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RESEARCH ARTICLE

Evaluation of Ocular Anterior Segment Parameters in Vitiligo Patients with Periocular Involvement

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ABSTRACT

Objective: This study aimed to quantitatively evaluate changes in the corneal and lenticular structures in vitiligo patients with periocular involvement.

Materials and Methods: Thirty patients with vitiligo and periocular involvement, along with 30 healthy volunteers, were included in the study. The anterior segment parameters were evaluated using specular microscopy and corneal topography. To evaluate the corneal endothelium, the mean cell area, mean endothelial cell density, coefficient of variation in the cell area, and central corneal thickness (CCT) were measured using specular microscopy. The mean anterior chamber depth (ACD), mean anterior chamber angle (ACA), mean keratometry (Km), and lens densitometry values were measured using corneal topography, and all parameters were compared between the groups.

Results: There were no statistically significant differences in endothelial parameters, CCT, ACD, ACA, and Km values between the vitiligo patients and the control group ($p>0.05$). Additionally, there was no statistically significant difference in lens densitometry values in any zone between patients with vitiligo and the control group ($p>0.05$).

Conclusion: Our results suggest that anterior segment parameters are not affected in patients with periocular vitiligo, and the pathological destruction seen in melanocytes in vitiligo is not observed in the neural crest-derived cells of the cornea.

Keywords: Cornea, endothelium, lens, periocular vitiligo

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INTRODUCTION

Vitiligo is a disease that causes depigmented, asymptomatic, and sharply demarcated macules and patches due to the destruction of melanocytes in the skin. It has a worldwide incidence of up to 2%.[1] Vitiligo affects both sexes equally and can develop at any age; however, 70–80% of cases are diagnosed before the age of 30.[2] Vitiligo lesions are typically caused by melanocyte deficiency.[3] Although the main pathophysiology of melanocyte loss is not fully understood, theories such as autoimmune disease, neural dysfunction, and metabolic diseases have been suggested.[4] Systemic destruction of melanocytes has also been reported not only in the skin but also in various tissues, particularly mucous membranes, the oculus, and the membranous labyrinth of the inner ear.[5]

Various ocular manifestations have been reported in vitiligo patients. The dense melanocyte content of the uveal tissues and retinal pigment epithelium may be targeted, leading to melanocyte loss in these areas. Hypopigmented spots on the iris and retina, atrophic changes, and chorioretinal degeneration in patients with vitiligo have been emphasized in previous studies.[6–8] In studies investigating the ocular surface, tear film abnormalities have been defined in patients with vitiligo, especially those with periocular involvement.[3,8–10] In a study conducted by Karadağ et al.,[8] which evaluated the anterior and posterior segments of vitiligo patients, it was suggested that choroidal and lenticular changes may occur in patients with vitiligo, while corneal parameters do not change.

Although posterior segment and uveal involvement in vitiligo patients have been clearly defined in the literature, stud-

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ies on corneal and lenticular involvement are scarce. Within the scope of our study, changes in the corneal and lenticular structures were evaluated using specular microscopy and corneal topography for the first time in patients with vitiligo and periocular involvement, and the measured parameters were compared with those in healthy volunteers.

MATERIALS and METHODS

This study was planned and executed at the Department of Dermatology and Ophthalmology the Sisli Hamidiye Etfal Training and Research Hospital, adhering to the guidelines outlined in the Declaration of Helsinki. Ethics committee approval was obtained (294/29.02.2024). All participants provided informed consent after being briefed on the study's objectives and procedures.

Thirty individuals with vitiligo affecting the area around the eyes (Group 1) and thirty healthy control subjects (Group 2) were part of the study. A dermatologist diagnosed vitiligo by observing white fluorescence of the skin lesions under a Wood's lamp (Dermlite Lumio UV). Patients with any corneal problems (neovascularization, scarring, etc.), cataracts, glaucoma, a history of contact lens usage, eye surgery, smoking, medication use that may affect ocular parameters, and systemic diseases other than vitiligo were excluded. The healthy control group consisted of individuals who regularly visited the ophthalmology outpatient clinic, had a best-corrected visual acuity (BCVA) of 20/20, and no ocular or systemic diseases.

Each participant underwent a detailed ophthalmological examination, including BCVA assessment with the help of a Snellen chart, intraocular pressure measurement, and biomicroscopic examinations.

Anterior segment evaluation, including corneal and lens densitometry measurements, was performed using a specular microscope (Topcon SP–1P, Japan) and a Pentacam HR Scheimpflug imaging system (Oculus, Wetzlar, Germany). Topographic maps of both the anterior and posterior surfaces of the cornea were created, and a three-dimensional assessment of the anterior chamber was conducted. All measurements were made using a specular microscope, and the Pentacam HR Scheimpflug imaging system was used by the same experienced clinician. Low-quality images were excluded from the analysis.

To evaluate the corneal endothelium, mean endothelial cell density (ECD) (cells/mm^2), mean cell area (MCA) (µm^2), coefficient of variation in the cell area (CV), percentage of hexagonality (HEX), and central corneal thickness (CCT) (µm) parameters were measured by specular microscopy.

The mean anterior chamber depth (ACD) (mm), mean anterior chamber angle (ACA), mean anterior chamber volume (ACV) (mm^3), and mean keratometry (Km) parameters were measured using corneal topography. The mean densitometry value was calculated by the analysis of predefined three-dimensional densitometry zones (Zone 1: 2.0 mm, Zone 2: 4.0 mm, and Zone 3: 6.0 mm) centered on the central pupil in the Pentacam HR system.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0 for Windows (SPSS Inc., Chicago, IL). Descriptive statistics for numerical variables are reported as mean, standard deviation, minimum, and maximum values, while categorical variables are presented as frequencies and percentages. Spearman's analysis was used for correlation analysis. Comparisons of numerical variables between the groups were performed using an independent sample t-test. Statistical significance was set at $p<0.05$.

RESULTS

The mean age of vitiligo patients (Group 1) and healthy volunteers (Group 2) was 25.5±12.4 and 24.2±11.3 years, respectively (p=0.823). Of the 30 patients with vitiligo, 14 were women and 16 were men; 13 healthy controls were women and 17 were men (p=0.770). The mean BCVA was 9.90±1.10 for Group 1 and 9.85±1.20 for Group 2 (p=0.980). The mean intraocular pressures of vitiligo patients and healthy volunteers were 13.5±11.4 and 14±12.3, respectively (p=0.710). There were no statistically significant differences between the vitiligo and control groups in terms of age, sex, BCVA, or intraocular pressure (p>0.05).

The specular microscopy measurements, anterior segment parameters, and mean keratometry values for both groups are presented in Table 1. No statistically significant differences were found between the vitiligo group and the control group regarding ECD, MCA, CV, HEX, CCT, ACD, ACA, or Km values (p>0.05).

The lens densitometry measurements of both groups are shown in Table 2. No statistically significant differences were found between the vitiligo group and the control group regarding lens densitometry values measured in zones 1, 2, and 3 (p>0.05).

DISCUSSION

Vitiligo is a condition characterized by depigmented spots and patches caused by the loss of epidermal melanocytes. Although the relationship of vitiligo with ocular pathologies is known from syndromes such as Vogt-Koyanagi-Harada, Waardenburg, and Alezzandrini, ocular involvement in nonsyndromic vitiligo patients has not yet been adequately defined. While

Table 1. Comparison of keratometry, anterior segment parameters and specular microscopy measurements in both groups

	Vitiligo group (n=30)	Control group (n=30)	p*
Km (D)	42.2±2.8	42.97±1.95	0.360
ACA	37.70±8.2	38.70±8.2	0.760
ACD (mm)	2.95±0.5	2.93±0.4	0.660
CCT (µm)	523.2±21.0	531.6 ±33.5	0.413
ECD (cell/mm^2)	2439.4±236.34	2433.0±230.0	0.776
MCA(µm^2)	395.5±32.1	395.9±32.3	0.887
CV	41.3±7.3	40.5±7.5	0.611
HEX (%)	43.2±5.1	43.6±5.1	0.412

*: Independent t-test. Km: Mean keratometry; ACA: Anterior chamber angle; ACD: Anterior chamber depht; CCT: Central corneal thickness; ECD: Endothelial cell density; MCA: Mean cell area; CV: Coefficient of variation in the cell area; HEX: Percentage of hexagonality

Table 2. Comparison of lens densitometry measurements in both groups

	Vitiligo group (n=30)	Control group (n=30)	p*
Zone 1 (%)	8.4±0.8	8.3±0.5	0.864
Zone 2 (%)	8.1±0.5	8.0±0.5	0.819
Zone 3 (%)	7.8±0.5	7.6±0.5	0.190
Mean (%)	8.7±1.1	8.7±0.8	0.944
Maximum LD (%)	32.1±13.1	35.1±18.5	0.456

*: Independent t-test. LD: Lens densitometry

many studies have clarified the involvement of the posterior segment in vitiligo, its impact on anterior segment structures, such as the cornea and lens, remains unclear. In this study, we investigated potential changes in the cornea and lens in patients with vitiligo affecting the area around the eyes. Based on the observation that patients with periorbital vitiligo were 58 times more likely to present with ocular findings than patients without periorbital depigmentation,[6] we selected the patient population from vitiligo patients with periocular involvement.

Consistent with our findings, a prior study assessing the cornea found no statistically significant difference in keratometry values between patients with vitiligo and the control group.[8] Similarly, earlier studies have not found statistically significant differences in intraocular pressure between vitiligo patients and healthy controls.[8,11–13] However, one study reported that the rate of normal tension glaucoma was 18.4% in patients with vitiligo and 0% in the control group, with two-thirds of the patients displaying periorbital lesions.[14] In a study conducted by Rogosic et al.[11] it was found that patients aged 56 and older had a 4.4 times higher risk of developing glaucoma. Additionally, when adjusted for age, the study indicated a 92% likelihood of an association between glaucoma development and the duration of vitiligo exceeding 13 years. However, it is known that the use of topical and pulse systemic corticosteroids, which are frequently used in the treatment of vitiligo, carries a risk of glaucoma development.[15,16]

In studies where the risk of glaucoma in vitiligo patients was found to be high, it was not stated that the patient groups were composed of untreated vitiligo patients. The development of glaucoma in vitiligo patients related to the duration of the disease might suggest more cumulative treatment damage. In our study, we did not find a statistically significant difference in intraocular pressure values between vitiligo patients with periocular involvement and the control group. Moreover, no studies have reported on the development of closed-angle glaucoma in patients with vitiligo. To clarify the relationship between vitiligo and glaucoma, studies designed with vitiligo patients with periocular involvement who have never received treatment are needed.

The main pathology in patients with vitiligo is the destruction of melanocytes originating from the neural crest. The endothelial layer, which plays an important role in corneal

transparency, also originates in the neural crest.[17] Considering this, unlike previous studies, we evaluated endothelial counts. We did not find a statistically significant difference in corneal endothelial parameters, such as ECD, MCA, CV, and HEX, between the groups. This suggests that the pathological destruction seen in melanocytes in vitiligo is not observed in the neural crest-derived cells of the cornea. Although the corneal endothelium shares the same embryological origin, its relatively avascular nature may contribute to its resilience against pathological destruction.

Similarly, while the precise pathogenesis of vitiligo remains unclear, there is a consensus that the pathological destruction of functioning melanocytes is a key factor. The observation that reactive oxygen species production, which plays an important role in the pathological destruction of melanocytes, occurs during the melanogenesis process indicates that functioning cells are targeted by the immune system.[18] Further studies at the molecular level are required to determine whether the prominence of this pathological process in uveal and retinal pigment epithelium, as opposed to neural crest-derived cells in the corneal endothelium, represents an immune tolerance mechanism arising from the avascular structure of the cornea or whether the corneal endothelium has functions beyond melanin pigment production.

In studies evaluating crystalline lenses in vitiligo patients, no statistically significant difference was found in cataract prevalence between patients with vitiligo and healthy controls.[12,19,20] In the study conducted by Ezzeldine et al.[21] with 40 vitiligo patients, no statistically significant difference was found between the patient group and volunteers in terms of visual acuity, although temporary refractive errors were observed. These results are consistent with those reported by Genedy et al.[22] and were attributed to the hypothesis that ocular melanocytes do not play a direct role in the detection or transmission of visual information.

Contrary to these studies, in a study conducted by Karadağ et al.[8] it was reported that point lenticular opacities were seen at a higher rate in patients with vitiligo, but these opacities did not interfere with vision. In addition, we assessed whether the lenticular opacities detected in young patients were risk factors for future cataract formation. In another study, it was reported that three patients with vitiligo developed posterior subcapsular cataracts in their 30s.[23]

We compared lens densitometry values of vitiligo patients with the control group using Pentacam HR to provide quantitative corneal and lens densitometry data that evaluated corneal and lens transparency. The lens densitometry values in vitiligo patients were comparable to those of the control group across all zones. Additionally, no patient in the study exhibited lenticular opacities. Comparison of patients with lenticular opacity to the control group, as reported in the study by Karadağ et al.[8] may be the subject of another study.

This study examined patients with periocular vitiligo for the first time using specular microscopy and lens densitometry, which we believe represents a strength of the present article. However, this study has some limitations. The study was conducted in a small patient group and included only Turkish participants. Studies conducted on larger patient groups with different ethnic backgrounds could yield different results regarding corneal and lens involvement in patients with vitiligo. The exclusion of images of unacceptable quality further reduced the sample size. In addition, prospective studies are still needed to better understand the correlation between clinical findings and corneal imaging findings, because our results do not provide information about the chronic course of the disease. The genetics and pathophysiology of vitiligo have not yet been clearly elucidated. Studies that reveal the molecular basis of the disease may also be important in the future.

CONCLUSION

No differences in corneal and anterior chamber parameters were observed in vitiligo patients with periocular involvement when compared to the control group. Likewise, corneal endothelial parameters were similar between the two groups. There was no statistically significant difference in lenticular involvement between vitiligo patients and those with periocular involvement. Our results suggest that the pathological destruction seen in melanocytes in vitiligo is not observed in the neural crest-derived cells of the cornea. We believe that the results of our study will reveal important findings that can serve as the basis for more comprehensive studies evaluating the effect of the disease on the cornea and lens in patients with vitiligo with and without periocular involvement.

Disclosures

Ethics Committee Approval: The study was approved by the Istanbul Medipol University Non-interventional Clinical Research Ethics Committee (No: 294, Date: 29/02/2024).

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