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Original Article

# Ocular complications in thalassemia major patients treated with deferoxamine: a hospital-based, cross-sectional study

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## Abstract

***Background & Aims*:** β-thalassemia is a severe hereditary disorder caused by defective globin synthesis. Patients suffering from β-thalassemia major require regular blood transfusion therapy to survive. Sight-threatening ocular abnormalities are quite common among these patients. This study was planned to evaluate the prevalence of ocular complications in multi-transfused patients with β-thalassemia who have been receiving deferoxamine.

***Materials & Methods*:** Thirty thalassemic patients receiving deferoxamine were studied in this cross-sectional descriptive study. All eligible subjects underwent an ophthalmologic examination, including the Humphrey visual field test, measurement of central corneal thickness (CCT), best-corrected visual acuity (BCVA), and central macular thickness (CMT).

***Results*:** Visual field defects were the most prevalent ocular abnormalities, observed in 50% of the studied subjects. Other ocular changes were as follows: bilateral cortical cataract (10%), macular pigmentary stippling (6.7%), punctate cortical opacity (3.3%), nuclear sclerosis cataract (3.3%), and macular pigmentary mottling (3.3%).

***Conclusion*:** The occurrence of ocular problems is common among thalassemic patients which necessitates long-term follow-up and regular ophthalmologic examination for these patients.

***Keywords*:** Cataract, Deferoxamine, Ocular manifestation, Thalassemia, Visual field defects

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## Introduction

Thalassemia is a severe genetic blood disorder caused by a defect in hemoglobin synthesis, leading to ineffective erythropoiesis due to a mutation in the globin gene. Patients with thalassemia major must receive frequent transfusions. However, multiple blood transfusions can result in iron toxicity, and may eventually lead to multi-organ dysfunction (1,2). Therefore, iron chelators are prescribed for patients receiving chronic transfusions to increase their long-term survival (3-5).

Deferoxamine is an iron-chelating agent specifically used in cases of iron overdose, hemosiderosis, and aluminum toxicity (6-8). It has been claimed that deferoxamine, at the recommended doses of 20-40 mg/kg/day, is safe and free of serious side-effects (9). However, there is evidence in the literature suggesting that the use of deferoxamine is

associated with an increased risk of a wide range of ocular abnormalities, such as night blindness, color vision anomalies, visual field defects, and optic neuropathy (10-11). The current investigation was undertaken to evaluate the prevalence of ocular abnormalities in multi-transfused β-thalassemic patients who were under treatment with deferoxamine.

## Materials & Methods

This is a cross-sectional descriptive study conducted on patients with a definitive diagnosis of thalassemia major who had been receiving chelation with deferoxamine for at least 12 months. Thirty consecutive multi-transfused β-thalassemia cases were recruited from September 2016 to May 2017 at Imam Khomeini Hospital, a referral center for eye diseases in Northwest Iran. The study was approved by the Ethics Committee of the Urmia University of Medical Sciences (IR.UMSU.REC.1396.11) and adhered to the tenets of the Declaration of Helsinki. All patients were informed about the nature of the study and written informed consent was obtained. In the case of minors, consent was obtained from their parents.

Subjects with ophthalmic diseases that may cause ocular abnormalities (e.g., aphakia, amblyopia, strabismus, and systemic diseases) were excluded. All eligible participants underwent an ophthalmologic examination including a Humphrey visual field test, measurement of central corneal thickness (CCT), best-corrected visual acuity (BCVA), and central macular thickness (CMT). BCVA was measured with a standard Snellen chart, CCT was assessed by ultrasound pachymetry, and CMT was measured using optical coherence tomography (OCT). The visual field test was performed using the automated perimetry test. In addition, slit lamp examination and dilated fundus evaluation were performed for all patients. The clinical and medical history of participants (i.e., duration of disease, number of blood transfusions, and weekly deferoxamine dosage) were recorded in specific checklists.

## Results

This study included 60 eyes from 30 patients with β-thalassemia, with a slight male predominance. Table 1 illustrates the demographic features of the participants. The mean age of patients was relatively young, and the duration of disease and deferoxamine use indicates long-term management of β-thalassemia. The high number of transfusions reflects the chronic nature of the disease and its treatment.

**Table 1.** Patient demographics

| Parameter | Value |
|---|---|
| Total number of eyes | 60 |
| Total number of patients | 30 |
| Gender (Male) | 17 (56.7%) |
| Gender (Female) | 13 (43.3%) |
| Age (years) | Mean ± SD: 18.1 ± 4.32 |
| Age range (years) | 7 to 34 |
| Duration of disease (years) | Mean ± SD: 16.33 ± 6.78 |
| Duration of deferoxamine use (years) | Mean ± SD: 14.13 ± 5.44 |
| Number of transfusions | Mean ± SD: 167.04 ± 45.31 |
| Transfusion range | 65 to 400 |
| Daily dosage of deferoxamine (mg/kg/day) | Mean ± SD: 33.5 ± 6.4 |

**Table 2.** Main Parameters

| Parameter | Value |
|---|---|
| BCVA (letters) | Mean ± SD: 30.6 ± 13.04 |
| CCT (μm) | Mean ± SD: 490 ± 54.3 |
| MCT (μm) | Mean ± SD: 288.76 ± 36.6 |
| Unreliable perimetry | 4 (13.3%) patients |
| Normal perimetry | 11 (36.7%) patients |
| Visual field defects | Both eyes in 15 (50%) cases |
| Paracentral scotoma | 8 patients |
| Central scotoma | 7 patients |
| Bilateral cortical cataract | 3 patients (10%) |
| Punctuate cortical opacity | 1 individual (3.3%) |
| Mild nuclear sclerosis cataract | 1 subject (3.3%) |
| Macular pigmentary stippling | 2 patients (6.7%) |
| Macular pigmentary mottling | 1 patient (3.3%) |

Visual acuity and corneal thickness measurements suggest a range of ocular impacts, with some patients experiencing significant visual field defects. The presence of paracentral and central scotoma in a combined 50% of cases indicates a notable prevalence of visual impairment among the participants (Table 2).

The slit lamp and ophthalmoscopic examinations revealed that a minority of patients had various forms of cataracts and macular changes (Table 2), which could be attributed to either the disease itself or its treatment. The finding of bilateral cortical cataracts in 10% of patients is particularly noteworthy and warrants further investigation into its association with β-thalassemia or deferoxamine use.

## Discussion

Patients suffering from thalassemia may present with various ocular abnormalities. These manifestations may correlate with the disease itself or may occur as a result of iron overload or as side effects of the chelating agents used (4, 12). Deferoxamine is the oldest and the most commonly used iron chelator. Despite the apparent benefits of deferoxamine for thalassemia patients, numerous sight-threatening ocular abnormalities have been reported to be caused by this iron-chelating drug. Ocular findings range from pigmentary retinopathy, cataracts, angioid streaks, and optic neuropathy, to ocular surface disorders, decreased visual acuity, thinning and tortuosity of retinal vessels, and retinal toxicity (13-17).

In the present research work, we evaluated the ocular complications in 30 multi-transfused thalassemic patients aged 7–34 receiving deferoxamine. The prevalence of ocular abnormalities among the studied population was 26.7% (i.e., 5 cases with lens opacities and 3 patients with macular pigmentary stippling/mottling). Prior investigations have reported different prevalence rates for ocular abnormalities, ranging from ~10.5% to ~75% (9, 14-16, 18-25). The cause of such discrepancies may be due to differences in the age of participants, the volume and frequency of blood transfusions, and the type and dosage of iron chelator (26).

Relative frequency of lens opacities in our population was 16.7% (n = 5). Gartaganis et al. (1989)

(16) reported lens opacities in 13.8% of cases, while Gaba et al. (1998)(19) found them in 45.7% of subjects. Cortical cataracts were found in 6.7% of subjects under treatment with deferoxamine in the study by Jafari et al (2015)(20). This is while Nowroozzadeh et al. (2011) observed lens opacities in 10.7% of cases who used deferoxamine (23).

Visual field defects were the most prevalent ocular manifestation among our studied patients, with half of them (n = 15) having either paracentral or central scotoma. This observation is consistent with that of Jafari et al. (2015) (20). In their study, the prevalence of visual field defects was 33.7% (20). Among these patients, 17.3% suffered from general depression and 6.7% had paracentral scotoma. Moreover, superior or inferior arcuate scotoma was found in ~10% of cases with visual field defects (20).

## Conclusions

In conclusion, the occurrence of ocular complications in patients suffering from thalassemia major is likely. Since the possibility of ocular abnormalities increases over time, long-term follow-up is essential for these patients and could help prevent or delay the development of further sight-threatening ocular abnormalities.

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## Authors' Contributions

Naser Samadi Aidenloo: Conceptualization, Methodology, Validation, Resources, Writing - Review & Editing, Supervision, Project Administration. Qader Motarjemizadeh: Conceptualization, Methodology, Investigation, Writing - Review & Editing, Funding Acquisition. Sina Hasani Shayan: Formal Analysis, Data Curation, Writing - Original Draft, Visualization.

## Data Availability

Data are not publicly available but can be obtained from the authors upon reasonable request.

## Conflict of Interest

The authors have no conflicts of interest associated with the material presented in this paper.

## Ethical Statement

The study was approved by the Ethics Committee of the Urmia University of Medical Sciences (IR.UMSU.REC.1396.11) and adhered to the tenets of the Declaration of Helsinki. All patients were informed about the nature of the study and written informed consent was obtained.

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