Topographic, Anterior Chamber Parameters and Corneal Endothelial Cell Density in Third Trimester Healthy Pregnant Women: Case-Control Study

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ABSTRACT

Purpose: This study aimed to investigate the effects of pregnancy on the corneal endothelium and epithelium, corneal topographic parameters, and anterior segment parameters.

Methods: This prospective cross-sectional study included 72 eyes of 72 healthy third-trimester pregnant women and 65 eyes of 65 age-matched healthy controls. Corneal topographic and anterior chamber parameters were obtained using a Placido-disc topographer (MS-39®, CSO, Badia a Settimo–Scandicci, Florence, Italy) and the Lenstar LS900 (Haag-Streit AG, Switzerland). Corneal specular parameters were evaluated using the NIDEK CEM-530 (Hiroishi-cho, Gamagori, Japan).

Results: No differences were observed in corneal topographic parameters or epithelial thickness between healthy third-trimester pregnant women and the control group. In the pregnant group, a significant negative correlation was observed between anterior maximum keratometry (Kmax) and minimum corneal thickness (minthick) ($r = -0.284$, $p = 0.016$; $r = -0.295$, $p = 0.012$, respectively). A significant positive correlation was found between anterior Kmax and anterior root mean square average (RMSA) ($r = 0.258$, $p = 0.028$). Endothelial cell density was lower in the pregnant group than in the control group ($p = 0.018$). When parameters were compared based on gravidity, a significant difference was found in the median coefficient of variation ($p = 0.017$).

Conclusion: No significant differences were found in corneal topographic parameters, corneal epithelial thickness, or anterior chamber parameters between healthy third-trimester pregnant women and healthy controls. Pregnancy-related hormonal changes may induce alterations in corneal endothelial cells. Further studies are needed to determine whether these corneal specular changes are permanent.

Keywords: Anterior chamber parameters; Keratoconus; Corneal endothelium; Corneal epithelium; Pregnancy

INTRODUCTION

Pregnancy induces physiological changes across all organ systems. These changes are most pronounced during the third trimester, when hormonal activity reaches its peak. The majority of pregnancy-related physiological alterations are temporary, and hormonal levels typically return to normal within a few weeks after delivery.[1] The eye is one of the organs that requires particular attention during pregnancy. Although most pregnancy-related ocular conditions are mild, some may result in significant visual impairment.[2,3] Previous studies have demonstrated a decrease in intraocular pressure as well as alterations in corneal biomechanics, corneal thickness and curvature, and anterior chamber parameters during pregnancy.[1,4–7] Several reports have indicated that these corneal changes return to pre-pregnancy values during the postpartum period.[8] How-

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ever, reports describing the progression of previously stable keratoconus during pregnancy[9] suggest that the effects of pregnancy on the anterior segment may not always be transient.

A previous study reported significant differences in corneal thickness, anterior chamber parameters, and keratometry values during pregnancy compared with the three-month postpartum period.[1] Another study demonstrated keratoconus progression during pregnancy and up to six months postpartum, suggesting that pregnancy may represent a potential risk factor for keratoconus progression.[6] In contrast, Naderan et al.[8] longitudinally evaluated the effects of pregnancy on corneal parameters and reported no statistically or clinically significant changes. Overall, studies investigating pregnancy-related alterations in corneal and anterior segment parameters have yielded conflicting results. Notably, no previous study has evaluated corneal epithelial thickness mapping in healthy pregnant women. Corneal epithelial thickness is non-uniform and dynamically remodels to maintain a smooth and regular ocular surface. Moreover, the corneal epithelium is highly responsive to underlying stromal irregularities and asymmetries.[10] Several studies have highlighted the clinical significance of corneal epithelial thickness mapping in the diagnosis and management of ectatic disorders, post-refractive surgery complications, and ocular surface diseases.[11,12]

The present study aimed to evaluate corneal topographic parameters, corneal epithelial thickness mapping, anterior chamber characteristics, and corneal endothelial cell density and morphology in healthy women during the third trimester of pregnancy, in comparison with a healthy control group.

MATERIALS AND METHODS

This prospective, cross-sectional, case–control study was conducted at the Ophthalmology and Obstetrics and Gynecology Clinics of Ankara Etlik City Hospital between May 2023 and January 2024. All participants were informed about the study, and written informed consent was obtained from each participant. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Etlik City Hospital (Ethics No: AEŞH-EK1-2023-317).

The study population consisted of 72 healthy pregnant women aged 18–39 years in the third trimester of pregnancy (28–38 weeks of gestation) and 65 age- and sex-matched healthy control subjects. Pregnant participants with systemic conditions such as gestational diabetes or hypertension were excluded, and only healthy pregnant women were enrolled. Healthy control subjects were recruited from individuals presenting to the outpatient clinic for routine ophthalmic examination. Exclusion criteria for both groups included elevated intraocular pressure; a history of ocular disease; dense media opacities; refractive errors exceeding ±3.5 diopters spherical or 2.5 diopters cylindrical; previous ocular trauma or surgery; a history of systemic vascular disease; or previous refractive surgery. Subjects diagnosed with keratoconus or other ectatic disorders on corneal topography were also excluded.

The number of pregnancies, height, and weight were recorded for all participants, and body mass index (BMI) was calculated. Only the right eye of each participant was included in the analysis. A comprehensive ophthalmologic examination was performed, including best-corrected visual acuity (BCVA), anterior and posterior segment examination using slit-lamp biomicroscopy with a 90 D lens (Volk Optical Inc., Mentor, OH, USA), and intraocular pressure measurement using a noncontact tonometer.

All participants underwent corneal assessment using a Placido disc–based topographer (MS-39®, CSO, Badia a Settimo–Scandicci, Florence, Italy) (Figure 1A, 1B). The MS-39 system integrates high-resolution spectral-domain optical coherence tomography with a 22-ring Placido disc and operates at a wavelength of 845 nm, providing high-resolution images of the cornea, including anterior chamber tomography and anterior and posterior corneal topography. The device analyzes the central 10 mm of the anterior corneal surface.[13]

All measurements were performed by a single experienced examiner, and a single measurement was obtained from each participant. The following parameters were analyzed as topometric indices: maximum keratometry (Kmax) values of the anterior and posterior corneal surfaces; anterior and posterior apex curvature; corneal pachymetry, including central corneal thickness (CCT) and minimum corneal thickness (minthick); anterior and posterior symmetry indices (SIf and SIb); anterior and posterior elevation-based in-

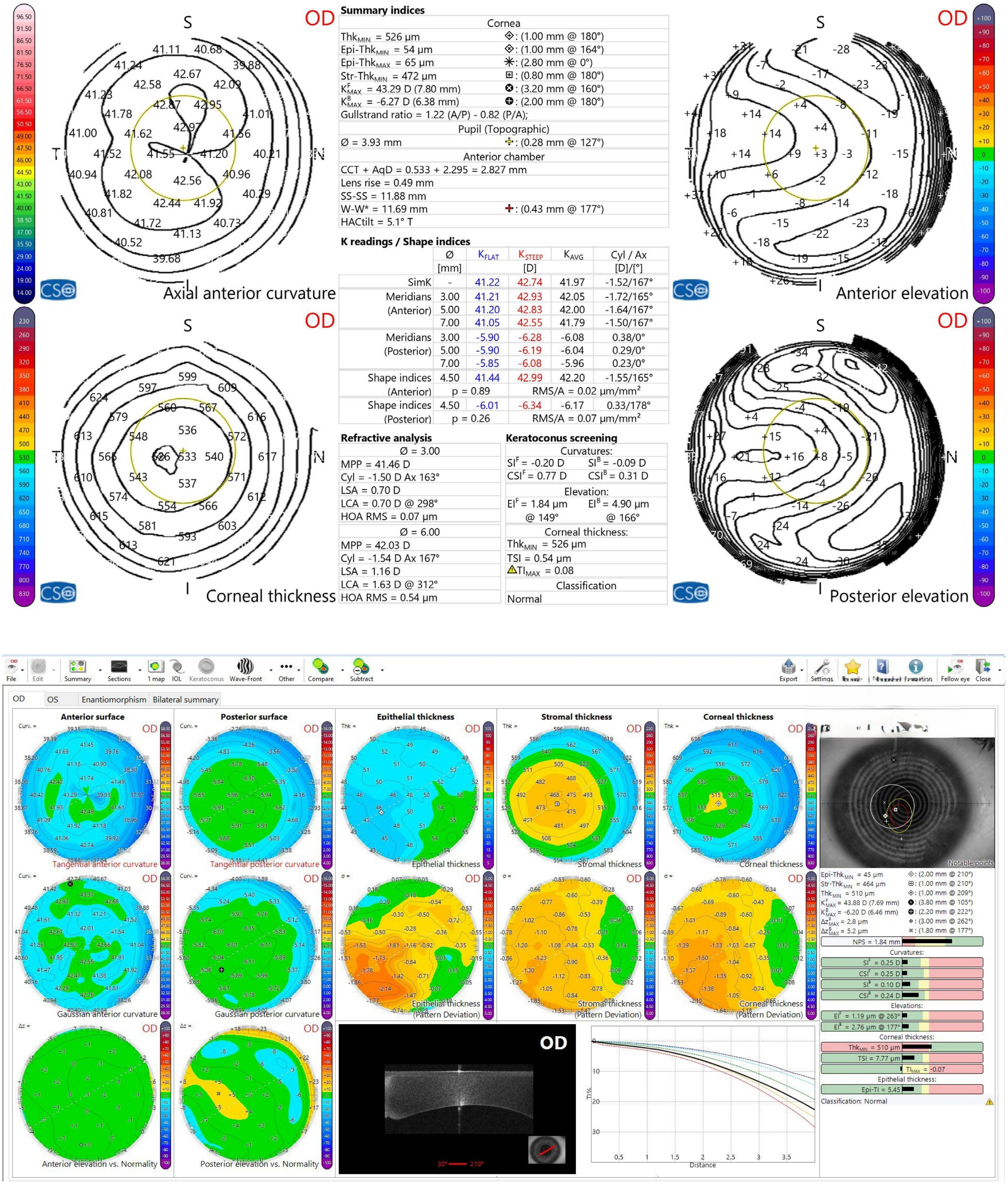

Figure 1A–B. *Corneal topographic images of the right eye of a pregnant woman.*

dices (EIf and EIb); mean pupillary power (MPP); anterior and posterior corneal root mean square average (RMSA); and epithelial thickness mapping (ETM). White-to-white diameter (WTW), aqueous depth (AqD), and anterior chamber depth (ACD) were also obtained using the same device. Corneal curvature values at the 3-mm zone were used for statistical analysis. Epithelial thickness was assessed in predefined concentric zones centered on the cornea, including the central (0–3 mm), paracentral (3–6 mm), and peripheral (6–8 mm) regions. Measurements in the paracentral and peripheral zones were recorded separately for the superior, inferior, nasal, and temporal quadrants.

Ocular biometry was performed using the Lenstar LS900 (Haag-Streit AG, Switzerland), and axial length and white-to-white diameter were measured. Corneal endothelial parameters, including endothelial cell density (cells/mm²), mean cell area (μm²), standard deviation of cell area (μm²), polymegathism, pleomorphism, and central corneal thickness, were evaluated using the NIDEK CEM-530 specular microscope (Hiroishi-cho, Gamagori, Japan). Unlike conventional specular microscopy, the paracentral mode of the CEM-530 allows detailed quantitative and structural evaluation of endothelial cells in the central, paracentral, and peripheral cornea.

STATISTICAL ANALYSIS

Statistical analyses were performed using IBM SPSS version 23 (SPSS Inc., Chicago, IL, USA). The Kolmogorov–Smirnov test was used to assess normality of data distribution. For comparisons between two groups, the independent samples t-test was used for normally distributed variables, whereas the Mann–Whitney U test was applied for non-normally distributed variables. For comparisons involving three or more groups, one-way analysis of variance was used for normally distributed variables, and the Kruskal–Wallis test was used for non-normally distributed variables, followed by Dunn's test for multiple comparisons. The Pearson chi-square test was applied to analyze categorical variables. Paired-sample t-tests were used to compare normally distributed measurements obtained using different devices. Agreement between measurements from different instruments was assessed using the intraclass correlation coefficient (ICC). Correlations between variables were analyzed using Pearson's or Spearman's correlation coefficients, as appropriate. The minimum required sample size was calculated as 101, assuming a margin of error of 0.05, a power of 0.80, and an effect size of 0.5. A p-value < 0.05 was considered statistically significant.

RESULTS

This study included 72 eyes of 72 healthy women in the third trimester of pregnancy and 65 eyes of 65 age-matched healthy nonpregnant women. The mean age was 28.0 ± 5.5 years in the pregnant group and 26.2 ± 4.9 years in the control group, with no statistically significant difference between the groups ($p = 0.055$). In the pregnant group, the mean gestational age was 31.68 ± 4.85 weeks and the mean gravidity was 2.17 ± 1.14. The mean gravidity in the control group was 0.5 ± 0.95, with no significant difference compared with the pregnant group ($p = 0.120$). The mean body mass index (BMI) was significantly higher in the pregnant group than in the control group (27.99 ± 4.07 vs. 22.44 ± 3.12, $p = 0.006$). Demographic and baseline characteristics of the participants are summarized in Table 1.

Comparisons of anterior chamber anatomical characteristics and corneal topographic parameters between the pregnant and healthy control groups are presented in Table 2. No significant differences were observed between the two groups in anterior and posterior corneal Kmax, SIf, anterior and posterior RMSA, EIf, EIb, MPP, minimum corneal thickness (minthick), aqueous depth (AqD), white-to-white diameter (WTW), or anterior chamber depth (ACD). The posterior symmetry index and axial length were significantly lower in the pregnant group compared with the control group ($p = 0.003$ and $p < 0.001$, respectively). Corneal epithelial thickness was evaluated in nine regions, including the central zone, four paracentral quadrants, and four peripheral quadrants. No significant differences in epithelial thickness were detected in any region between the two groups ($p > 0.05$) (Table 3).

Correlations between anterior and posterior corneal curvature and minimum corneal thickness, central corneal thickness (CCT), anterior and posterior RMSA, mean pupillary power (MPP), and symmetry indices were analyzed separately for the pregnant group, the healthy control group, and the overall study population (Table 4). A strong negative correlation between anterior and posterior Kmax values was observed in the pregnant group, the control group, and in all participants combined (r = −0.751, p < 0.001; r = −0.648, p < 0.001; and r = −0.722, p < 0.001, respectively).

In the pregnant group, anterior Kmax showed a significant negative correlation with both minimum corneal thickness and CCT (r = −0.284, p = 0.016; and r = −0.295, p = 0.012, respectively). Anterior Kmax was positively correlated with anterior RMSA and MPP (r = 0.258, p = 0.028; and r = 0.820, p < 0.001, respectively). Posterior Kmax demonstrated significant negative correlations with posterior RMSA and MPP (r = −0.244, p = 0.039; and r = −0.716, p < 0.001, respectively) (Table 4).

In the healthy control group, anterior Kmax was positively correlated with MPP, whereas posterior Kmax was negatively correlated with MPP (r = 0.892, p < 0.001; and r = −0.687, p < 0.001, respectively).

When all participants were analyzed together, anterior Kmax was negatively correlated with minimum corneal thickness and CCT (r = −0.184, p = 0.032; and r = −0.201, p = 0.018, respectively) and positively correlated with anterior RMSA and MPP (r = 0.176, p = 0.040; and r = 0.825, p < 0.001, respectively). Posterior Kmax showed significant negative correlations with posterior RMSA and MPP (r = −0.217, p = 0.011; and r = −0.707, p < 0.001, respectively) (Table 4).

The mean CCT values measured using the NIDEK CEM-530 and the Placido-disc topographer for all participants were 546.47 ± 34.44 µm and 538.64 ± 33.36 µm, respectively, and the difference between the measurements was statistically significant (p < 0.001). However, excellent agreement was observed between the two devices (ICC = 0.989, p < 0.001) (Table 5).

When parameters were analyzed according to gravidity, the coefficient of variation (polymegathism) was significantly higher in pregnant women with a gravidity of four (p = 0.017). Gravidity was not found to have a significant effect on other evaluated parameters (p > 0.050) (Table 6).

In the corneal endothelial cell analysis, endothelial cell density was significantly lower and mean cell area was significantly higher in the pregnant group compared with the healthy control group (p = 0.018 and p = 0.006, respectively) (Table 7).

Table 1. *Demographic Characteristics of the Groups.*

Variables	Groups				Total		Test Statistics	P value
	Third Trimester Pregnant (n=72)		Healthy Nonpregnant (n=65)					
	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)		
Age (years)	28.01 ± 5.54	28 (18 - 39)	26.28 ± 4.93	26 (17 - 39)	27.19 ± 5.31	27 (17 - 39)	1896.5	0.055*
Gestational week	31.68 ± 4.85	33 (19 - 40)	---	---	31.68 ± 4.85	33 (19 - 40)	---	---
Gravida	2.17 ± 1.14	2 (1 - 6)	0.5±0.95	0(0-4)	1.41 ± 1.32	1 (0 - 6)	---	0.120
Height (cm)	162.49 ± 5.69	163 (148 - 175)	163.8 ± 5.2	163 (154 - 176)	163.11 ± 5.48	163 (148 - 176)	-1.405	0.162**
Weight (kg)	74.01 ± 12.13	74 (45 - 101)	60.2 ± 8.51	60 (47 - 98)	67.46 ± 12.6	65 (45 - 101)	746.5	**<0.001***
BMI(kg/m²)	27.99±4.07	27.73(16.73-36.11)	22.44±3.12	21.83(17.47-27.34)	-	-	7.936	**0.006****

*Mann Whitney U Test; **Independent Sample t-test; BMI, body mass ındex

Table 2. *Patient Clinical Characteristics*.

Variables	Groups				Total		Test Statistics	P value
	Third trimester pregnant (n=72)		Healthy nonpregnant (n=65)					
	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)		
Minthick (µm)	529.65 ± 37.32	526 (441 - 600)	535.23 ± 28.94	534 (471 - 597)	532.3 ± 33.6	529 (441 - 600)	-0.970	0.334**
Kmax front (D)	45.69 ± 2.07	45.48 (41.47 - 50.82)	45.36 ± 1.99	44.88 (42.09 - 51.38)	45.54 ± 2.03	45.34 (41.47 - 51.38)	2061.5	0.230*
Kmax back (D)	-6.68 ± 0.56	-6.55 (-9.55 - -6.06)	-6.82 ± 1.47	-6.53 (-17.57 - -6.03)	-6.74 ± 1.09	-6.55 (-17.57 - -6.03)	2241	0.670*
Front Apex Curvature (mm)	7.4 ± 0.33	7.42 (6.64 - 8.14)	7.45 ± 0.32	7.52 (6.57 - 8.02)	7.43 ± 0.33	7.44 (6.57 - 8.14)	2061	0.229*
Back Apex Curvature (mm)	6.03 ± 0.42	6.11 (4.19 - 6.61)	5.99 ± 0.62	6.13 (2.28 - 6.63)	6.01 ± 0.52	6.11 (2.28 - 6.63)	2237.5	0.659*
AqD (mm)	3.07 ± 0.26	3.08 (2.24 - 3.6)	3.08 ± 0.33	3.11 (2.01 - 3.74)	3.07 ± 0.3	3.08 (2.01 - 3.74)	-0.224	0.823**
ACD (mm)	3.6 ± 0.26	3.61 (2.76 - 4.09)	3.62 ± 0.33	3.64 (2.52 - 4.26)	3.61 ± 0.29	3.63 (2.52 - 4.26)	-0.344	0.732**
WTW (mm)	11.66 ± 0.36	11.69 (10.5 - 12.7)	11.69 ± 0.37	11.69 (10.91 - 12.56)	11.67 ± 0.37	11.69 (10.5 - 12.7)	-0.496	0.620**
RMSA Anterior (µm/mm²)	0.02 ± 0.01	0.02 (0.01 - 0.06)	0.03 ± 0.01	0.02 (0.01 - 0.1)	0.03 ± 0.01	0.02 (0.01 - 0.1)	2258.5	0.705*
RMSA Posterior (µm/mm²)	0.08 ± 0.03	0.07 (0.04 - 0.21)	0.08 ± 0.03	0.07 (0.04 - 0.19)	0.08 ± 0.03	0.07 (0.04 - 0.21)	2064	0.225*
MPP (D)	43.4 ± 1.65	43.5 (39.32 - 47.07)	42.94 ± 1.36	42.73 (40.47 - 47)	43.18 ± 1.53	43.19 (39.32 - 47.07)	1.789	0.076**
SI Front (D)	0.11 ± 0.35	0.07 (-0.68 - 1.01)	0.17 ± 0.39	0.16 (-0.8 - 1.31)	0.14 ± 0.37	0.11 (-0.8 - 1.31)	-0.844	0.400**
SI Back (D)	0.01 ± 0.09	0.01 (-0.18 - 0.32)	0.06 ± 0.1	0.04 (-0.18 - 0.59)	0.03 ± 0.1	0.02 (-0.18 - 0.59)	-3.053	**0.003****
EI Front (µm)	2.07 ± 1.87	1.24 (0.17 - 8.57)	2.63 ± 2.16	2.09 (0.21 - 10.69)	2.34 ± 2.02	1.47 (0.17 - 10.69)	1965.5	0.106*
EI Back (µm)	3.33 ± 3.31	2.2 (0.42 - 17.76)	4.12 ± 3.43	2.53 (0.36 - 12.83)	3.7 ± 3.38	2.39 (0.36 - 17.76)	1983.5	0.124*
AL (mm)	23.12 ± 1.1	22.99 (20.79 - 29.15)	23.63 ± 0.94	23.73 (21.44 - 25.31)	23.36 ± 1.06	23.21 (20.79 - 29.15)	1528	**<0.001***
WTW (mm) (NIDEK)	12.1 ± 0.38	12.14 (11.25 - 13.17)	12.19 ± 0.38	12.18 (11.17 - 13.1)	12.14 ± 0.38	12.16 (11.17 - 13.17)	-1.372	0.172**

*Mann Whitney U Test; **Independent Sample t-test

D; diopter, Kmax; maximum keratometry, Minthick; minimum corneal thickness, CCT; central corneal thickness, SI; symmetry indices, RMSA; root mean square average, EI; elevation based indices. MPP; mean pupillary power, WTW; White to White diameter, AqD; aqueous depth. ACD; anterior chamber depth, AL; axial length.

Table 3: *Differences in Epithelial Thickness in Pregnant and Nonpregnant Women*			
Variable	**Third Trimester Pregnant (Mean±SD)**	**Healthy Nonpregnant (Mean±SD)**	**P value**
Central ET	52.37± 3.22	53.54± 3.08	0.550*
Paracentral ET			
Superior	51.62 ± 2.71	52.30± 3.10	0.406*
Temporal	52.01 ± 3.00	52.80± 3.16	0.772*
Inferior	53.91 ± 3.25	54.06 ± 3.36	0.750*
Nasal	52.46 ± 3.48	53.11 ± 2.99	0.501*
Peripheral ET			
Superior	49.75 ± 3.76	49.70± 3.79	0.872*
Temporal	52.94 ± 3.62	52.80 ± 2.92	0.107*
Inferior	55.00± 3.90	54.70 ± 3.30	0.312*
Nasal	53.46 ± 3.74	52.99 ± 2.96	0.311*

*Independent Sample t-test
ET; Epithelial thickness

Table 4: *Correlations Between Anterior and Posterior Corneal Power with Other Parameters in Each Group and All Volunteers.*					
		Kmax Front		Kmax Back	
		r	p	r	p
Third trimester pregnant	Minthick (µm)	-0.284	**0.016**	0.013*	0.915
	CCT (µm)	-0.295	**0.012**	0.017*	0.885
	RMSA Anterior (µm/mm²)	0.258*	**0.028**	-0.037*	0.757
	RMSA Posterior (µm/mm²)	0.185*	0.119	-0.244*	**0.039**
	MPP (D)	0.820	**<0.001**	-0.716*	**<0.001**
	SI Front (D)	-0.003	0.983	-0.034*	0.777
	SI Back (D)	0.180	0.130	-0.007*	0.955
Healthy nonpregnant	Minthick (µm)	-0.084*	0.508	0.096*	0.448
	CCT (µm)	-0.113*	0.371	0.109*	0.387
	RMSA Anterior (µm/mm²)	0.088*	0.487	-0.035*	0.781
	RMSA Posterior (µm/mm²)	0.049*	0.698	-0.181*	0.150
	MPP (D)	0.892*	**<0.001**	-0.687*	**<0.001**
	SI Front (D)	-0.008*	0.948	0.088*	0.486
	SI Back (D)	-0.029*	0.821	0.139*	0.271
All cases	Minthick (µm)	-0.184	**0.032**	0.043*	0.620
	CCT (µm)	-0.201	**0.018**	0.052*	0.548
	RMSA Anterior (µm/mm²)	0.176*	**0.040**	-0.034*	0.696
	RMSA Posterior (µm/mm²)	0.123*	0.152	-0.217*	**0.011**
	MPP (D)	0.825	**<0.001**	-0.707*	**<0.001**
	SI Front (D)	-0.022	0.797	0.027*	0.757
	SI Back (D)	0.013*	0.885	0.064*	0.456

r: Pearson Correlation Coefficient; r*Spearman's rho Correlation Coefficient
Kmax; maximum keratometry, Minthick; minimum corneal thickness, CCT; central corneal thickness, SI; symmetry indices, RMSA; root mean square average.

Table 5: *Differences and Agreement in Terms of Measurements in Devices.*

	CCT (MS-39)	CCT (NIDEK)	Test Statistics	p*	ICC (%95 CI) / p
Mean ± SD	538.64 ± 33.36	546.47 ± 34.44	-17.887	**<0.001**	0.989 (0.984 - 0.992) / **<0.001**
Median (min - max)	537 (451 - 607)	542 (454 - 612)			

*Paired Two Sample t-test; ICC Intraclass Correlation Coefficient

Table 6. *Comparison of Parameters According to Gravidity in the Pregnant Group.*

	Gravidity (mean±SD; median (min –max)				**Test statistics**	**p**
Variables	**1**	**2**	**3**	**4**		
Minthick (µm)	524.12 ± 32.65	535.7 ± 40.88	529.06 ± 42.87	536.89 ± 35.07	0.464	0.708*
	521 (446 - 583)	525.5 (473 - 597)	533.5 (441-600)	527 (487 - 590)		
Kmax front (D)	45.73 ± 1.63	45.3 ± 2.47	46.04 ± 1.78	45.47 ± 2.72	0.414	0.744*
	45.59 (42.47 - 49.92)	45.11 (41.58 - 50.82)	45.68 (43.68 - 49.56)	46.06 (41.47 - 48.96)		
Kmax back (D)	-6.56 ± 0.21	-6.68 ± 0.64	-6.75 ± 0.45	-6.85 ± 1.07	1.160	0.763**
	-6.57 (-7.05 - -6.14)	-6.53 (-8.86 - -6.1)	-6.59 (-7.85 - -6.31)	-6.42 (-9.55 - -6.06)		
CCT (µm)	531.04 ± 31.13	540.45 ± 40.95	535.44 ± 42.6	543.56 ± 34.53	0.373	0.773*
	526.5 (472 - 586)	531.5 (476 - 601)	540 (451 - 607)	536 (495 - 596)		
ACD (mm)	3.64 ± 0.22	3.64 ± 0.29	3.59 ± 0.24	3.43 ± 0.34	1.584	0.201*
	3.62 (3.26 - 4.08)	3.66 (2.83 - 4.09)	3.58 (3.22 - 3.98)	3.48 (2.76 - 3.83)		
SI Front (D)	0.09 ± 0.36	0.14 ± 0.37	0.19 ± 0.38	0.01 ± 0.29	0.602	0.616*
	0.08 (-0.68 - 0.79)	0.06 (-0.53 - 1.01)	0.12 (-0.61 - 0.84)	-0.03 (-0.29 - 0.61)		
SI Back (D)	0.01 ± 0.07	0.01 ± 0.09	0.03 ± 0.11	-0.01 ± 0.07	0.894	0.827**
	0 (-0.18 - 0.1)	-0.01 (-0.16 - 0.23)	0.01 (-0.13 - 0.32)	0.01 (-0.1 - 0.09)		
Cell Density (cell/mm²)	2865.15 ± 236.09	2766.45 ± 308.5	2745.56 ± 243.35	2728.22 ± 130.1	1.180	0.324*
	2840.5 (2286 - 3447)	2788.5 (2351 - 3422)	2668 (2384 - 3192)	2642 (2595 - 2925)		
Coefficient Variation (%)	28.23 ± 3.35	27.9 ± 3.32	27.94 ± 3.17	33.22 ± 4.35	10.167	**0.017****
	27 (23 - 35)[b]	28 (22 - 36)[b]	27.5 (23 - 34)[b]	33 (26 - 41)[a]		
Hexagonality (%)	66.92 ± 5.49	67.65 ± 5.38	68.25 ± 4.17	64.67 ± 6.19	2.324	0.508**
	66.5 (57 - 78)	68.5 (59 - 79)	69 (59 - 75)	65 (54 - 74)		

*One Way Anova Test; **Kruskal Wallis Test; Mean ± standard deviation; Mean(minimum – maximum); a-b: there is no difference between groups having same letters.

Kmax; maximum keratometry, Minthick; minimum corneal thickness, CCT; central corneal thickness, ACD; anterior chamber depth, SI; symmetry indices.

Table 7 : *Corneal Endothelial Cell Properties of the Study Groups.*

	Third trimester pregnant		Healthy nonpregnant		Test Statistic	P value
Variables	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)		
Cell Density (cells/mm²)	2794.33 ± 250.55	2802.5 (2286 - 3447)	2906.23 ± 298.05	2934 (2141 - 3455)	-2.386	**0.018***
Cell Area (µm²)	341.25 ± 31.18	337 (275 - 410)	329.31 ± 38.82	320 (272 - 451)	1699.0	**0.006****
Standard Deviation (µm²)	98.03 ± 15.21	94 (71 - 146)	95.48 ± 15.64	96 (63 - 130)	2192.5	0.525**
Coefficient Variation (%)	28.68 ± 3.77	28 (22 - 41)	29 ± 3.78	29 (21 - 37)	2184.0	0.500**
Hexagonality (%)	67.14 ± 5.24	68 (54 - 79)	66.09 ± 4.58	66 (56 - 76)	2041.0	0.197**

*Independent Samples t-test; **Mann Whitney U Test

DISCUSSION

In the present study, corneal topographic parameters, corneal epithelial thickness mapping, anterior segment characteristics, and corneal endothelial cell parameters of healthy women in the third trimester of pregnancy were evaluated and compared with those of healthy nonpregnant controls.

During pregnancy, estrogen and progesterone levels increase to approximately 15 times those observed in non-gravid women.[14] Experimental studies have demonstrated that elevated estrogen levels stimulate the production of prostaglandins, matrix proteinases, and collagenolytic enzyme activators, thereby influencing the biomechanical properties of the cornea. High estrogen levels may also promote the production of hyaluronic acid in corneal cells, leading to increased corneal thickness as a result of stromal overhydration. In contrast, progesterone inhibits prostaglandin synthesis and may counterbalance the effects of estrogen by suppressing matrix degradation.[7] Estrogen has been detected in tears and aqueous humor at approximately half the plasma concentration. Due to its small molecular size, estrogen can diffuse into ocular tissues, bind to receptors in keratocytes, and stimulate protein synthesis. Consequently, the cornea is considered an estrogen-sensitive tissue, and estrogen plays an important role in corneal biomechanical stability. However, estrogen may also weaken corneal collagen by stimulating matrix metalloproteinases and collagenolytic enzymes.[15,16] Several studies have reported pregnancy-related progression of keratoconus. In a case series, post–laser-assisted in situ keratomileusis (LASIK) ectasia was reported in 17 cases, and worsening of keratoconus was observed in three cases during pregnancy.[17]

In the current study, corneal topographic parameters, with the exception of the posterior symmetry index (SIb), did not differ significantly between pregnant women and healthy controls, and none of the evaluated parameters varied according to the number of pregnancies. Previous studies investigating the relationship between pregnancy and keratometry values have reported conflicting results. Park et al.[18] observed increased corneal curvature in pregnant women during the second and third trimesters, whereas Manges et al.[19] reported no changes in corneal curvature or thickness throughout pregnancy, findings that are consistent with our results. Naderan et al.[8] reported clinically insignificant changes in corneal curvature and thickness during the third trimester, which returned to baseline values by the twelfth postpartum month. It has been suggested that pregnancy-related corneal changes regress as estrogen levels decline during the postpartum period.[9,20,21] Hypothetically, hormonal fluctuations during pregnancy may influence corneal curvature by altering corneal biomechanical stability or modifying the pressure exerted by surrounding soft tissues.[22] In our study, SIb values were higher in the healthy control group. Correlation analyses revealed that corneal curvature was positively correlated with RMSA and mean pupillary power (MPP) and negatively correlated with central corneal thickness, as expected. These findings suggest that presumed corneal changes during pregnancy may be overemphasized and that, in most individuals, pregnancy-related alterations are clinically insignificant. The corneal stiffness–reducing effect of estrogen may not be clinically evident in normal corneas but may become apparent in biomechanically compromised eyes, such as those with keratoconus or a history of refractive surgery.[15]

To the best of our knowledge, no previous studies have evaluated corneal epithelial thickness mapping in pregnant women. In the present study, epithelial thickness across all nine evaluated regions did not differ significantly between third-trimester pregnant women and nonpregnant controls. The inferior peripheral and inferior paracentral regions were the thickest, whereas the superior peripheral region was the thinnest. The mean central epithelial thickness was 52.3 µm in pregnant women and 53.5 µm in nonpregnant women. Haque et al.[23] reported a mean central epithelial thickness of 54 µm in healthy individuals. Alturki et al.[24] demonstrated that males have a thicker corneal epithelium than females, a difference attributed to hormonal factors. Numerous studies have reported epithelial thinning over the cone apex in keratoconus, typically located inferiorly or inferotemporally, in contrast to the inferior epithelial thickening pattern observed in normal corneas.[25] Our findings in both groups were consistent with the epithelial thickness distribution of normal corneas. Increased superior-to-inferior epithelial thickness differences in the 6-mm and 8-mm zones have been described as a diagnostic feature of keratoconus.[26]

Alterations in anterior chamber parameters during pregnancy are expected due to systemic fluid retention and increased aqueous humor outflow. Karatepe et al.[27] evaluated anterior chamber parameters throughout the menstrual cycle and reported changes in anterior chamber volume and angle, with significantly increased anterior chamber depth on the 26th day of the cycle. Another study demonstrated greater anterior chamber volume, angle, and depth during pregnancy compared with the third postpartum month.[1] Pota et al.[28] reported a significant increase in anterior chamber volume during the second trimester, followed by a decrease postpartum. In contrast, Goldich et al.[22] found no significant differences in anterior chamber depth or volume between third-trimester pregnant women and nonpregnant controls. Consistent with these findings, we observed no significant differences in anterior chamber depth, aqueous depth, or white-to-white diameter between pregnant women and healthy controls. The longer axial length observed in the control group was considered likely coincidental.

In the present study, endothelial cell density was significantly lower and mean cell area was significantly greater in pregnant women compared with healthy controls. Additionally, when parameters were analyzed according to gravidity, a significant increase in polymegathism was observed in pregnant women with higher gravidity. These findings may be related not only to gravidity but also to factors such as age and sample distribution, making it difficult to attribute the observed differences solely to gravidity. Other factors influencing corneal endothelial characteristics, including age, may also play a role and warrant further investigation. Ornek et al.[29] evaluated corneal endothelial cell density and morphology across all three trimesters and reported stable endothelial cell density throughout pregnancy, with transient increases in hexagonality and cell volume during the first trimester. Uzun et al.[30] similarly reported no significant differences in endothelial cell parameters between pregnant women and controls, although decreased hexagonality was noted in the first trimester. Karaküçük et al.[31] observed no substantial changes in corneal densitometry across trimesters, supporting the notion that endothelial function remains relatively stable during pregnancy. Because we did not assess endothelial parameters during the first or second trimesters or during the pre- or postpartum periods, our findings should be confirmed in longitudinal studies with repeated measurements.

In our study, no significant differences in corneal thickness were observed between third-trimester pregnant women and healthy controls. Previous studies evaluating corneal thickness during pregnancy have reported inconsistent results. Some studies have demonstrated increased corneal thickness during pregnancy,[1,21,28,32] whereas others have reported no significant changes,[19,30,32–34] consistent with our findings. Weinreb et al.[5] reported a 3% increase in corneal thickness during pregnancy that remained stable throughout gestation and returned to baseline within weeks postpartum, attributing this change to increased stromal fluid retention. Efe et al.[35] found increased corneal thickness during the second and third trimesters compared with the first trimester and postpartum period, with values returning to first-trimester levels after delivery.

Accurate measurement of corneal thickness is of particular importance in clinical practice, especially in the context of refractive surgery. In the present study, central corneal thickness measurements obtained using the Placido-disc topographer (MS-39) and the NIDEK CEM-530 specular microscope differed significantly but demonstrated excellent agreement. Consistent with our findings, previous studies comparing CEM-530 and Pentacam HR measurements reported thicker corneal values with the CEM-530 device.[36]

This study has several limitations. First, the sample size was relatively small. Second, the cross-sectional design precluded evaluation of the longitudinal effects of pregnancy on corneal parameters, and measurements were not obtained across all trimesters or during the pre- and postpartum periods. The third trimester was selected because hormonal activity peaks during this period. Third, only the right eye of each participant was included in the analysis. Finally, menstrual cycle phases, which may influence corneal biomechanics, could not be standardized in the control group.

In conclusion, pregnancy may be associated with changes in corneal endothelial cell density and morphology. However, in healthy women during the third trimester of pregnancy, corneal topographic parameters, corneal epithelial thickness, and anterior segment characteristics were comparable to those of healthy nonpregnant women. Larger, longitudinal studies are warranted to further clarify the effects of pregnancy on corneal and anterior segment parameters.

Authors' Note

This study was conducted under the research program of Ankara Etlik City Hospital. The study did not involve animal subjects.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Standards

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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Informed Consent

Informed consent was obtained from all individual participants included in the study.

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