ORIGINAL ARTICLE

Evaluation of Anterior Segment Parameters and Retinal Nerve Fiber Layer Thickness According to Pregnancy Trimester

Kuddusi Teberik[1]
Alper Başbuğ[2]
Hakan Sağlam[3]
Musa Karaaslan[1]
Murat Kaya[1]

[1] Düzce University Faculty of Medicine Department of Ophthalmology, Düzce, Turkey
[2] Duzce University Faculty of Medicine Department of Obstetrics and Gynecology, Duzce, Turkey
[3] Department of Ophthalmology, Yozgat State Hospital, Yozgat, Turkey

Corresponding Author:
Kuddusi Teberik
Orhangazi Mah., Konuralp 500.Cd, No: 125/7, 81450, Düzce, Turkey
Tel:+90 505 636 13 15
E-mail: kuddusiteberik@yahoo.com

ABSTRACT

Objective: To analyze the effects of pregnancy on anterior segment parameters and retinal nerve fiber layer (RNFL) thickness.

Methods: The study designed prospectively conducted among 122 singleton pregnant women and 49 non-pregnant women. Intraocular pressure (IOP) was measured via the Goldman applanation tonometry. Central corneal thickness (CCT), axial lenght (AxL) and anterior chamber depth (ACD) measurement were performed with Echoscan US 500. For investigating the thickness of RNFL in detail, the optical coherence tomography was used. One Way ANOVA test was used to make a comparison between normal distribution groups.

Results: There was no statistically significant difference regarding age. The IOP were 16.0 mmHg in the 1st trimester, 14.6 mmHg in the 2nd trimester, 13.6 mmHg in the 3rd trimester and 15.56 mmHg in the non-pregnant. Statistically, the findings of the 2nd and the 3rd trimester were significantly different from that of the 1st trimester ($p = 0.033$, $p = 0.001$, respectively). CCT averages were 554 μm, 564 μm and 552 μm, respectively, according to the trimester, while it was 542 μm in non-pregnant women. The difference between CCT averages between pregnancies in the 2nd and 3rd trimesters and non-pregnant women was statistically significant ($p = 0.022$, $p = 0.041$, respectively). The comparison of average thickness of four RNFL showed no difference between the pregnant and non-pregnant.

Conclusions: During gestation, there was an increase in CCT with a decrease in IOP. We also determined that the ACD, AxL, and RNFL thickness measurements do not change with pregnancy.

Keywords: Central Corneal Thickness, Intraocular Pressure, Retinal Nerve Fiber Layer Thickness, Optical Coherence Tomography

Gebelik Trimesterine Göre Ön Segment Parametrelerinin ve Retina Sinir Lifi Tabaka Kalınlığının Değerlendirilmesi

ÖZET

Amaç: Gebeliğin ön segment parametreleri ve retina sinir lifi kalınlığı (RNFL) üzerindeki etkilerini incelemek.

Gereç ve Yöntem: Bu prospektif çalışma, 122’si tekil gebe ve 49’u gebe olmayan kadınlar arasında yürütüldü. Göz içi basıncı (GİB) Goldman Aplanasyon Tonometresi ile ölçüldü. Santral kornea kalınlığı (SKK), aksiyel uzunluk (AxL) ve ön kamara derinliği ölçümleri (ÖKD) Echoscan US 500 ile yapıldı. RNFL kalınlığının ayrıntılı olarak araştırılması için optik koherens tomografi kullanıldı. Normal dağılım grupları arasında bir karşılaştırma yapmak için One Way ANOVA testi kullanıldı.

Bulgular: Yaşa bakımından istatistiksel olarak anlamlı fark yoktu. GİB, birinci trimesterde 16.0 mmHg, 2. trimesterde 14.6 mmHg, 3. trimesterde 13.6 mmHg ve gebe olmayanlarda 15.56 mmHg idi. İstatistiksel olarak, 2. ve 3. trimesterlerin bulguları 1. trimesterden anlamlı olarak farklıydı ($p = 0.033$, $p = 0.001$, sırasıyla). Gebe olmayan kadınlarda 542 μm iken, trimestere gore SKK ortalaması sırasıyla 554 μm, 564 μm ve 552 μm idi. 2. ve 3. trimesterdeki gebeliklerin ve gebe olmayan kadınların SKK ortalamaları arasındaki fark istatistiksel olarak anlamlıydı ($p = 0.022$, $p = 0.041$, sırasıyla). Dört RNFL'nin ortalama kalınlığının karşılaştırılması, gebe ve gebe olmayan arasında fark göstermedi.

Sonuç: Gebelik esnasında, GİB’de azalma ile SKK’da bir artış bulundu. ÖKD, AxL ve RNFL kalınlık ölçümlerinin hamilelik ile birlikte değişmediği de tespit edildi.

Anahtar Kelimeler: Santral Kornea Kalınlığı, Göz İçi Basıncı, Retina Sinir Lifi Tabakası Kalınlığı, Optik Koherens Tomografi

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

INTRODUCTION

Metabolic, hormonal and vascular changes that happen in pregnancy additionally influence the visual structures (1). Some of these changes are physiologic (corneal shape, corneal sensitivity, intraocular pressure, etc.) and some are pathologic (preeclampsia and amniotic fluid embolism), while prenatal diseases such as diabetic retinopathy and glaucoma may differ.

During pregnancy, the amount of fluid in many body tissues increases due to changes in the endocrine system (1). Decrease in intraocular pressure in the eye is predicted to increase in total macular volume, foveal thickness and retinal nerve fiber thickness (3-4). There is an expansion in central corneal thickness and a decline in corneal sensitivity because of liquid maintenance (3). It is still under investigation whether how these changes affect the visual function.

In this study, we aimed to analyze the effects of pregnancy on anterior segment parameters and retinal nerve fiber layer thickness.

MATERIAL AND METHODS

The study designed prospectively was performed after obtaining the approval of the Ethical Board of Medical School of Duzce University (registration number, 2015/160). Informed consent form was collected from all participants. Besides, all procedures in the studies involving human participants were performed in accordance with the ethical standards of the institutional research committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Women admitted to the obstetrics and gynecology, and the ophthalmology departments of Medical School of Duzce University between January 2016- June 2016 were included and evaluated in the study. The study group was constituted of 122 females with singleton pregnancies, in total, 40 of them being in the 1st and 2nd trimester and 42 of them, in the 3rd trimester. The control group consisted of 49 healthy and non-pregnant women. Women in both groups with disorders such as diabetes mellitus, hypertension, hyperlipidemia, coronary heart disease, Cushing's syndrome, malignancy; and who had been taking systemic steroids antidepressants or emotion-regulating medications such as lithium or valproic acid, within the last six months; besides, those who smoke, use alcohol and have a history of ocular trauma or surgical interventions, and those with refraction disorder of spheric area more than ±1 dioptric, amblyopia, retinal dystrophy, retinal vasculitis, ocular hypertension or glaucoma were excluded out of the criteria. All patients were meticulously examined by a single ophthalmologist. After performing refraction measurements, the best-corrected visual acuity (BCVA) was tested in all cases through the Snellen chart. 0.5% proparacaine (Alcaine, AlconPharma) drops were applied for topical anesthesia. Intraocular pressure (IOP) was measured via the Goldman applanation tonometry (GAT) (Nikon, Japan). Biomicroscopic and fundoscopic examination without dilatation were performed. 5 minutes after this operation, central corneal thickness and anterior chamber depth measurement were performed with Echoscan US 500 (Nidek Co. Ltd, Aichi, Japan). In the analyses of the thickness of RNFL (superior, nasal, temporal and global) in detail, the optical coherence tomography (OCT) (Topcon 3D OCT-1000, Tokyo, Japan) was used. Compliance with the normal distribution of data that can be measured was assessed by Shapiro - Wilk testing. One Way ANOVA test was used to make a comparison between normal distribution groups. Pearson's correlation analysis was used to measure the strength and direction of the linear relationship between the two variables. Descriptive statistics were given as median ± standard deviation (SD). Statistical analyses were performed through SPSS v.22 (IBM, NY) package program, and the significance level was accepted to be 0.05.

RESULTS

Average age of the participants in the study was 28.5 ± 5.4 in the 1st trimester, 28.05 ± 6.1 in the 2nd trimester, 28.8 ± 6.7 in the 3rd trimester and 27.2 ± 7 in the non-pregnant women. There was no statistically significant difference regarding age ($p = 0,653$). The intraocular pressures measured by GAT were 16.05 ± 2.74 mmHg in the 1st trimester, 14.62 ± 2.04 mmHg in the 2nd trimester, 13.69 ± 1.81 mmHg in the 3rd trimester and 15.56 ± 2.51 mmHg in the non-pregnant. Statistically, the findings of both the 2nd and the 3rd trimester were significantly different from that of the 1st trimester ($p = 0.033$, $p = 0.001$, respectively). Also, the intraocular pressure difference between the 3rd trimester and non-pregnant women was statistically significant ($p = 0.001$). Central corneal thickness averages were 554 ± 35.6 μm, 564 ± 33.4 μm and 552 ± 33.6 μm, respectively, according to the trimester, while it was542 ± 39 μm in non-pregnant women. The difference between central corneal thickness averages between pregnancies in the 2nd and 3rd trimesters and non-pregnant women was statistically significant ($p = 0.022$, $p = 0.041$, respectively) (Table 1). Although the mean central corneal thickness of 1st-trimester pregnancies was 11.94 μm higher than that of non-pregnant women, the difference was not notable in statistical terms ($p = 0.143$). A weak correlation was found between the decrease in intraocular pressure, which was seen in the progressive trimester of pregnancy, and the increase in the corneal thickness that occurred simultaneously (Pearson correlation coefficient: 0.390, $p = 0.001$). When the anterior chamber depth and axial lengths of pregnant and non-pregnant women were compared, we saw that the difference between the groups was not statistically significant (p = 0.566, p = 0.294), (Table 2). No difference between pregnant and non-pregnant women was detected when the average thicknesses of the four retinal nerve fiber layers (superior, inferior, nasal, and temporal) were compared (p= 0.784, p = 0.575, p = 0.550, p = 0.351, respectively) (Table 3).

Table 1. Change in the difference between intraocular pressure and central corneal thickness averages in pregnant and non-pregnant women, respectively

	Mean ± SD			*p-value*			
Parameters	2nd Trimester	3rd Trimester	Non pregnancy	1stTrimester vs 2ndTrimester	1st Trimester vs 3rdTrimester	2nd Trimester vs Non pregnancy	3rd Trimester vs Non pregnancy
IOP from 1st rimester	1.42 ± 1.34	2.35±1.32	0.48 ± 1.27	0.033*	0.001*	0. 236	0.001*
CCT from 1st rimester	-10.25 ± 21.15	-8.16 ± 20.54	11.93 ± 19.81	0.577	0.731	0.022*	0.041*

IOP: Intraocular pressure, CCT: Central corneal thickness
* p<0,05 indicates statistical significance.

Table 2. Comparison of age and anterior segment parameters in pregnant and non-pregnant

Right eye	1 st (n=40)	2nd (n=40)	3rd (n=42)	Non pregnancy (n=49)	*p-value*
Age (years)	28.5 ± 5.4	28.05 ± 6.1	28.8 ± 6.7	27.2 ± 7	0.653
IOP (mmHg)	16.05 ± 2.74	14.62 ± 2.04	13.69 ± 1.81	15.56 ± 2.51	0.001*
CCT (μm)	554 ± 35.6	564 ± 33.4	552 ± 33.6	542 ± 39	0.015*
ACD (mm)	3.20 ± 0.32	3.30 ± 0.35	3.21 ± 0.25	3.20 ± 0.40	0.566
AxL (mm)	22.75 ± 0.81	22.74 ± 0.68	22.63 ± 0.76	22.96 ± 0.99	0.294

IOP: Intraocular pressure, CCT: Central corneal thickness, ACD: Anterior chamber depth, Axl: Axial length
* p<0,05 indicates statistical significance.

Table 3: RNFL thickness values of pregnant and non-pregnant women

RNFL/quadrant (μm)	1rd trimester	2nd trimester	3rd trimester	Non- pregnancy	*p-value*
Superior	114.43 ± 13.89	114.21 ± 11.25	113.26 ± 11.56	115.96 ±13.53	0.784
Inferior	120.05 ± 11.35	121.11 ± 12.58	119.02 ± 14.06	117.43 ± 12.54	0.575
Nasal	77.70 ± 10.89	77.55 ± 10.90	77.76 ± 13.75	74.73 ± 11.87	0.550
Temporal	70.40 ± 8.97	67.32 ± 5.80	68.36 ± 8.25	68.02 ± 8.30	0.351

RNFL: Retina nerve fiber layer

DISCUSSION

Significant changes occur in all systems affected by hormones released from the placenta in pregnancy as in the ocular system (5-6). The majority of these progressions are short-lived and rarely perpetual. The most notable changes are intraocular pressure and central corneal thickness (7-9). In our study, as the gestational week progressed, the intraocular pressures decreased, and the central corneal thickness increased, in comparison to the non-pregnant women. Davis stated that the intraocular pressure has continued to decline from the 2nd trimester of pregnancy to the postpartum period (10). A research carried out by Efe et al. reported an increase in CCT accompanied by a decrease in significant IOP in the 2nd and 3rd trimester of pregnancy (11). Green et al. additionally detailed that the intraocular pressure diminished while pregnancy and postnatal come back to the typical level in the third month (9). The ocular hypotensive impact in the third trimester, which we found to have the most reduced intraocular pressure in our research, is consistent with different studies (12-13). Pregnancy has been associated with a 10% reduction in IOP in healthy eyes (8). In our study, the intraocular pressure drop rate we found between the 1st and third trimester was 14%. Although the physiological mechanism responsible for the decrease in IOP during pregnancy is not exactly known, many possible mechanisms have been proposed. A conceivable component that could decrease IOP includes an expansion in aqueous outflow because of changes in hormone levels (e.g., estrogen, relaxin, progesterone, and beta-human chorionic gonadotrophin); a reduction in systemic vascular resistance, prompting diminished episcleral venous pressure; summed up expanded tissue flexibility, prompting diminished scleral rigidity; and summed up acidosis amid pregnancy (14). Metabolic acidosis amid pregnancy can hypothetically change the formation of aqueous humor, on the other hand flow rate of the aqueous humor is still constant during pregnancy period (9). Finally, connective tissue loosening affects the corneoscleral wall, visible throughout the body at the end of pregnancy. This can lead to a mistakenly low measurement of the applanation tonometry (13). For these reasons, it seems difficult to reach a definite conclusion about the causes of the hypothesis of intraocular pressure that occurs in pregnancy.

In our study, CCT measurements using ultrasonic pachymetry were higher in all trimester than in non-pregnant women. While there were no significant differences in the CCT measurements of the 1st-trimester pregnancies and non-pregnant women, differences between that of the 2nd and 3rd-trimester pregnancies, and the non-pregnant women were statistically significant. While they were working with the Pentacam front segment analyzer, Ataş and his colleagues reported that the difference between the 3rd trimester and the CCT averages of the postpartum 3rd month of the pregnancy (4 µm), was statistically significant (15). Weinreb et al. reported that ultrasonic pachymetry was used and that this difference was statistically significant, in eyes of non-pregnant women the thickness of the central cornea is 3% (16 µm) higher than the others (8). Efe et al. showed that the difference between the average measurements of CCT during 1st trimester and 2nd and 3rd trimester was statistically different and postnatal third month measurements were not different (11). It was not statistically significant that the average CCT rate in pregnant women was higher than that of the non-pregnant in the study conducted by Sen and collegues (16).

It is hypothesized in the study of Weinreb et al. that fluid retention related to pregnancy can lead to higher corneal thickness (8). Lately, nuclei of stromal and endothelial cells of human cornea includes estrogen, progesterone and androgen receptors (17-19). Corneal thickness and estrogen levels were found to be related in a different study (20-22). Hormones have been suggested to have direct effects or secondary effects, such as systemic water retention due to estrogen-induced upregulation of the renin-aldosterone system, on the cornea. During pregnancy, changes in anterior chamber parameters are expected due to both fluid retention in the body and increased aqueous humor outflow. However, there are not many studies in this field in literature. In our study, the anterior camera depth and axial lengths of pregnant and non-pregnant women were measured with ultrasound biometer, and statistically, no difference was found. Ataş and his colleagues performed by using Pentacam in their study, anterior chamber volume, anterior chamber depth, and anterior chamber angle were significantly higher during pregnancy compared with the 3rd month postpartum. It is reported in the study that axial length measurements from IOL Master 500 (Carl Zeiss Meditec Inc., Jena, Germany) did not show a difference (16).

There might be a rise in fluid volume in many tissues of the body due to pregnancy hormone levels (1). In pregnancy, especially in the 2nd and third trimesters, fluid retention may also cause a thickness increase in the retinal nerve fiber layer. Demir et al. reported that there was no difference in the mean peripapillary RNFL thickness of pregnants in their last three months and non-pregnant participants in their study conducted using OCT (RTVue-100, Optovue Inc, Fremont, CA) (1). Ataş and colleagues found that the mean RNFL thickness was significantly higher in healthy participants when spectral-area OCT was used than in the non-pregnant group (15). Statistically, the nonsignificant difference was found between the superior, nasal, inferior and temporal RNFL thicknesses of pregnant and non-pregnant women in our study.

In this study, we evaluated both anterior and posterior segment eye parameters unlike similar studies in the literature. The main limitation of this study was the small number of cases, and the subjects in the study group were formed from different people.

As a result, as the week of gestation progresses, there was an increase in CCT with a decrease in IOP. We also determined that the ACD, Axl, and RNFL thickness measurements not change with pregnancy. These changes may be due to hormonal changes that occur during pregnancy. Both obstetricians and ophthalmologists should cooperate in the management of these changes in pregnancy.

REFERENCES

1. Demir M, Oba E, Can E, et al. Foveal and parafoveal retinal thickness in healthy pregnant women in their last trimester. Clin Ophthalmol 2011;5:1397-1400.
2. Grant AD, Chung SM, The eye in pregnancy: ophthalmologic and neuro-ophthalmologic changes. Clin Obstet Gynecol 2013;56(2):397-412.
3. Sertan G, Ahmet B, Yasar S, et al. Measurement of choroid thickness in pregnant women using enhanced depth imaging optical coherence tomography. Arq. Bras. Oftalmol 2014;77(3):148-51.
4. Omoti AE, Waziri-Erameh JM, Okeigbemen VW. A review of the changes in the ophthalmic and visual system in pregnancy. Afr J Reprod Health 2008;12(3):185-96.

5. Fuchsjager-Mayrl G, Nepp J, Schneeberger C, et al. Identification of estrogen and progesterone receptor mRNA expression in the conjunctiva of premenopausal women. Invest Ophthalmol Vis Sci 2002;43(9):2841-4.
6. Esmaeli B, Harvey JT, Hewlett B. Immunohistochemical evidence for estrogen receptors in meibomian glands. Ophthalmology 2000;107(1):180-4.
7. Weinreb RN, Lu A, Key T. Maternal ocular adaptations during pregnancy. Obstet Gynecol Surv 1987;42(8):471-83.
8. Weinreb RN, Lu A, Beeson C. Maternal corneal thickness during pregnancy. Am J Ophthalmol 1988;105(3):258-60.
9. Green K, Phillips CI, Cheeks L, et al. Aqueous humor flow rate and intraocular pressure during and after pregnancy. Ophthal Res 1988;20(6): 353-7.
10. Davis E. Dana reza pregnancy and eye. In: Albert D, Jakobiec FA, ed. Principles and practice of ophthalmology. Philadelphia, WB Saunders 2000;4767-8474.
11. Efe YK, Ugurbas SC, Alpay A, et al. The course of corneal and intraocular pressure changes during pregnancy. Can J Ophthalmol 2012;47(2):150-4.
12. Kass MA, Sears ML. Hormonal regulation of intraocular pressure. Surv Ophthalmol 1977;22(3):153-76.
13. Phillips CI, Gore SM. Ocular hypotensive effect of late pregnancy with and without high blood pressure. Br J Ophthalmol 1985;69(2):117-9.
14. Afekhide E.O., Joseph M. W., Valentina W. O. A Review of the Changes in the Ophthalmic and Visual System in Pregnancy. Afr J Reprod Health 2008; 12(3):185-96.
15. Atas M, Duru N, Ulusoy DM, et al. Evaluation of anterior segment parameters during and after pregnancy. Cont Lens Anterior Eye 2014;37(6):447-50.
16. Sen E, Onaran Y, Nalcacioglu-Yuksekkaya P, et al. Corneal biomechanical parameters during pregnancy. Eur J Ophthalmol 2014;24(3):314-9.
17. Gupta PD, Johar K, Nagpal K, Vasavada AR. Sex hormone receptors in the human eye. Surv Ophthalmol 2005;50(3):274-84.
18. Suzuki T, Kinoshita Y, Tachibana M, et al. Expression of sex steroid hormone receptors in human cornea. Curr Eye Res 2001;22(1):28-33.
19. Wickham LA, Gao J, Toda I, Rocha EM, Ono M, Sullivan DA. Identification of androgen, estrogen and progesterone receptor mRNAs in the eye. Acta Ophthalmol Scand 2000;78(2):146-53.
20. El-Hage SG, Beaulne C. Changes in central and peripheral corneal thickness with menstrual cycle. Am J Optom Arch Am Acad Optom 1973;50(11):863-71.
21. Kiely PM, Carney LG, Smith G. Menstrual cycle variations of corneal topography and thickness. Am J Optom Physiol Opt 1983;60(10):822-9.
22. Giuffrè G, Di Rosa L, Fiorino F, Bubella DM, Lodato G. Variations in central corneal thickness during the menstrual cycle in women. Cornea 2007;26(2):144-6.