be controlled or prevented through regular ophthalmic examination (2).

Several studies have evaluated anthropometric changes in thalassemic patients and found marked retardation in growth parameters. In line with the results of this study, Shamsirsaz and colleagues, (12) Fahim and coworkers, (9) Elkitkat *et al.*, (3) Nowroozzadeh *et al.*, (11) and Kundu *et al.*, (10) found that thalassemic patients had lower weight, height, and BMI compared to normal people, indicating a significant delay in their growth in response to growth hormone deficiency (12,14,15). The results of this study, similar to the findings of a study by Heydarian *et al.*, (1) showed that the mean UCVA was worse in the thalassemia group compared to the control group while there was no difference in BCVA between the two groups, which could be secondary to lack of or insufficient eye care services. Aksoy *et al.*, (2) found that the mean BCVA (LogMAR) was higher in the thalassemia versus the control group, while Nowroozzadeh *et al.*, (11) found no difference in UCVA and BCVA between the two groups.

Another finding of the present study was a significant difference in refractive indexes between the two groups, such that a significant myopic shift was observed in thalassemic patients, which was independent of age and sex. Although this finding was in line with the results of a study by Elkitkat *et al.*, (3), but the other studies (1,2,10,11,13,20) found no significant difference in SE between the two thalassemia and normal subjects. To explain this finding, it can be stated that in thalassemic patients, due to ocular growth retardation that is usually associated with a shorter axial length, to maintain emmetropization and neutralize the hyperopic effect resulting from the shorter axial length, the compensation process is associated with corneal steepening and lens thickening. Because this process occurs in an exaggerated form, it causes a myopic shift. The higher corneal power in thalassemic patients, which was also reported by Nowroozzadeh *et al.*, (11) and Kundu *et al.*, (10), and an indirect relationship between SE and Kmax ($r = -0.378$; $P = 0.001$) and Kmin ($r = -0.348$; $P = 0.003$) may support this hypothesis.

This study also found that independent of age and sex, corneal astigmatism and refractive astigmatism were significantly more prevalent in thalassemic patients compared to control subjects, which is consistent with the study conducted by Nowroozzadeh *et al.*, (11). This study also found a significant difference in the pattern of total astigmatism between the two groups as the against the rule pattern (47.88%) and with the rule pattern

(75.15%) were the most common patterns in the thalassemia and control group, respectively. This finding was comparable to the findings of other studies; for example, the prevalence of against the rule pattern was 52.8% in the study by Heydarian *et al.*, (1) and 57.5% in the study conducted by Nowroozzadeh *et al.*, (11). In a study in India, Kundu *et al.*, (10) showed that the prevalence of astigmatism was 9.18% in thalassemic children while 5.78% of the control subjects had astigmatism, but they did not specify which pattern was more common. On the other hand, Elkitkat *et al.*, (3) found a tendency towards the against the rule pattern in normal and thalassemic subjects. It seems that in thalassemic patients, upper eyelid laxity results in a higher prevalence of vertical astigmatism (10).

The results of the present study showed a worse tear function in thalassemic patients compared to the control group (a lower mean TBUT in thalassemic patients), which was consistent with studies conducted by Gartaganis *et al.*, (16) Aksoy *et al.*, (2) and Jafari *et al.*, (13). It seems that in thalassemic patients, loss of goblet cells and conjunctival squamous metaplasia on the one hand (16,23) and systemic dehydration on the other hand⁵ decrease the quality and quantity of the tear film. Jafari *et al.*, (13) found a significant positive correlation between dry eye and the serum ferritin level and since increased iron deposition in glands results in cytotoxic effects and endocrine and exocrine dysfunction, iron overload leads to lacrimal glands dysfunction causing tear film deficiency (16) Repanti *et al.*, (24) studied 40 rats and found that iron overload led to hemosiderin deposits in macrophages, especially in the connective tissue of lacrimal glands, causing tear film dysfunction. Several studies have reported that the prevalence of pinguecula, which has no relationship with the use of chelator agents or thalassemia, is higher in thalassemic patients, which could be due to tear film disorders and dry eye (4,13).

In the presents study, NPA, NPC, and accommodative amplitude were compared between thalassemia and control groups and contrary to expectations, (25) NPA and NPC were smaller in thalassemic patients. In other words, the amplitude of accommodation was higher in thalassemic patients. Since the above parameters were investigated in thalassemic patients for the first time, other studies with larger sample sizes are required to confirm the results.

It was not possible to compare biometric parameters between thalassemic and normal subjects like other studies due to the lack of facilities and infrastructures, which could be considered a weakness of this study. The

Ocular problems in thalassemia

strengths of this study include conducting examinations by trained staff and comparison of the binocularity index between the two groups for the first time.

Ocular characteristics were compared between thalassemia patients and normal subjects in this study. It seems that due to systemic dehydration and iron overload, the quality and quantity of the tear film decreases in thalassemic patients. Compared to the control group, thalassemia patients suffer from significant retardation in general and ocular growth, and although ocular growth changes result in compensatory biometric changes including corneal steepening to maintain emmetropization, exaggeration of this process causes a myopic shift. On the other hand, the prevalence of vertical astigmatism is higher in thalassemic patients due to eyelid laxity, which calls for more attention during ophthalmic and optometric examinations. Considering the increased survival of thalassemia patients and the detrimental effects of this disease on the visual status of the patients, regular ophthalmological examinations are recommended to detect visual system changes in the early stages and improve the quality of life of the patients.

References

1. Heydarian S, Jafari R, Karami H. Refractive errors and ocular biometry components in thalassemia major patients. *Int Ophthalmol* 2016;36:267-71.
2. Aksoy A, Aslankurt M, Aslan L, Gül O, Garipardıç M, Celik O, et al. Ocular findings in children with thalassemia major in Eastern Mediterranean. *Int J Ophthalmol*. 2014;7:118-21.
3. Elkitkat RS, El-Shazly AA, Ebeid WM, Deghedy MR. Relation of anthropometric measurements to ocular biometric changes and refractive error in children with thalassemia. *Eur J Ophthalmol* 2018;28:139-43.
4. Hashim ZA, Mutlag SS. Ophthalmologic Changes in Thalassemia Patients. *Int J Pharm Sci Rev Res* 2017;9:2237-9.
5. Schrier SL. Pathophysiology of the thalassemsias. The Albion Walter Hewlett Award presentation. *West J Med* 1997;167:82-9.
6. Cao A, Galanello R. Beta-thalassemia. *Genet Med* 2010;12:61-76.
7. Voskaridou E, Terpos E. New insights into the pathophysiology and management of osteoporosis in patients with beta thalassaemia. *Br J Haematol* 2004;127:127-39.
8. Weatherall DJ, Clegg JB. Historical perspectives. In: *The Thalassemia syndromes*. 4th ed. Oxford, UK: Blackwell Scientific, 2001.
9. Fahim FM, Saad K, Askar EA, Eldin EN, Thabet AF. Growth Parameters and Vitamin D status in Children with Thalassemia Major in Upper Egypt. *Int J Hematol Oncol Stem Cell Res* 2013;7:10-4.
10. Kundu A, Purban Ganguly D, Sinharay A, Patil P, Sharma K, Bandyopadhyay M. A Study to Assess the Ocular Biometric Parameters and Prevalence of Refractive Errors among Thalassemic Children in a Rural Based Tertiary Hospital. *Int J Med Health Sci Res* 2017;7:160-5.
11. Nowroozzadeh MH, Kalantari Z, Namvar K, Meshkibaf MH. Ocular refractive and biometric characteristics in patients with thalassaemia major. *Clin Exp Optom* 2011;94:361-6.
12. Shamshirsaz AA, Bekheirnia MR, Kamgar M, Pourzahedgilani N, Bouzari N, Habibzadeh M, et al. Metabolic and endocrinologic complications in beta-thalassemia major: a multicenter study in Tehran. *BMC Endocr Disord* 2003;3:4.
13. Jafari R, Heydarian S, Karami H, Shektaei MM, Dailami KN, Amiri AA, et al. Ocular abnormalities in multi-transfused beta-thalassemia patients. *Indian J Ophthalmol* 2015;63:710-5.
14. Kassab-Chekir A, Laradi S, Ferchichi S, Khelil AH, Feki M, Amri F, et al. Oxidant, antioxidant status and metabolic data in patients with beta-thalassemia. *Clin Chim Acta* 2003;338:79-86.
15. Vogiatzi MG, Macklin EA, Trachtenberg FL, Fung EB, Cheung AM, Vichinsky E, et al. Differences in the prevalence of growth, endocrine and vitamin D abnormalities among the various thalassaemia syndromes in North America. *Br J Haematol* 2009;146:546-56.
16. Gartaganis SP, Georgakopoulos CD, Exarchou A, Mela EK, Psachoulia C, Eliopoulou MI, et al. Alterations in conjunctival cytology and tear film dysfunction in patients with beta-thalassemia. *Cornea* 2003;22:591-7.
17. Parentin F, Perissutti P. Congenital Growth Hormone Deficiency and Eye Refraction: A Longitudinal Study. *Ophthalmologica* 2005;219:226-31.
18. Parentin F, Tonini G, Perissutti P. Refractive evaluation in children with growth defect. *Curr Eye Res* 2004;28:11-5.
19. Abolghasemi H, Amid A, Zeinali S, Radfar MH, Eshghi P, Rahiminejad MS, et al. Thalassemia in Iran: epidemiology, prevention, and management. *J Pediatr Hematol Oncol* 2007;29:233-8.
20. Khalaj M, Sarokhani MR, Mahyar A, Jahan Hashemi H, Godsi F. Assessing the Refractive Errors in Beta-Thalassemia Major Patients. *Jour Guilan Uni Med Sci* 2009;17:42-9.

21. Ghazanfari A, Jafarzadehpour E, Heydarian S, Dailami KN, Karami H. Comparison of contrast sensitivity in β -thalassemia patients treated by deferoxamine or deferasirox. *J Optom* 2019;12:168-73.
22. Hashemi H, Khabazkhoob M, Pakzad R, Yekta A, Heravian J, Nabovati P, et al. The prevalence of color vision deficiency in the northeast of Iran. *J Curr Ophthalmol* 2019;31:80-5.
23. Liaska A, Petrou P, Georgakopoulos CD, Diamanti R, Papaconstantinou D, Kanakis MG, et al. β -Thalassemia and ocular implications: a systematic review. *BMC Ophthalmol* 2016;16:102.
24. Repanti M, Gartaganis SP, Nikolakopoulou NM, Ellina A, Papanastasiou DA. Study of the eye and lacrimal glands in experimental iron overload in rats in vivo. *Anat Sci Int* 2008;83:11-6.
25. Hashemi H, Pakzad R, Yekta A, Asharlous A, Aghamirsalim M, Ostadimoghaddam H, et al. The distribution of near point of convergence in an Iranian rural population: A population-based cross-sectional study. *Saudi J Ophthalmol* 2019;33:148-52.