

# Comparison of anterior segment parameters, endothelial cell density, and their coefficient of variation in COVID-19 patients and healthy individuals

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## ABSTRACT

This study aimed to evaluate anterior segment parameters, corneal endothelial cell density (ECD), and the coefficient of variation (CV) of endothelial cells in patients who had recovered from COVID-19 compared to healthy individuals. The right eyes of 34 patients (mean age  $44.97 \pm 6.74$  years; range 25 to 55 years) who had been hospitalized with COVID-19 and had a negative PCR test at least two months prior were examined. A comprehensive optometric evaluation was performed, including autorefractometry, retinoscopy, ophthalmoscopy, slit-lamp examination, and assessments using Topcon Specular and Oculus Pentacam devices. The control group consisted of 34 healthy individuals (mean age  $44.71 \pm 4.65$  years) who had tested negative for COVID-19 via PCR at least three times over the past two years. Both groups had a history of COVID-19 vaccination. The mean corneal endothelial cell density was significantly lower in the patient group ( $2503.78 \pm 311.76$  cells/mm<sup>2</sup>) compared to the healthy group ( $2710.04 \pm 184.93$  cells/mm<sup>2</sup>;  $P = 0.005$ ). The coefficient of variation of endothelial cells was slightly higher in the patient group ( $37.30 \pm 5.31$ ) than in controls ( $36.20 \pm 4.08$ ), but this difference was not statistically significant ( $P = 0.451$ ). Other anterior segment parameters, such as central corneal thickness, anterior chamber angle, keratometry, horizontal corneal diameter, and pupil diameter, showed no significant differences between the two groups ( $P > 0.05$ ). The study demonstrated a reduction in corneal endothelial cell density and a non-significant increase in the coefficient of variation among individuals recovered from COVID-19. These findings may provide insight into the systemic ocular effects associated with COVID-19.

**Keywords:** Anterior segment parameters, Endothelial cell density, Coefficient of variation, COVID-19.

## Introduction

The coronavirus SARS-CoV-2, first identified in 2019, quickly evolved into a global pandemic, profoundly impacting public health, healthcare systems, and the global economy. As a member of the coronavirus family, this virus primarily spreads through respiratory droplets, direct contact with infected individuals, and contaminated surfaces (1). COVID-19 triggers severe inflammatory responses that can affect the vascular system, leading to complications such as thrombosis and organ failure (2). Numerous reports have documented ocular

symptoms in COVID-19 patients, including conjunctivitis, dry eye, conjunctival inflammation, visual disturbances, and reduced corneal sensitivity. Moreover, studies indicate that the virus can reach ocular tissues via the bloodstream and tear ducts, causing direct or indirect damage to the eye, highlighting a potential link between COVID-19 and visual health, and emphasizing the need to explore the virus's effects on ocular structures (3).

Among the ocular components, corneal endothelial cells are crucial for maintaining corneal transparency and function, and these cells may be vulnerable to viral infection. Limited studies have explored the impact of COVID-19 on corneal endothelial

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cell density and the coefficient of variation. Some evidence suggests that the virus might impair endothelial cell function through inflammatory and systemic mechanisms (4). Potential pathways include increased oxidative stress, disruption of the corneal barrier, and microvascular alterations caused by immune responses. Since reduced corneal endothelial cell density can lead to visual impairments and elevate the risk of corneal opacity, understanding the systemic effects of COVID-19 on the eye is critical (5). Additionally, some research points to COVID-19 causing ocular inflammation and anterior segment changes, which may increase the risk of corneal abnormalities and impact long-term vision. These findings underscore the necessity for more comprehensive and detailed investigations into the disease's effects on the visual system (6).

In a study by Oren *et al.* (2022), 68 individuals (34 recovered COVID-19 patients and 34 healthy controls) were evaluated. The patient group had a mean age of  $50.14 \pm 1.6$  years, and the control group averaged  $48.9 \pm 7.1$  years; the patient group included 18 women and 16 men, while the controls had 16 women and 18 men. Corneal endothelial cell density was lower in patients ( $2278.186 \pm 50.78$  cells) compared to controls ( $2420.222 \pm 15.25$  cells), accompanied by an increased coefficient of variation. These results suggest that COVID-19 may significantly affect the structure and function of the corneal endothelium (7).

Erdem *et al.* (2021) examined 80 recovered COVID-19 patients and 72 healthy controls, with a mean age of  $36.7 \pm 37.70$  and  $34.66 \pm 5.89$  years, respectively. The patient group included 44 women and 36 men; the control group had 37 women and 35 men. Endothelial cell density was  $2713.46 \pm 56.25$  cells in patients versus  $2845.299 \pm 80.27$  in controls. The coefficient of variation was higher in patients ( $42.6 \pm 92.79$ ) than in controls ( $40.5 \pm 16.97$ ). The percentage of hexagonal cells decreased from 49.12% in controls to 46.51% in patients ( $p = 0.024$ ). Additionally, central corneal thickness increased significantly from 526.84 to 553.00 micrometers ( $p = 0.005$ ). These findings indicate that COVID-19 may affect both the structure and function of the corneal endothelium (8).

Kaushik *et al.* (2022) assessed 129 recovered COVID-19 patients and 123 healthy controls. The patient group's mean age was  $43.88 \pm 17.13$  years, and controls averaged  $49.31 \pm 15.65$  years. In patients, mean endothelial cell density was 2586.74 in the right eye and 2610.36 in the left eye, compared to 2616.79 and 2618.74 in controls, respectively. The coefficient of variation in patients was  $37.75 \pm 6.03$  (right eye) and  $36.25 \pm 4.66$  (left eye), compared to  $35.23 \pm 3.75$  and  $34.77 \pm 3.64$  in controls. The study observed decreased endothelial cell density and hexagonal cell count (pleomorphism), alongside increased coefficient of variation (polymegathism) in patients, suggesting notable alterations in corneal endothelial morphology following COVID-19 infection (9).

Elshalkami *et al.* (2022) examined the right eyes of 64 recovered COVID-19 patients and 53 healthy controls. The mean ages were  $41.8 \pm 11.97$  years for the patient group and  $42.11 \pm 02.16$

years for the control group. Males comprised 50% of the patient group and 45.3% of the control group. Endothelial cell density was  $197 \pm 2943.89$  cells/mm<sup>2</sup> in patients and  $270 \pm 2925.63$  cells/mm<sup>2</sup> in controls. The coefficient of variation (CV) was  $29.3 \pm 66.88$  in patients and  $30.4 \pm 59.49$  in controls. No significant differences were observed in any of the measured parameters between the two groups (10).

Siu and Agrawal (2020) conducted a comprehensive review investigating the potential effects of COVID-19 on ocular health. Their analysis of human and animal coronavirus studies revealed that the murine coronavirus (MHV) caused retinal inflammation and damage in laboratory models, suggesting that coronaviruses, including SARS-CoV-2, might exert similar effects on the human eye (3).

Shokouhi-Rad *et al.* (2022) studied the impact of COVID-19 on the anterior segment of the eye. Their results indicated a significant increase in anterior chamber volume among recovered patients, though the clinical implications of this remain uncertain. The study involved 20 non-hospitalized patients with mild COVID-19, who underwent Pentacam imaging at least two weeks after recovery, with follow-up measurements at one and three months. Anterior chamber volume increased from  $177.68 \pm 8.36$  mm<sup>3</sup> to  $182.58 \pm 25.39$  mm<sup>3</sup> ( $P = 0.048$ ). While corneal curvature and thickness also increased, these changes were not statistically significant (11).

Roehrich *et al.* (2020) employed immunohistochemistry to examine the distribution of ACE2, TMPRSS2, DC-SIGN, and DC-SIGNR proteins in ocular surface tissues, including the cornea, limbus, and conjunctiva. Their findings demonstrated that ACE2 and TMPRSS2 are expressed in the superficial epithelium of these tissues as well as in the corneal endothelium. This suggests a possible route for SARS-CoV-2 entry through the ocular surface and raises concerns about virus transmission via corneal transplantation (12).

Multiple studies have documented that COVID-19 infection can induce significant structural and functional changes in the corneal endothelium. Commonly reported alterations in recovered patients include decreased endothelial cell density, increased variation in cell size (coefficient of variation), reduced hexagonality of cells, and increased corneal thickness. Although some studies have found no significant differences between recovered patients and healthy controls, the overall evidence points to potential ocular effects of the virus. These findings underscore the necessity of long-term studies to understand the clinical significance of these changes. Additionally, further investigation into the underlying mechanisms may enhance understanding of coronavirus-related corneal alterations and support the development of targeted therapeutic approaches.

## Materials and Methods

This cross-sectional study was conducted in 2023 (the year 1402 in the Iranian calendar) in Mashhad. Thirty-four right eyes of patients aged 25 to 55 years, previously hospitalized for COVID-

19 at Qaem and Imam Reza Hospitals, were examined alongside 34 right eyes of healthy individuals as a control group over six months.

Sample size calculations were based on data from Oren *et al.*, who reported mean endothelial cell density (ECD) values of  $2278.186 \pm 50.78$  cells/mm<sup>2</sup> in COVID-19 patients and  $2420.222 \pm 15.25$  cells/mm<sup>2</sup> in healthy controls. Assuming a 5% error rate and 80% statistical power, the minimum required sample size per group was calculated as 34 using a formula for comparing means of two independent populations. Notably, sample sizes calculated based on the coefficient of variation (CV) and the percentage of hexagonal cells (HEX) were smaller (5 and 15 per group, respectively).

Inclusion criteria were: age between 25 and 55 years; at least two months since a negative PCR test; history of moderate to severe COVID-19 requiring hospitalization within the past two years; no history of ocular diseases such as keratoconus or corneal refractive surgery; and no use of medications affecting corneal thickness or structure. Exclusion criteria included the development of new ocular diseases during the study, initiation of medications affecting the cornea, lack of cooperation with examinations or follow-ups, or diagnosis of systemic diseases potentially influencing the outcomes.

During the study, 3 to 4 patients per week with a prior history of severe COVID-19 (requiring hospitalization based on criteria including oxygen saturation <94%, shortness of breath, chest pain, dizziness, impaired consciousness, or prolonged fever) were fully examined, ensuring at least two months had passed since a negative PCR test.

Complete ophthalmic evaluations included autorefractometry, retinoscopy, ophthalmoscopy, slit lamp examination, and measurement of corneal endothelial cell density and coefficient of variation using a specular microscope (TOPCON SP-3000P, Japan). Central corneal thickness, anterior chamber angle, keratometry, horizontal corneal diameter, and pupil diameter were measured using a Pentacam device (OCULUS, Germany). These examinations were similarly performed on the 34 healthy controls who had tested negative for COVID-19 by PCR three times over the previous two years.

Among the 68 participants, 58 had received vaccination, including 50 who received the Sinopharm vaccine and 8 who received the Barakat vaccine.

After data collection and entry into SPSS software version 26, the data were analyzed descriptively and analytically. A significance level of 5% was considered.

This study was reviewed and approved by the university's Research and Ethics Committees before implementation. The ethical code of the research project is IR.MUMS.FHMPM.REC.1402.006.

## Results and Discussion

The mean age in the COVID-19 history group was  $44.97 \pm 6.74$  years, and in the control group was  $44.71 \pm 4.65$  years. The

Mann-Whitney test showed no significant difference in age between the two groups ( $p = 0.956$ ), and the two groups were homogeneous in terms of age (Table 1).

**Table 1. Mean and standard deviation of participants' age in the hospitalized history and control groups**

		Group		Test-result	
		Control (n = 34)	With hospitalization history (34 persons)	Mann-Whitney	P
Age (years)	Mean $\pm$ Standard Deviation	44.71 $\pm$ 4.65	44.97 $\pm$ 6.74	z = -0.055	0.956
	Median [Q3, Q1]	46 (41.50, 48)	44.5 (39.50, 50.25)		

The number of women and men was equal in both groups. The chi-square test results showed that there was no significant difference between the two groups in terms of gender ( $p = 1.00$ ), and the two groups were homogeneous in this regard (Table 2).

**Table 2. Frequency distribution of participants by gender in the hospitalized history and control groups**

Variable	Group		Test-result
	Control group (34 individuals)	Control group (34 individuals)	
Gender	Number (Percentage)	Number (Percentage)	
	Male	5 (14.7)	$\chi^2 < 0.001$
	Female	29 (85.3)	$P = 0.999$
<b>Total</b>	34 (100.0)	34 (100.0)	Chi-square test

In both groups, the number of vaccinated individuals was similar. The chi-square test results showed that there was no significant difference between the two groups in terms of vaccination status ( $p = 1.00$ ), and the two groups were homogeneous in this regard (Table 3). Additionally, in both groups, among the vaccinated individuals, 25 people (73.5%) had received the Sinopharm vaccine, and 4 people (11.8%) had received the Barakat vaccine.

**Table 3: Frequency distribution of participants by vaccination status in the hospitalized history and control groups**

variable	Group		Test-result
	Control group (34 individuals)	Control group (34 individuals)	
Vaccine	Number (Percentage)	Number (Percentage)	
	No	(14.7) 5	$\chi^2 < 0.001$
	Yes	(85.3) 29	$P = 0.999$
<b>Total</b>	(100.0) 34	(100.0) 34	Chi-square test

Based on the findings, 70.6% of the control group and 76.5% of the hospitalized group were classified as having astigmatism. Fisher's exact test indicated no significant difference between the

two groups regarding refractive errors ( $p = 0.082$ ), demonstrating homogeneity in this aspect (Table 4).

**Table 4. Frequency distribution of participants by refractive errors in the hospitalized history and control groups**

Variable	Group		Test result
	Control group (34 individuals)	With a history of hospitalization (34 individuals)	
	Number (Percentage)	Number (Percentage)	
Hyperopia (Farsightedness)	(0.0) 0	(2.9) 1	
Myopia (Nearsightedness)	(0.0) 0	(2.9) 1	F = 6.078
Astigmatism	(0.0) 0	(5.9) 2	P = 0.082
Hyperopic Astigmatism	(29.4) 10	(11.8) 4	Fisher's test
Myopic Astigmatism	(70.6) 24	(76.5) 26	
Total	(100.0) 34	(100.0) 34	

The Mann-Whitney test indicated significant differences between the two groups in endothelial cell parameters, including cell count, average cell size, and cell density. Specifically, the hospitalized group had a significantly lower cell count (mean  $\pm$  SD:  $93.59 \pm 18.57$ ) compared to the control group ( $110.38 \pm 16.06$ ) ( $p = 0.001$ ). Moreover, the average cell size was significantly larger in the hospitalized group ( $406.42 \pm 58.72$ ) than in controls ( $356.46 \pm 35.17$ ) ( $p < 0.001$ ). Cell density was also significantly reduced in the hospitalized group ( $2503.78 \pm 311.76$ ) relative to the control group ( $2710.04 \pm 184.93$ ) ( $p = 0.005$ ) (Table 5).

**Table 5. Mean and standard deviation of endothelial cell characteristics in the hospitalized history and control groups**

Variable	Group		Test- result
	Control group (34 individuals)	With a history of hospitalization (34 individuals)	
Mean $\pm$ SD	$0.51 \pm 0.03$	$0.51 \pm 0.03$	$651/0 t = t = 0.651$
Corneal thickness	(Q3, Q1) Median: (0.53, 0.49) 0.51	(0.53, 0.50) 0.51	$z = 3.222^{**}$ P = 0.001 Mann-Whitney test
Cell count	Mean $\pm$ SD: $110.38 \pm 16.06$	$93.59 \pm 18.57$	$z = -3.778^{**}$

	(Q3, Q1) Median	(124, 98) 108.50	(106.50, 85.0) 98.50	P < 0.001 Mann-Whitney test $z = -0.908$ P = 0.364 Mann-Whitney test
Mean $\pm$ SD		$356.46 \pm 35.17$	$406.42 \pm 58.72$	$z = -0.754$ P = 0.451 Mann-Whitney test
Mean cell size	(Q3, Q1) Median	(381.60, 323.73) 354.50	(427.95, 358.15) 388.65	$z = 2.809^{**}$ P = 0.005 Mann-Whitney test
Mean $\pm$ SD		$139.86 \pm 14.99$	$147.89 \pm 27.49$	$t = -0.969$ P = 0.336 Independent t-test
Standard deviation of cell size	(Q3, Q1) Median	(149.35, 126.43) 139.60	(158.68, 126.35) 146.75	$t = 0.651$ P = 0.517 Independent t-test
Mean $\pm$ SD		$36.20 \pm 4.08$	$37.30 \pm 5.31$	$z = 3.222^{**}$ P = 0.001 Mann-Whitney test
Coefficient of variation of cell size	(Q3, Q1) Median	(40.17, 32.70) 35.15	(40.10, 33.30) 35.80	$z = -$ $3.778^{**}$ P < 0.001 Mann-Whitney test
Mean $\pm$ SD		$2710.04 \pm 184.93$	$2503.78 \pm 311.76$	$z = -0.908$ P = 0.364 Mann-Whitney test
Cell density	(Q3, Q1) Median	(2876.50, 2558.03) 2736.95	(2792.23, 2337.32) 2573.15	$z = -0.754$ P = 0.451 Mann-Whitney test
Mean $\pm$ SD		$52.97 \pm 9.89$	$50.76 \pm 8.85$	$z = 2.809^{**}$ P = 0.005 Mann-Whitney test
Hexagonality	(Q3, Q1) Median	(60.50, 46.00) 52.00	(56.00, 44.00) 51	

\*\*Statistically significant at the 1% level

The test results revealed that among anterior segment parameters, individuals with a history of hospitalization due to COVID-19 exhibited a significantly lower anterior chamber volume (mean  $\pm$  SD:  $135.94 \pm 30.53$ ) compared to the control group ( $160.91 \pm 32.82$ ;  $P = 0.002$ ). Additionally, anterior chamber depth was significantly reduced in the hospitalized COVID-19 group ( $3.20 \pm 0.29$ ) relative to controls ( $3.36 \pm 0.21$ ;  $P = 0.014$ ) (Table 6).

**Table 6. Mean and standard deviation of anterior segment parameters in two groups with a history of hospitalization and control**

	Group		Test- result				
	Control group (34 individuals)	Control group (34 individuals)		Mean ± SD	(28.80, 37.88): Median	(29.55, 35.95): 34.75	32.40
Vortex Clarity	Mean ± SD	539.09 ± 32.50	540.03 ± 30.75				
	Median (Q1, Q3)			t = 0.123 P = 0.903			
				Independent t- test			
Keratometry	Mean ± SD	(511.50, 568.25):	Median (519.00, 557.25):				
	Median (Q1, Q3)			t = 0.181 P = 0.857			
				Independent t- test			
Corneal Volume	Mean ± SD	45.11 ± 0.82	45.17 ± 1.81				
	Median (Q1, Q3)			z = -0.802 P = 0.425			
				Independent t- test			
Anterior Chamber Volume	Mean ± SD	160.91 ± 32.82	135.94 ± 30.53				
	Median (Q1, Q3)	(134.50, 180.00):	(117.00, 161.75):	**z = -3.248 P = 0.002**			
				Independent t- test			
Anterior Chamber Depth	Mean ± SD	3.36 ± 0.21	3.20 ± 0.29				
	Median (Q1, Q3)	(3.22, 3.48):	(2.98, 3.40):	*z = -2.514 P = 0.014*			
				Independent t- test			
Intraocular Pressure (IOP)	Mean ± SD	0.41 ± 1.27	0.40 ± 1.23				
	Median (Q1, Q3)			z = -0.058 P = 0.954			
				Independent t- test			
Horizontal Corneal Diameter	Mean ± SD	11.69 ± 0.37	11.58 ± 0.40				
	Median (Q1, Q3)			z = -1.161 P = 0.250			
				Independent t- test			
Anterior Chamber Angle	Mean ± SD	33.93 ± 5.05	32.79 ± 5.91				
	Median (Q1, Q3)			z = -0.860 P = 0.393			
				Independent t- test			

\*Significant at the 5% level \*\* Significant at the 1% level

This study demonstrated that patients recovered from COVID-19 exhibited significant alterations in certain corneal and anterior chamber parameters, reflecting possible systemic effects of SARS-CoV-2 on ocular microanatomy, particularly at the endothelial cellular level.

A key finding was the significant reduction in endothelial cell density (ECD) among recovered patients compared to healthy controls. This decrease may be attributed to direct viral cytopathic effects, systemic inflammatory responses, or secondary sequelae of the infection. Since corneal endothelial cells play a critical role in maintaining corneal transparency through their pump function, reduced cell density can predispose patients to complications such as corneal edema and vision impairment. Notably, despite the decline in cell density, the coefficient of variation (CV) and the percentage of hexagonal cells (HEX) did not differ significantly from controls, suggesting that endothelial cell morphology and uniformity remained largely intact. This pattern may reflect an early or mild endothelial insult without substantial structural degeneration.

Central corneal thickness (CCT) was comparable between groups, indicating preserved endothelial function in fluid regulation despite decreased cell density. This contrasts with conditions like Fuchs' endothelial dystrophy, where reduced cell numbers typically correspond with increased corneal thickness. Similarly, keratometric values and corneal volume showed no significant differences, underscoring the stability of corneal geometry and suggesting no direct COVID-19-related impact on these parameters.

Anterior chamber metrics—including angle, depth, and volume—were slightly reduced in patients but remained mostly within normal ranges. A narrowed anterior chamber angle in some individuals may raise concerns about an increased risk for angle-closure glaucoma, particularly in anatomically predisposed eyes, warranting further detailed longitudinal assessment. Intraocular pressure (IOP) measurements showed no significant group differences, though minor variations could relate to individual or inflammatory factors inherent to the disease. Pupil diameter and horizontal corneal diameter (HWTW) also remained similar between groups, with some borderline values potentially reflecting neurological sequelae of COVID-19.

Unlike prior studies which mainly focused on superficial ocular inflammation or syndromic ocular manifestations, this investigation provided a comprehensive assessment of anterior segment structures using advanced imaging modalities: specular microscopy for endothelial analysis and Pentacam for corneal and

anterior chamber evaluation. This methodological rigor allowed for precise detection of subtle corneal changes potentially linked to COVID-19 and offers a valuable framework for early diagnosis and clinical management of post-COVID ocular complications. The absence of significant differences in keratometric values between recovered COVID-19 patients and healthy controls aligns with the findings of Smith *et al.* (2021), suggesting that COVID-19 likely does not affect the anterior corneal curvature. However, potential confounding factors—such as disease severity, time elapsed since recovery, and medication use—necessitate further controlled investigations to clarify these relationships and their clinical implications.

In contrast, this study identified significant changes in multiple corneal and anterior chamber parameters in recovered patients compared to controls. These include a notable decrease in corneal endothelial cell density (ECD), number of endothelial cells, anterior chamber volume and depth; a significant increase in mean cell size and coefficient of variation (CV), decreased percentage of hexagonal cells (pleomorphism), and increased central corneal thickness (CCT). These findings are consistent with previous studies by Oren *et al.* (2022), Erdem *et al.* (2021), and Kaushik *et al.* (2022) (7, 8, 9). For example, Oren and colleagues, in a study involving 68 recovered patients, similarly reported reduced ECD and increased CV, mirroring the current results (7). Likewise, Erdem *et al.* (80 patients) and Kaushik *et al.* (129 patients) observed comparable changes in endothelial parameters and corneal thickness, indicating a pattern of COVID-19-related endothelial disruption (8, 9).

Conversely, Elshalkami *et al.* (2022), analyzing 64 eyes from recovered patients and 53 from controls, found no significant differences in these parameters. This discrepancy may stem from differences in examination timing (closer to infection versus post-recovery), variations in disease severity among study populations, or less sensitive instrumentation compared to the specular microscopy and Pentacam technologies used here. Moreover, insufficient control for confounding factors such as corticosteroids or other drug treatments may have influenced their findings (10).

The concordance between the current study and those by Oren, Erdem, and Kaushik likely reflects the shared focus on endothelial cell parameters using high-resolution imaging, enabling precise measurement and comparison. Mechanistically, these results are supported by known SARS-CoV-2 effects: viral entry via ACE2 receptors on corneal endothelial cells, induction of local inflammation, and disruption of the Na<sup>+</sup>/K<sup>+</sup>-ATPase pump function. These processes impair corneal hydration regulation, resulting in decreased ECD and increased CCT. The systemic cytokine storm and oxidative stress triggered by infection may further accelerate endothelial apoptosis and reduce pleomorphism, while increased CV reflects greater heterogeneity in cell size due to ongoing cellular damage and repair. These pathophysiological mechanisms are corroborated by this and aligned studies, underscoring the combined role of direct viral injury and inflammation.

Age was identified as an important confounding factor since ECD naturally declines with age (Carlson *et al.*, 1988), whereas sex differences in ECD have been generally dismissed by prior research. Other potential confounders include intraocular pressure and refractive errors (13).

Limitations of the present study include the absence of inflammatory biomarker measurements, incomplete control of confounding variables, lack of assessment of long-term ocular effects, no stratification by COVID-19 severity, and omission of sex-based analyses. These gaps warrant attention in future research.

Given the observed alterations, periodic clinical evaluation of recovered COVID-19 patients using specular microscopy and Pentacam to monitor ECD and CCT is advisable. Early detection protocols and long-term follow-up, particularly for patients with severe COVID-19, could facilitate timely identification and management of potential ocular complications.

## Conclusion

This study demonstrated that individuals recovered from COVID-19 exhibit decreased corneal endothelial cell density and increased variability in endothelial cell size, as measured by specular microscopy and Pentacam. These findings contribute to understanding the systemic ocular effects of COVID-19 and highlight the importance of ongoing ophthalmic monitoring in this population.

**Acknowledgments:** Not applicable.

**Conflict of interest:** The authors declare no conflict of interest.

**Financial support:** This work was supported by the “Mashhad University of Medical Science.

**Ethics statement:** The research adhered to the tenets of the Declaration of Helsinki and Written informed consent was obtained from the participants in the present study. Also, the Ethics Committee of Mashhad University of Medical Sciences approved the study with ID IR.MUMS.FHMPM.REC.1402.006.

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