Ann Med Res

Current issue list available at AnnMedRes

Annals of Medical Research

journal page: www.annalsmedres.org

Effects of pre-eclampsia on corneal tomography and specular microscopy parameters: A prospective study

Ayna Sariyeva Ismayilov[a,*], Neslihan Parmak Yener[a], Hafize Gokben Ulutas[b], Burcu Dincgez[c]

[a] *University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Ophthalmology, Bursa, Türkiye*
[b] *University of Health Sciences, Bursa City Hospital, Department of Ophthalmology, Bursa, Türkiye*
[c] *University of Health Sciences, Bursa Yuksek Ihtisas Research and Training Hospital, Department of Obstetrics and Gynecology, Bursa, Türkiye*

ARTICLE INFO

Keywords:
Corneal tomography
Intraocular pressure
Preeclampsia
Pregnancy
Specular microscopy

Received: Dec 23, 2024
Accepted: Mar 24, 2025
Available Online: 25.04.2025

DOI:
10.5455/annalsmedres.2024.12.275

Abstract

Aim: To evaluate the effect of preeclampsia on corneal tomography and specular microscopy parameters.

Materials and Methods: A total of 22 preeclamptic women were evaluated prospectively. Patients were evaluated at prepartum and postpartum third months. Best-corrected visual acuity (BCVA), intraocular pressure (IOP), slit lamp, optical coherence tomography, corneal tomography, and specular microscopy were recorded and compared.

Results: Prepartum BCVA was 0.065±0.638 logMAR, and postpartum BCVA was 0.050±0.823 logMAR, which was significantly different (p=0.033). The mean spherical equivalent was -0.68±1.27 diopter at prepartum and 0.00±1.41 diopter at postpartum period (p<0.001). While prepartum IOP was 16.90±2.92 mmHg, post-partum IOP was 15.40±3.17 mmHg (p=0.041). No significant changes were detected between the prepartum and postpartum period in terms of flat keratometry, steep keratometry, average keratometry, max keratometry, topographic astigmatism, and mean corneal endothelial cell density (ECD). The mean ACV (p=0.012), ACD (p=0.035), and ACA (p=0.032), the mean coefficient variation (CV) (p=0.030) were significantly lower at postpartum period (p=0.032). The percentage of hexagonal cells (HEX) increased (p=0.008) at postpartum period. The mean CCT was 572.81±66.79µm in the prepartum period and 553.90±51.51µm in the postpartum period (p=0.039).

Conclusion: This study indicates that preeclampsia affects corneal cell morphology including CV and HEX, and significant changes in BCVA, IOP, and CCT postpartum. Depending on the change in IOP, it may suggest that the ocular hypotensive effect of pregnancy may have been eliminated by preeclampsia. However, no significant differences were found in corneal topography parameters. Further long-term studies with larger patient cohorts are needed to determine whether these effects are persistent and clinically significant.

Copyright © 2025 The author(s) - Available online at www.annalsmedres.org. This is an Open Access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Introduction

Pregnancy, which is a significant challenge for the woman body, is associated with various physiological and pathological changes. One of the most critical pathologies that can occur during pregnancy is the hypertensive disorders. Hypertensive disorders of pregnancy, affecting nearly 10% of pregnancies, remain the leading cause of perinatal morbidity and fatality worldwide. It can be divided into groups such as chronic hypertension, gestational hypertension, preeclampsia, and superimposed preeclampsia. Preeclampsia complicates 3-5% of pregnancies [1]. Preeclampsia is defined as a new onset of hypertension after 20 weeks of gestation accompanied by proteinuria or maternal end-organ disorders in the absence of proteinuria [2]. Eclampsia is characterized by the coexistence of preeclampsia and seizures [3]. Preeclampsia and eclampsia have not only perinatal adverse outcomes but also they are related to future life complications.

Preeclampsia has been claimed to be a multisystemic disorder characterized by blood vessel construction, metabolic disease, endothelial disorder, onset of the coagulation cascade, and activated inflammatory response [4]. It is known that 25% of preeclamptic patients have visual impairment. In severe preeclampsia and eclampsia, there is an increased risk of hypertensive, hemorrhagic, and em-

*Corresponding author:
Email address: myusufova@cu.edu.tr (Ayna Sariyeva Ismayilov)

bolic strokes, presenting with visual symptoms [5]. The most well-known retinal changes in preeclampsia are abnormal retinal vascularity, such as arterio-venous crossing changes, focal vascular narrowing, and generalized attenuation of arterioles. In severe preeclampsia, serous retinal detachment and choroidal infarcts may develop secondary to hypertensive retinopathy [6].

Changes in sex hormones that occur during normal pregnancy affect both the anterior segment and fundus. Previous studies have shown that there are receptors for estrogen, progesterone, and androgen in the nuclei of human corneal epithelial, stromal, and endothelial cells [7-9]. Due to possible fluid retention, corneal thickness and corneal curvature have been reported to increase during pregnancy [10-11]. A recent study has shown higher anterior flat and steep keratometry, central corneal thickness (CCT), corneal volume, anterior chamber depth, angle, and volume, and lower IOP during pregnancy than three months postpartum period [12]. In contrast , another study has reported no statistically significant differences between corneal topographic and biomechanical parameters before pregnancy, during pregnancy, and postpartum. This study showed that prenatal ocular changes returned to fundamental characteristics after the postpartum period [13].

The physiology and hormonal status of preeclampsia pregnant women are quite different from normal pregnants. In preeclampsia, the body's ability to respond to vasoactive agents is initially lost, leading to a reduction in vasoconstriction. This results in a increase in intravascular volume, which then shifts to the extravascular compartments. Furthermore, there is a disruption in the balance between proangiogenic and antiangiogenic factors. Soluble vascular endothelial growth factor (VEGF) and soluble endoglin are two key proangiogenic factors involved in preeclampsia. Additionally, nitric oxide signaling, which is crucial for vascular relaxation, is impaired in this condition [14-15]. We thought that ocular physiology might be affected by existing hormonal changes in preeclampsia, which is a different process from normal pregnancy.

Although anterior segment parameters in pregnant women have been frequently examined in the literature, the effects of preeclampsia have not been investigated. This study prospectively analyzed the impact of preeclampsia on corneal tomography and specular microscopy parameters.

Materials and Methods

This is a prospective, non-interventional and observational study performed at a university-affiliated hospital. The primary endpoint of the study was the change in anterior segment parameters in preeclamptic women after postpartum period. The present study was approved by Bursa Yüksek İhtisas Training and Research Hospital Ethics Committee (Protocol number: 2011-KAEK-25 2022/06-18). The study adhered to the principles of the Declaration of Helsinki, and informed consent was obtained from the patients.

A total of 31 patients diagnosed with preeclampsia between July 2022 and July 2023 and hospitalized in the Obstetrics and Gynecology Clinic of Bursa Yuksek Ihtisas Training and Research Hospital were admitted to the study. G*Power software was used for sample size and power analysis. Convenience sampling, a non-probability sampling method, was used in this study. Participants were selected based on their availability and willingness to participate. Preeclampsia was diagnosed in pregnant women with new-onset hypertension (systolic blood pressure (BP) $\geq$ 140 mm Hg and/or diastolic BP $\geq$ 90 mm Hg (twice evaluation at least four hours interval)) after 20 weeks of gestation along with the presence of proteinuria, as defined by one of the following: $\geq$300 mg protein in a 24-hour urine, protein/creatinine ratio $\geq$ 0.3 mg/dL, dipstick protein $\geq$ +2. In the absence of proteinuria, new onset hypertension accompanied by one of the following criteria: thrombocytopenia (platelet count less than 100 000/uL), elevated serum transaminases (twice the upper level of normal), creatinine >1.1 mg/dl, pulmonary edema and/or visual symptoms. If a new-onset tonic-clonic seizure was added to preeclampsia, it was diagnosed as eclampsia [2].

Patients were consulted with the Ophthalmology Clinic at prepartum period and postpartum 3 months. Patients with contact lens use, glaucoma, a history of ocular surgery and trauma, atopy, corneal ectasia, spherical refractive errors of more than 4.00 diopter (D), cylindrical refractive errors of more than 2.00 D, two patients with serous retinal detachment due to preeclampsia having systemic disease such as hypertension, diabetes mellitus, and thyroid disease and patients who do not have regular follow-up were excluded from the study. Finally, a total of 22 patients (44 eyes) were included in the study.

A detailed history and routine ophthalmologic examination were done. Best-corrected visual acuity (BCVA) (Snellen converted to logMAR), intraocular pressure (IOP), slit lamp, dilated fundoscopy, and optical coherence tomography (OCT) (RTVue XR AVANTI, Optovue, Inc., Fremont, CA, USA) were evaluated. The combined Scheimpflug–Placido disc corneal topography system (Sirius, CSO, Florence, Italy) performed the corneal tomography parameters. K1 (flat keratometry), K2 (steep keratometry), Kavg (average keratometry), maximum keratometry (Kmax), anterior chamber volume (ACV), anterior chamber depth (ACD), anterior chamber angle (ACA) were taken. Corneal endothelial cell density (ECD) (cells/ mm^2), polymegathism, hexagonality, and CCT were evaluated automatically using a noncontact specular microscopy (NSP-9900, NonconRobo, Konan, Japan) analyzing at least 100 cells (Figure 1). Evaluations were taken from the central cornea in a suitable head position while the patient sat. Three images were taken, and the best image was recorded for analysis. All measurements were taken during the daytime to prevent diurnal variation (02:00-04.00 PM).

Statistical analysis

Statistical analyses were performed using the SPSS software version 22 (IBM Corp., Armonk, NY, USA). The distribution of variables was tested by using the Shapiro-Wilk test. Continuous, normally distributed data were presented as mean ± standard deviation, while categorical variables were presented as numbers and percentages.

Since the constant data shows normal distribution, the paired sample t-test was performed to compare prepartum and postpartum values. A p-value of <0.05 was considered statistically significant.

Results

The mean age of the patients was 32.22±6.56 (21-42) years. The gestational week was ranged between 20 and 39 weeks. A total of 6 patients (27.2%) were primigravidas, 13 patients (59%) were multigravidas, and 3 patients (13.6%) were grand multiparas. Two patients (9%) were diagnosed with eclampsia while 18 patients (81%8) had mild and 2 patients (9%) had severe preeclampsia.

At the time of ophthalmological examination, mean systolic BP was 149.54±23.39 (120-200), and mean diastolic BP was 88.40±17.68 (60-120) mm Hg. When the symptoms were searched, headache was present in 9 (40.9%) patients, abdominal pain in 2 (9.1%) patients, blurred vision in 8 (36.3%) patients, scotoma in 1 (4.5%) patient, diplopia in 1 (4.5%) patient, transient sudden vision loss in 1 (4.5%) patient and subconjunctival hemorrhage in 2 (9.1%) patients. There was a constriction of retinal arteriole in 6 eyes (13.6%), flame-shaped hemorrhage in 3 (6.8%) eyes, optic disc edema in 2 (4.5%) eyes, cotton-wool spots in 3 (6.8%) eyes, hard exudates in 1 (2.27%) eye.

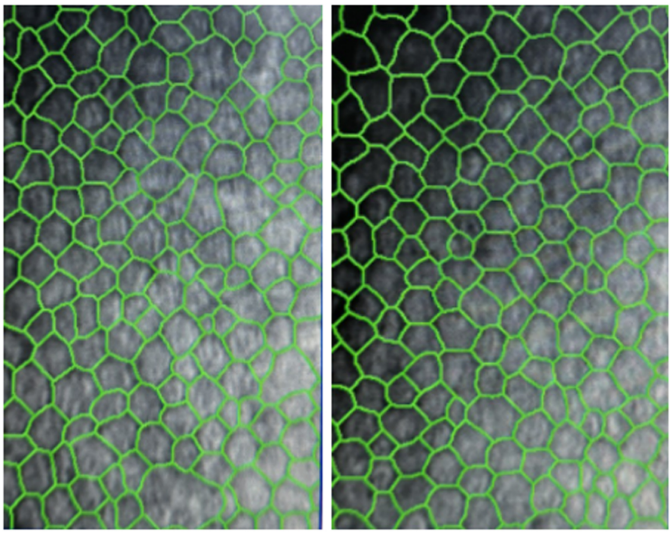

Figure 1. Specular microscopy of a 32-year-old pregnant woman with preeclampsia during the prepartum and postpartum periods.

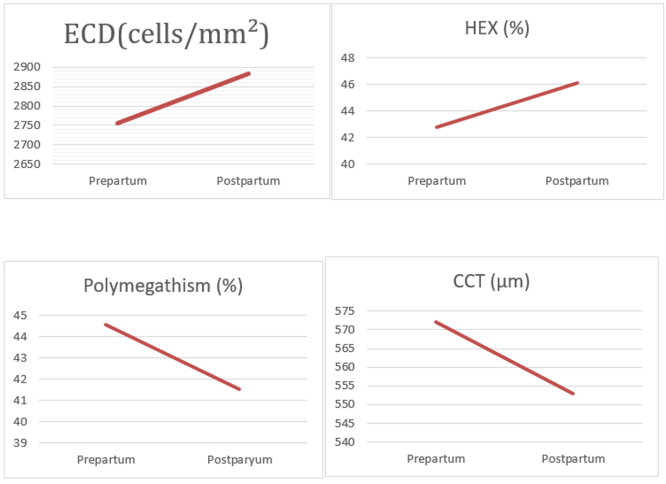

Figure 2. Changes in specular microscopy parameters in the postpartum period.

Table 1. Comparison of corneal tomography parameters in prepartum and postpartum periods.

	Prepartum	Postpartum	
	Average±SD (range)	Average±SD (range)	p value
Flat keratometry (K1) (D)	43.17±1.77 (40.00-46.50)	43.00±1.85 (40.0-46.25)	0.618
Steep keratometry (K2) (D)	44.39±1.92 (41.50-47.50)	44.14±1.93 (41.50-47.50)	0.075
Average keratometry (Kavg) (D)	44.16±1.45 (40.25-47.0)	44.06±1.63 (40.25-47.0)	0.534
Maximum keratometry (Kmax)	46.46±2.28 (44.25-47.75)	45.93±1.62 (44.00-47.75)	0.457
Topographic astigmatism (D)	0.98±2.06 (-2.0-0)	0.94±0.71 (-2.0-0)	0.381
Anterior Chamber Volume (mm^3)	175.45±35.9 (115-252)	164.98±12.4 (121-198)	**0.012***
Anterior Chamber Depth (mm)	3.224±0.765 (2.999-3.987)	2.876±0.355 (2.675-3.654)	**0.035***
Anterior Chamber Angle (°)	42.65±7.91 (29-45)	41.87±5.67 (28-45)	**0.032***

D: Diopter. Paired sample t-test, * p<0.05.

Table 2. Analysis of Endothelial Cell Characteristics in prepartum and postpartum periods.

	Prepartum	Postpartum	
	Average±SD (range)	Average±SD (range)	p value
ECD (cells/mm^2)	2755.47±251.05 (2128-3096)	2883.42±620.90 (2519-3268)	0.125
Polymegathism (CV) (%)	44.57±7.52 (40-59)	41.52±6.61 (29-56)	**0.030***
Pleomorphism (HEX) (%)	42.80±5.43 (39-50)	46.10±5.98 (33-55)	**0.008***
CCT (µm)	572.81±66.79 (408-770)	553.90±51.51 (400-612)	**0.039***

ECD: endothelial cell density, CV: coefficient variation of cell area, HEX: percentage of hexagonal cells, CCT: Central corneal thickness, paired sample t-test, * p<0.05.

Prepartum BCVA was 0.065±0.638 (0-0.698) logMAR, and postpartum BCVA was 0.050±0.823 (0-0.154) logMAR, which was statistically significant (p=0.033). While prepartum IOP was 16.90±2.92 (10-26) mmHg, postpartum IOP was 15.40±3.17 (10-21) (p=0.041). The mean spherical equivalent was -0.68±1.27 (-3.0-2.0) diopter in the prepartum period and 0.00±1.41 (-2.0-3.0) diopter in the postpartum period (p<0.001). Changes in K1, K2, Kavg, Kmax, and topographic astigmatism were not sta-

tistically significant at postpartum period. The mean ACV (p=0.012), ACD (p=0.035), and ACA (p=0.032) decreased statistically significantly at the postpartum third month (Table 1).

The mean ECD values were not statistically significant (p=0.125) between the prepartum and postpartum periods, while the mean CV values decreased (p=0.030) and the mean HEX values increased (p=0.008) significantly after delivery. The mean CCT was 572.81±66.79 µm at the prepartum period and 553.90±51.51 µm at the postpartum period (p=0.039) (Table 2 and Figure 2).

Discussion

Preeclampsia is a multisystem disease secondary to generalized vasoconstriction and endothelial injury. The clinical spectrum of preeclampsia includes hemolysis, low platelets, proteinuria, elevated liver enzymes, and HELLP syndrome [16]. It is well known that preeclampsia causes loss of vision due to changes in the neurological system and retina. The present study evaluated the effects of preeclampsia on the anterior segment. Blurred vision was detected in 36.3% of the preeclamptic patients, and retinal changes due to hypertensive retinopathy were diagnosed in 34%. Postpartum visual acuity increase was found to be statistically significant.

In a study searching IOP in pregnant women, IOP was found to be lower in pregnant women as compared to nonpregnant women [11]. In a study by Atas et al., lower IOP were reported during pregnancy than that the 3-month postpartum period. Moreover, this study claimed higher ACD, ACA, and ACV values during pregnancy as compared to the postpartum period [12]. Similarly, a study searching 25 healthy pregnant women in the second and third trimesters found a significant decline in the IOP and a reciprocal rise in CCT [10]. Since all values returned to the 1st-trimester values at three months postpartum. In the present study, unlike uncomplicated pregnancies, prepartum IOP was higher in preeclamptic pregnancies. The IOPs of the patients decreased significantly by 8.8% after delivery. In addition, it was observed that the ACD, ACA, and ACV measured during pregnancy were greater than in the postpartum period. Although the cause of the reduction in IOP during pregnancy is not fully understood, higher estrogen, progesterone, relaxin, and β-human chorionic gonadotropin levels leading to increased outflow of aqueous humor through the unconventional track are claimed to be the primary mechanism [12,17]. Another possible factor is decreased systemic vascular resistance and episcleral venous pressure. In parallel with this hypothesis, increased systemic vascular resistance in preeclampsia may increase episcleral venous pressure and cause an increase in IOP. Additionally, lower circulating estrogen and progesterone levels in women with preeclampsia may affect the outflow of aqueous humor [18].

Different results exist regarding ACV, ACA, and ACD measurements during pregnancy. Goldich et al. found no difference in ACV, ACD, and ACA measurements between pregnant women in the last trimester and nonpregnant women [11]. Erkan Pota's [19] and Atas's [12] studies reported a significant rise in ACV in the last two trimesters and a reduction in the postpartum period. The present study observed that ACV, ACA, and ACD measurements decreased statistically significantly after delivery.

In this study, we found a hyperopic shift in refractive errors in women with preeclampsia in the postpartum period. The change to hypermetropia may be due to a slight decrease in corneal curvatures. Although lens thickness was not measured in this study, it is known that the lens swells during pregnancy and is a catharogenic process [20]. The hyperopic shift may occur since this situation disappears in the postpartum period. This agrees with Erkan Pota's study [19], which reported that myopia rising to the 3rd trimester and reducting in the postpartum period. Pizzarello et al. [20] reported a tendency to myopia during pregnancy. However, another study showed that refractive measurements were similar in the 3rd trimester and postpartum period [12].

Some studies have reported that estrogen, progesterone, and androgen receptors exist in human corneal epithelial, stromal, and endothelial cell nuclei [7-9]. Hormonal changes during pregnancy can cause corneal curvature steepening and increased CCT [10,21,22]. Consistent with the literature, we found higher CCT values in pregnant women with preeclampsia at prepartum period. A study reported a significant decrease in K2, while no statistical changes were present in K1 and Kmean at the postpartum period [19]. In some studies [10,17], no significant alterations in keratometry parameters were observed due to pregnancy. The present study demonstrated that flat keratometry, steep keratometry, and average and maximum keratometry values did not significantly change in the postpartum period as compared to the prepartum period.

The most essential function of the corneal endothelium is to supply corneal transparency. It ensures the balance between the flow of aqueous humor into the stroma and the pumping of aqueous humor into the anterior chamber. The age-related decrease in ECD is compensated by increased Na, K-ATPase activity, which is the basis of endothelial pump function [23]. Corneal endothelial self-renewal is very limited, and the healthy indicators are higher ECD and HEX and lower polymegatism (CV) [24]. In this study, the mean ECD value changes were not statistically significant, but the mean CV and CCT values decreased, and the mean HEX values increased significantly at postpartum period. It is unclear why the transient high CV and low HEX values were measured in pregnant women with preeclampsia. We speculate that this may be due to general inflammation in the preeclampsia. In preeclampsia, placental oxidative stress appears because there is insufficient blood flow to the placenta. This results in the excess release of soluble fms-like tyrosine kinase-1 (sFlt-1), the soluble receptor for vascular endothelial growth factor (VEGF), into the maternal circulation, triggering an inflammatory response and endothelial dysfunction [25]. Monocyte and granulocyte activity and proinflammatory cytokines TNF-alpha, IL-6, and soluble phospholipase A2 increase in circulation [26,27]. It is known that anterior chamber inflammation results in alterations to the shape and size of the cells and a decrease in ECD [28]. Lower ECDs are associated with higher levels of specific cytokines, including IL-1α, IL-4, IL-13, MIP-1β, TNF-α, and

E-selectin [29]. Systemic inflammation during preeclampsia may have caused increased levels of cytokines in the aqueous humor and morphologically affected endothelial cells or endothelial cells may have been exposed to hypoxia during this inflammatory process. Although a study reported that the ophthalmic microenvironment continues immune concession by manipulating local innate and adaptive immunity far from inflammatory responses [30], it has also been shown that severe systemic hypertension in animals increases NADPH oxidase activity and reactive oxygen radicals in the cornea [31].

The present study has some limitations. The number of participants was small, there was the absence of a normal pregnant group, a single eye examination was performed before and after delivery, not measuring axial length and lens thickness, the patients' systemic BP was not recorded at the postpartum period, and the correlation between blood pressure and ocular measurements could not have been determined. The majority of the patient group were mild preeclampsia cases. Patients with retinal changes, except for serous retinal detachment due to preeclampsia, were included.

Conclusion

In conclusion, this study indicates that preeclampsia affects corneal cell morphology including CV and HEX, and significant changes in BCVA, IOP, and CCT postpartum. The ocular hypotensive effects of pregnancy may be eliminated by preeclampsia due to the increase in systemic vascular pressure, which can affect episcleral venous pressure. Alternatively, unlike in normal pregnancies, in preeclampsia the reduced levels of estrogen and progesterone may impair aqueous outflow. In addition, no significant differences were found in corneal topography parameters. Further long-term studies with larger patient cohorts are needed to determine whether these effects are persistent and clinically significant.

Disclosures

Ethics Committee Approval: The present study was approved by Bursa Yüksek İhtisas Training and Research Hospital Ethics Committee (Protocol number: 2011-KAEK-25 2022/06-18).

Informed Consent: Informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: ASI, BD; Design: ASI, HGU; Supervision: NPY, BD; Materials: ASI, NPY, HGU, BD; Data Collection and/or Processing: ASI, NPY, HGU, BD; Analysis and Interpretation: ASI; Literature Review: ASI, NPY, HGU; Writing Manuscript: ASI, BD; Critical Review: ASI, BD.

Conflict of Interest: None of the authors have any potential conflicts of interest to disclose.

Financial Disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Ananth CV, Keyes KM, Wapner RJ. Pre-Eclampsia Rates in the United States, 1980–2010: Age-Period-Cohort Analysis. *BMJ.* 2013;347:f6564. https://doi.org/10.1136/bmj.f6564.
2. American College of Obstetrics and Gynecology (ACOG): ACOG Practice Bulletin, Number 222: Gestational Hypertension and Preeclampsia, *Obstet Gynecol.* 2020;135(6):e237-60. https://doi.org/10.1097/aog.0000000000003891.
3. National Guideline Alliance (UK) Hypertension in Pregnancy: Diagnosis and Management (NG133);2019 Available online: https://www.nice.org.uk/guidance/ng133.
4. Roberts JM, Pearson G, Cutler J, Lindheimer M. Summary of the NHLBI Working Group on Research on Hypertension During Pregnancy. *Hypertension.* 2003;41(3):437–445. https://doi.org/10.1161/01.hyp.0000054981.03589.e9.
5. Gilbert AL, Prasad S, Mallery RM. Neuro-ophthalmic disorders in pregnancy. *Neurol. Clin.* 2019; 37(1):85–102. https://doi.org/10.1016/j.ncl.2018.09.001.
6. Practice Bulletin No. 222: Gestational hypertension and preeclampsia. *Am Coll Obstet Gynecol.* 2020;135(6):e237–60. https://doi.org/10.1097/aog.0000000000003891.
7. Gupta PD, Johar K, Nagpal K, Vasavada AR. Sex hormone receptors in the human eye. Surv. Ophthalmol. 2005;50(3):274–284. https://doi.org/10.1016/j.survophthal.2005.02.005.
8. Suzuki T, Kinoshita Y, Tachibana M, Matsushima Y, Kobayashi Y, Adachi et al. Expression of sex steroid hormone receptors in human cornea. *Curr Eye Res.* 2001;22(1):28–33. https://doi.org/10.1076/ceyr.22.1.28.6980.
9. Wickham LA, Gao J, Toda I, Rocha EM, Ona M, Sullivan DA. Identification of androgen, estrogen and progesterone receptor mRNAs in the eye. *Acta Ophthalmol Scand.* 2000;78(2):146–153. https://doi.org/10.1034/j.1600-0420.2000.078002146.x.
10. Efe YK, Ugurbas SC, Alpay A, Ugurbas SH. The course of corneal and intraocular pressure changes during pregnancy. *Can. J. Ophthalmol.* 2012;47(2):150–154. https://doi.org/10.1016/j.jcjo.2012.01.004.
11. Goldich Y, Cooper M, Barkana Y, Tovbin J, Ovadia KL, Avni I, et al. Ocular anterior segment changes in pregnancy. *J. Cataract. Refract. Surg.* 2014;40(11):1868–1871. https://doi.org/10.1016/j.jcrs.2014.02.042.
12. Ataş M, Duru N, Ulusoy DM, Altınparmak H, Duru Z, Açmaz G, et al. Evaluation of anterior segment parameters during and after pregnancy. *Cont. Lens. Anterior. Eye.* 2014;37(6):447–450. https://doi.org/10.1016/j.clae.2014.07.013.
13. Naderan M, Jahanrad A. Anterior, posterior and biomechanical parameters of cornea during pregnancy in healthy eyes: a cohort study. *The British journal of ophthalmology.* 2018;102(3):309–312. https://doi.org/10.1136/bjophthalmol-2017-310247.
14. Dieckman WJ. The toxemias of pregnancy. 2nd ed. Mosby; *St Lousi.* 1952; 240-249.
15. Sunness JS. The pregnant woman's eye. *Surv Ophthalmol.* 1988;32(4):219-238. https://doi.org/10.1016/0039-6257(88)90172-5.
16. 1Kongwattanakul K, Saksiriwuttho P, Chaiyarach S, Thepsuthammarat K. Incidence, characteristics, maternal complications, and perinatal outcomes associated with preeclampsia with severe features and HELPP syndrome. *Int. J. Womens. Health.* 2018;10:371–377. https://doi.org/10.2147/ijwh.s168569.
17. Taradaj K, Ginda T, Ciechanowicz P, Maciejewicz P, Suchońska B, Szymusik I, et al. Changes in the parameters of the anterior segment of the eye in pregnant women—literature review. *Ginekol. Pol.* 2018;89(3):169–173. https://doi.org/10.5603/gp.a2018.0028.
18. Wan J, Hu Z, Zeng K, Yin Y, Zhao M, Chen M, et al. The reduction in circulating levels of estrogen and progesterone in women with preeclampsia. *Pregnancy Hypertension.* 2018;11:18-25. https://doi.org/10.1016/j.preghy.2017.12.003.
19. Erkan Pota Ç, Çetinkaya Yaprak A. Evaluation of anterior segment parameters between pregnancy trimesters and postpartum with pentacam scheimflug ımaging: a prospective study. *International ophthalmology.* 2024;44(1):268. https://doi.org/10.1007/s10792-024-03173-y.
20. Pizzarello LD. Refractive changes in pregnancy. Graefes Arch. Clin. Exp. *Ophthalmol.* 2003; 241(6):484–488. https://doi.org/10.1007/s00417-003-0674-0.
21. Spoerl E, Zubaty V, Raiskup-Wolf F, Pillınat LE. Oestrogen-induced changes in biomechanics in the cornea as a possible reason for keratectasia. *Br. J. Ophthalmol.* 2007;91(11):1547–50. https://doi.org/10.1136/bjo.2007.124388.

22. Bilgihan K, Hondur A, Sul S, Ozturk S. Pregnancy-induced progression of keratoconus. *Cornea.* 2011;30(9):991–994. https://doi.org/10.1097/ico.0b013e3182068adc.
23. Watsky MA, McDermott ML, Edelhauser HF. In vitro corneal endothelial permeability in rabbit and human: the effects of age, cataract surgery and diabetes. *Exp. Eye. Res.* 1989;49(5):751–67. https://doi.org/10.1016/s0014-4835(89)80036-3.
24. Garza-Leon, M. Corneal endothelial cell analysis using two non-contact specular microscopes in healthy subjects. *Int. Ophthalmol.* 2016;36(4):453-461. https://doi.org/10.1007/s10792-015-0133-z.
25. Borzychowski A, Sargent I, Redman C. Inflammation and pre-eclampsia. *Seminars in Fetal and Neonatal Medicine.* 2006;11(5):309-316. https://doi.org/10.1016/j.siny.2006.04.001.
26. Vince GS, Starkey PM, Austgulen R, Kwiatkowski D, Redman CW. Interleukin-6, tumor necrosis factor, and soluble tumor necrosis factor receptors in women with pre-eclampsia. *Br J Obstet Gynaecol.* 1995;102(1):20-25. https://doi.org/10.1111/j.1471-0528.1995.tb09020.x.
27. Lim KH, Rice GE, de Groot CJ, Taylor RN. Plasma type II phospholipase A2 levels are elevated in severe preeclampsia. *American journal of obstetrics and gynecology.* 1995;172(3):998-1002. https://doi.org/10.1016/0002-9378(95)90033-0.
28. Alfawaz AM, Holland GN, Yu F, Margolis MS, Giaconi JA, Aldave AJ. Corneal endothelium in patients with anterior uveitis. *Ophthalmol.* 2016;123(8):1637-1645. https://doi.org/10.1016/j.ophtha.2016.04.036.
29. Yamaguchi T, Higa K, Suzuki T, Aketa N, Dogru M, Satake Y, et al. Association between corneal endothelial cell densities and elevated cytokine levels in the aqueous humor. *Scientific Reports.* 2017;7(1):1-8. https://doi.org/10.1038/s41598-017-14131-3.
30. Taylor AW. A review of the influence of aqueous humor on immunity. *Ocular Immunology and Inflammation.* 2003;11(4):231–241. https://doi.org/10.1076/ocii.11.4.231.18269.
31. Santana-Garrido Á, Reyes-Goya C, Arroyo-Barrios A, André H, Vázquez CM, Mate A. Hypertension secondary to nitric oxide depletion produces oxidative imbalance and inflammatory/fibrotic outcomes in the cornea of C57BL/6 mice. *J. Physiol. Biochem.* 2022;78(4):915-932. https://doi.org/10.1007/s13105-022-00916-2.