

Evaluation of Choroidal Thickness during Pregnancy and Postpartum: A Longitudinal Study

Yousef Alizadeh¹, Zahra Moravvej^{1,2}, Reza Soltani-Moghadam¹, Maryam Dourandeesh¹, Mitra Akbari¹, Ebrahim Azaripour¹, Abdolreza Medghalchi¹, Ziba Zahiri Sorouri³, Zahra Motaghinia⁴

¹Department of Eye, Eye Research Center, Amiralmomenin Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran, ²Department of Ophthalmology, Hakim Hospital, Neyshabour University of Medical Sciences, Neyshabour, Iran, ³Department of Obstetrics and Gynecology, Reproductive Health Research Center, Alzahra Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran, ⁴Department of Ophthalmology, School of Medicine, Arak University of Medical Sciences, Arak, Iran

Abstract

Purpose: To assess the longitudinal changes of choroidal thickness using enhanced depth imaging optical coherence tomography (EDI-OCT) during pregnancy and postpartum.

Methods: The study included 23 eyes of 23 healthy pregnant women and 23 eyes of 23 healthy nonpregnant women. Choroidal thickness was measured manually with EDI-OCT at seven locations: The fovea, 500, 1000, and 1500 μm temporal (T) from the fovea and 500, 1000, and 1500 μm nasal (N) from the fovea. Measurements were obtained at each pregnancy trimester and 6 weeks postpartum and in the follicular phase of the menstrual cycle for the control group.

Results: The mean subfoveal choroidal thickness was $410.2 \pm 82.4 \mu\text{m}$, $434.8 \pm 79.6 \mu\text{m}$, $433.5 \pm 80.3 \mu\text{m}$, and $395.0 \pm 71.1 \mu\text{m}$ in the first, second, and third trimesters and 6 weeks postpartum, respectively. In all seven measured locations, statistically significant changes were noted during pregnancy and postpartum in the choroidal thickness ($P < 0.001$). Choroidal thickness increased from the first trimester to the second and third trimester, after which it decreased at postpartum. Choroidal thickness was greater in the pregnant group during pregnancy and postpartum compared to the control group ($P < 0.001$).

Conclusions: This study indicated significant change in choroidal thickness at seven locations measured with EDI-OCT throughout pregnancy and 6 weeks after delivery. We showed that 6 weeks after delivery, choroidal thickness remains significantly higher than nonpregnant subjects.

Keywords: Choroid, Optical coherence tomography, Postpartum, Pregnancy, Trimester

Address for correspondence: Zahra Motaghinia, Department of Ophthalmology, School of Medicine, Arak University of Medical Sciences, Arak, Iran.
E-mail: motaghini@m@gmail.com

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INTRODUCTION

Pregnancy is a period associated with many physiologic changes throughout the body.¹ The majority of these changes occur in the hormonal, hematologic, and cardiovascular systems. As it is well understood, the blood volume is increased during pregnancy, reaching 40%–45% higher than prepregnancy volumes by the 32–34 weeks of gestation.² Furthermore, an increase in the cardiac output and reduction

of peripheral vascular resistance provide a suitable situation for fetus development.

The impact of these hormonal and hemodynamic alterations on the ocular structure has been studied in the literature. Changes in central corneal thickness, corneal curvature, and intraocular pressure (IOP) have been well documented.^{3,4} Since the choroid has the highest blood flow per unit weight

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in the body and supplies much of the nutritional needs of the retina, choroidal changes may lead to various ophthalmic conditions.^{5,6} Investigating choroidal changes during pregnancy offers insight to ocular pathologies encountered in this period such as central serous chorioretinopathy (CSC) and eclampsia-associated retinopathy.^{7,8} The extent of these choroidal changes and its reversibility after pregnancy is of great clinical significance.

Optical coherence tomography (OCT) is an essential device for diagnosing retinal and choroidal pathologies and evaluating treatment. New-generation OCT devices perform scans much faster, hence providing higher resolution imaging with extensive detail. Studies have shown the great reproducibility and repeatability of spectral-domain OCT (SD-OCT) in retinal and choroidal thickness assessment.⁹⁻¹¹ The enhanced depth imaging (EDI) technique of SD-OCT is a precise and noninvasive method, ideal for documenting the choroidal morphology.^{12,13} The choroidal thickness is a useful parameter in indicating physiologic and pathologic ocular changes as it is affected by the blood flow and ocular perfusion pressure (OPP). Various studies with controversial results have reported choroidal thickness in pregnancy and pregnancy-associated states.^{3,14-16} A review of current literature indicated inadequate longitudinal research which determines choroidal thickness during pregnancy and postpartum. Therefore, the purpose of this study was to longitudinally monitor the changes in choroidal thickness during each trimester and postpartum and also compare the results with a control group.

METHODS

This prospective, longitudinal study included 23 eyes of 23 healthy pregnant women and 23 eyes of 23 healthy nonpregnant women. To ensure unbiased results, only one eye (right eye) was included for each study participant. Participants from both groups were recruited from the Gynecology and Obstetrics clinic at the same university hospital between January and August 2018. All participants provided written informed consent, and the purpose of the research was fully explained. The research protocol was approved by the local ethics committee (IR.GUMS.REC.1395.282) and adhered to the Declaration of Helsinki principles.

The inclusion criteria for the study group were healthy pregnant women in the first trimester, who attended prenatal care and completed pregnancy without any complications (including gestational diabetes, preeclampsia, or eclampsia). All the pregnancies were singleton and all participant were primigravid with no history of abortion. The control group consisted of healthy nulligravid women with regular menstrual cycles. All participants were between 18 and 40 years old and had refractive errors less than ± 1.0 diopters with a best-corrected visual acuity (BCVA) of $\geq 20/20$ (Snellen chart), and IOP below 21 mmHg at the time of enrollment. Subjects with a history of anemia, diabetes, hypertension, polycystic ovarian syndrome, thyroid dysfunction, collagen vascular, renal, or cardiovascular

diseases and smoking and those with any ocular pathology including any previous ocular intervention were excluded from the study.

Demographic and previous medical history of participants was obtained. A complete ophthalmic examination was performed, including refraction (Topcon KR-8000 autorefractor) and visual acuity testing, slit-lamp biomicroscopy, IOP measurement by Goldmann applanation tonometry, and dilated fundus examination. Axial length measurement was performed using an optical biometer (Lenstar 900, Haag-Streit AG, Switzerland). Data regarding patients systolic and diastolic blood pressure (BP), anthropometric data, and fasting blood sugar, blood urea nitrogen, creatinine and ferritin were also obtained. OPP was calculated based on the following formula: Mean BP-IOP.

For the pregnant group, choroidal thickness was measured at the first trimester (at 6–12 GA weeks), second trimester (at 16–22 GA weeks), and third trimester (at 28–34 GA weeks), and 6 weeks postpartum and for the control group in the follicular phase of the menstrual cycle. Participants were asked to avoid any caffeine containing diet, such as coffee, tea, and chocolate for 24 h before image acquisition. Measurements were acquired in the morning between 9 and 11 A.M. to avoid diurnal variations and after 15 min of rest in the sitting position. Choroidal thickness was measured using SD-OCT with the EDI technique (Spectralis; Heidelberg Engineering, Heidelberg, Germany). The macular region was scanned using a horizontal 1-line raster scan ($30^\circ \times 5^\circ$) centered on the fovea, generated from 7 B-scans with 100 frames averaged per scan. The choroidal thickness was measured as the vertical distance from Bruch's membrane to the choroid-sclera interface (hyperreflective line of the inner surface of the sclera) using the manual caliper in the Heidelberg software. All OCT imaging were separately assessed by two ophthalmologists.

Choroidal thickness measurements were obtained at seven locations: At the fovea, 500, 1000, and 1500 μm temporal (T) from the fovea and 500, 1000, and 1500 μm nasal (N) from the fovea.

Statistical analyses were performed using the SPSS Statistics version 21 (IBM-SPSS, Chicago, IL, USA). Variables are presented as mean \pm standard deviation were appropriate. To compare variables between groups, Student's *t*-test and Mann-Whitney test was used for normally and nonnormally distributed data, respectively. Changes in choroidal thickness were analyzed using Repeated Measures analysis of variance (ANOVA). Furthermore, multiple comparisons with Bonferroni adjustment were performed. The *post hoc* Dunnett test was performed for comparison between each time point in the pregnancy group and the control group. Subjects with missing data were omitted from the analysis. A linear regression analysis with choroidal thickness as a dependent parameter and ocular and general parameters as independent parameters was performed. All *P* values were 2-sided, and a *P* < 0.05 was considered statistically significant.

RESULTS

The study enrolled 23 eyes of pregnant women and 23 eyes of age-matched women for the control group. Two participants in the pregnant group did not complete follow-up for the third trimester and postpartum imaging, and thus, analyzed as missing data. One patient who had premature delivery was excluded from the study, and another healthy pregnant woman was recruited for replacement. All other participants in the pregnant group had normal vaginal delivery.

The mean age was 26.1 ± 3.6 years (range, 22–34) at the time of the first examination in the pregnant group and 26.7 ± 4.0 (range, 21–34) in the control group. IOP was within the normal range in both groups. The BCVA was 20/20 or better for all participants. Baseline clinical evaluations were not statistically different between the two groups, except for the body mass index (BMI), which was higher in the pregnant group. This difference in BMI was probably due to the weight gain which occurs in pregnancy. Hemoglobin was also in the normal range for all subjects of both groups, although significantly lower in the pregnant group. Table 1 shows demographic and baseline clinical data in the two groups.

Table 2 shows the mean choroidal thickness in the pregnancy and control group in each measured location. The mean subfoveal choroidal thickness was $410.2 \pm 82.4 \mu\text{m}$, $434.8 \pm 79.6 \mu\text{m}$, $433.5 \pm 80.3 \mu\text{m}$, and $395.0 \pm 71.1 \mu\text{m}$ in the first, second, and third trimesters, and 6 weeks postpartum, respectively. The temporal choroid was thicker compared to the nasal choroid in all pregnancy time points and also the control group.

Based on the repeated-measures ANOVA, there was statistically significant change during pregnancy and postpartum in the choroidal thickness in all seven locations [Table 2 and Figure 1].

Table 1: Demographic and baseline clinical parameters in the pregnant and control groups

	Pregnant group (n=23)	Control group (n=23)	P
Age	26.1±3.6	26.7±4.0	0.723 [†]
RE (diopters)	-0.21±0.3	-0.17±0.3	0.560 [†]
AL (mm)	23.5±1.4	23.4±0.3	0.195 [†]
IOP (mmHg)	12.9±1.9	13.5±2.7	0.750 ^a
Systolic BP (mmHg)	114.1±7.3	112.6±6.9	0.402 [†]
Diastolic BP (mmHg)	74.1±3.9	74.5±4.2	0.787 [†]
MABP (mmHg)	87.3±4.4	87.0±4.0	0.721 [†]
OPP (mmHg)	47.7±3.8	49.3±3.1	0.129 ^a
Hemoglobin (g/dL)	12.2±0.3	13.3±0.4	0.001 ^a
Ferritin (μg/L)	31.4±5.9	29.5±6.2	0.291 ^a
BUN (mg/dL)	13.6±3.1	14.3±2.0	0.342 ^a
Cr (mg/dL)	0.6±0.1	0.6±0.1	0.062 [†]
BMI (kg/m ²)	23.2±1.5	22.1±2.3	0.050 ^a

[†]Mann-Whitney-U, ^aIndependent samples t-test. RE: Refractive error, AL: Axial length, IOP: Intraocular pressure, BP: Blood pressure, OPP: Ocular perfusion pressure, MABP: Mean arterial blood pressure, BMI: Body mass index, BUN: Blood urea nitrogen, Cr: Creatinine

We noted an increase in mean choroidal thickness from the first trimester to the second trimester, which was statistically significant only in the temporal 500 μm from fovea region [Table 3]. In the 3rd trimester, the thickness remained nearly the same as the 2nd trimester, with no significant difference in multiple comparison of 2nd and 3rd trimesters [Table 3]. The mean choroidal thickness decreased significantly after delivery. Table 3 shows P values for multiple pairwise comparisons of mean choroidal thickness in pregnancy trimesters and postpartum.

Choroidal thickness was greater in all 7 locations during pregnancy and postpartum compared to the control group ($P < 0.001$ for all time points). Mean subfoveal, nasal, and temporal (500–1500 μm from fovea) choroidal thickness is shown in box plots in the pregnant women and control groups [Figure 1].

Correlation between the choroidal thickness in different locations and baseline BMI, BP, OPP (the first trimester for pregnant group) was evaluated using Pearson's correlation. No significant correlation was found between the choroidal thickness and BP and OPP, whereas choroidal thickness in all seven locations was positively correlated with BMI [Table 4].

DISCUSSION

Pregnancy-related hormonal, hemodynamic, and cardiovascular changes can affect the ocular structures.¹⁷ The complex vascular structure of the choroid makes it vulnerable to pregnancy-related alterations, either the physiologic or pathologic events. Choroidal thickness changes can be expected due to the increased blood volume and water retention during pregnancy.^{18,19} Certain ocular conditions such as CSC, serous retinal detachment, and retinal vascular events have an increased prevalence during pregnancy.^{20,21}

There is no definite consensus on whether pregnancy can change choroidal structure and thickness and whether these changes are reversible. Previous studies have shown controversial results regarding choroidal thickness in pregnant women. Studies by Rothwell *et al.*, Kara *et al.*, Ataş *et al.*,²² Sayin *et al.*, and

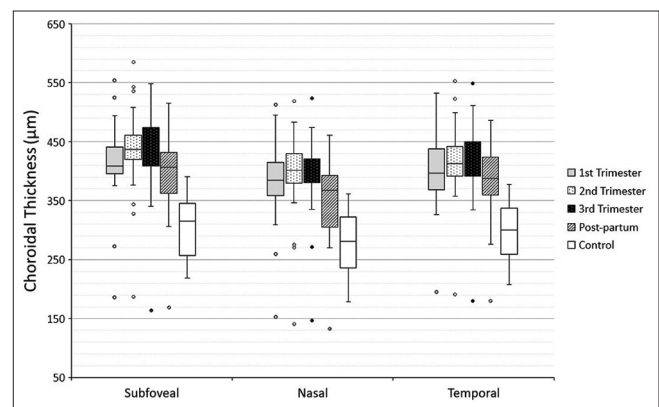


Figure 1: Subfoveal, temporal, and nasal choroidal thickness distribution in the pregnant group at different study time-points and the control group

Table 2: Choroidal thickness in different locations in the pregnant group at study time-points and control group

Location (μm from fovea)	Time points in pregnant group				Control (n=23)	P	
	1 st trimester (n=23)	2 nd trimester (n=23)	3 rd trimester (n=21)	Postpartum (n=21)		Pregnancy group [†]	Pregnancy versus control [‡]
Subfovea	410.2±82.4	434.8±79.6	433.5±80.3	395.0±71.1	304.5±52.6	0.001	<0.001
Nasal 500	402.7±79.8	420.6±80.9	421.8±80.2	379.9±71.5	296.0±60.5	0.001	<0.001
Nasal 1000	384.5±74.3	391.2±79.6	393.0±77.5	351.8±70.2	285.2±50.9	<0.001	<0.001
Nasal 1500	352.9±74.8	340.4±106.0	350.4±72.0	314.6±68.0	253.8±49.8	<0.001	<0.001
Temporal 500	415.8±73.4	433.2±74.6	430.1±77.0	375.0±96.0	304.6±52.5	0.001	<0.001
Temporal 1000	405.9±70.7	418.8±69.3	416.2±72.0	381.3±71.7	306.5±53.1	0.001	<0.001
Temporal 1500	387.2±67.9	396.9±64.2	396.6±67.6	365.2±63.2	288.0±49.3	0.004	<0.001

[†]Repeated measures ANOVA (in the pregnant group time points), [‡]Same P values for each time point were observed. Dunnett test (values in pregnancy group time points compared against control). ANOVA: Analysis of variance

Table 3: Multiple comparisons of choroidal thickness between pregnancy trimesters and postpartum

Location (μm from fovea)	P value in pairwise comparisons [†]					
	1 st versus 2 nd trimester	1 st versus 3 rd trimester	2 nd versus 3 rd trimester	1 st versus postpartum	2 nd versus postpartum	3 rd versus postpartum
Subfovea	0.119	0.324	1.000	1.000	0.001	0.003
Nasal 500	0.191	0.298	1.000	0.186	0.000	0.001
Nasal 1000	1.000	1.000	1.000	0.008	0.002	0.002
Nasal 1500	1.000	1.000	1.000	0.007	0.007	0.014
Temporal 500	0.036	0.592	1.000	0.317	0.002	0.010
Temporal 1000	0.127	1.000	1.000	0.221	0.003	0.012
Temporal 1500	0.541	1.000	1.000	0.380	0.018	0.020

[†]Adjustment for multiple comparisons with Bonferroni

Table 4: Pearson's correlation coefficient for choroidal thickness and body mass index

Location (μm from fovea)	Pearson's correlation coefficient	P
Subfovea	0.371	0.011
Nasal 500	0.382	0.009
Nasal 1000	0.363	0.013
Nasal 1500	0.353	0.016
Temporal 500	0.389	0.007
Temporal 1000	0.313	0.034
Temporal 1500	0.340	0.021

Acmaaz *et al.* have shown increased choroidal thickness in the third trimester of pregnancy compared to controls,^{14,22-25} whilst Takahashi *et al.*, Benfica *et al.*, Su *et al.*, and Kim *et al.* found no significant difference between choroidal thickness of healthy pregnant women in the third trimester and the control group.²⁶⁻²⁹ A recent meta-analysis concluded that choroidal thickness is significantly higher in healthy pregnant patients over 24 weeks of GA compared to controls.³⁰

The case-control and cross-sectional design of most of these previous studies has limited the achievement of definite results due to individual bias. The choroidal thickness is affected by various factors including age, sex, systemic or local diseases, diurnal variation, IOP, axial length, menstrual cycle, and pregnancy trimester.³¹⁻³³ In our study, we considered these

confounding variables, and their effect was eliminated to a great extent. Other factors such as previous pregnancy were regarded in our study. We only included nulligravid women (no prior pregnancy) for the control group and primigravid women for our pregnant group, whereas most aforementioned studies have not accounted for this factor.^{23,24,26,34}

To date, very few studies have investigated choroid thickness changes in different trimesters and postpartum. Goktas *et al.* investigated choroidal thickness in the three trimesters but in different sets of pregnant patients at 3 points (subfoveal and 3 mm nasal and temporal to the fovea).³⁵ Their results showed significantly greater choroidal thickness in the 2nd trimester group in comparison with the 1st and 3rd trimester and control groups. They did not find any statistical difference between the 2nd and 3rd trimester groups and the control. Greene and Capkin also conducted a study with a similar design but used the average measurement of subfoveal, 500 μm nasal and temporal choroidal thickness.¹⁵ The choroidal thickness was significantly lower in the 3rd trimester compared to the 1st and 2nd trimester and also compared to the control group. They did not find any statistical difference between the 1st and 2nd trimester groups and the control. In our study, on the other hand, we observed significantly thicker choroids in all three pregnancy trimesters compared to control. We also demonstrated increasing choroidal thickness from the first trimester into the second and third trimesters. The fact that Goktas *et al.* and Greene and Capkin included different patients

for each trimester may have caused the dissimilar results.^{15,35} Moreover, as choroidal thickness is affected by the menstrual cycle, we measured the choroidal thickness of the control group in the follicular phase. This issue was not addressed in neither of the two mentioned studies.

Dadaci *et al.* compared choroidal thickness of pregnant women in the first trimester (6–8 GA weeks) with the third trimester (32–37 GA weeks).³⁶ Similar to our findings, they reported thicker choroids during pregnancy compared to control. However, choroidal thickness decreased significantly in the third trimester compared to the first trimester. As we noted in our study, the choroidal thickness in the 3rd trimester was similar to that of the 2nd trimester and greater than the 1st trimester. We believe different sampling time points in the 3rd trimester may have caused this disagreement, as our measurements were taken between 28 and 34 weeks GA, and theirs was between 32 and 37 GA weeks. Reasons for this finding may be that toward the end of pregnancy, blood flow is redistributed to vital organs and increase in adrenoreceptor activity leads to vasoconstriction.^{37,38}

It has been proposed that increased blood flow, enhanced arterial compliance, and decreased vascular resistance during pregnancy leads to an increase in choroidal thickness.¹⁶ Furthermore, fluid retention in the choroidal layer may affect the thickness.³⁹ Kim *et al.*, Benfica *et al.*, and Sharudin *et al.* noted significantly greater choroidal thickness in patients with pre-eclampsia compared to the healthy pregnancy group.^{27,40,41} This may suggest a correlation between choroidal thickness and OPP, rather than pregnancy itself. However, other studies in line with ours did not find a correlation between OPP and choroidal thickness.^{23,34,35} This issue may highlight the influence of hormones, particularly estrogen, progesterone and cortisol, on choroidal thickness.^{5,33}

In the present longitudinal study, we also measured choroidal thickness after delivery. Previous studies on choroidal thickness before and after delivery have displayed conflicting results. Ulusoy *et al.* examined subfoveal choroidal thickness in third trimester (36 weeks GA) pregnant woman and prospectively 3 months after delivery.³⁴ They reported significant decrease in the thickness 3 months after delivery. In contrast Taradaj *et al.*, which assessed choroidal thickness at 36 weeks GA and at 6th week after delivery, reported greater choroidal thickness at 6th week postpartum compared to 36 weeks GA.⁴² In addition, they evaluated choroidal thickness changes depending on the mode of delivery and reported more noticeable changes in the cesarean section group compared to normal labor. Therefore, mode of delivery is presumed to affect the choroidal thickness postpartum. As mentioned, all our participants had normal vaginal delivery.

Takahashi *et al.* were the first to evaluate choroidal thickness from early pregnancy until after delivery in the same group of patients.⁴³ They measured the subfoveal choroidal thickness of 25 eyes of pregnant women in the 1st and 3rd trimesters, shortly after delivery, and 1 month postpartum. Their results

indicated that the choroidal thickness increases in the first trimester and decreases in the third trimester and remains subsequently unchanged until the 1st month after delivery. In comparison to our study, in which we measured choroidal thickness in seven locations, Takahashi *et al.* only measured the subfoveal choroidal thickness. Moreover, their study did not include measurements at the 2nd trimester of pregnancy.⁴³

In contrast to Takahashi *et al.*,⁴³ we showed that the choroidal thickness changed significantly during pregnancy and postpartum, with increased thickness until the 3rd trimester and subsequent reduction at 6 weeks postpartum in all seven measured locations. Takahashi *et al.* postpartum measurements were done at 4 weeks after delivery, this issue is of clinical relevance as the regression of pregnancy-related physiological changes takes place at 6–7 weeks postpartum.^{1,43} In our study, we also noted that postpartum choroidal thickness was still greater than the control. Takahashi *et al.*, however, did not include a control group.

To the best of our knowledge, the present study is the first longitudinal design to evaluate the changes in choroidal thickness at several locations throughout pregnancy and postpartum and in comparison with nonpregnant healthy women. As there are considerable choroidal thickness variations between individuals, the longitudinal design of our study is of great value. To add to the strength of our study, we included a group of healthy nonpregnant women to compensate for the absent prepregnancy measurements. However, a study including prepregnancy choroidal measurements of the same group of patients would be the ideal and optimal design. Another advantage of our study was that all pregnant participants were primigravid. As it is debated whether previous pregnancy-related choroidal changes are reversible, this matter may act as a confounding factor.⁴⁴

Our study also had some limitation. The first was the relatively small number of subjects as well as the drop-outs. However, previous studies also had a similar sample size, and drop-out is an inevitable part of longitudinal studies of this kind. Another limitation was the lack of patients' prepregnancy choroidal measurements and data. Further studies including prepregnancy choroidal thickness and longer postpartum follow-up measurements are needed to determine precise choroidal changes and reversal. Moreover, evaluating choroidal thickness in patients with pregnancy-related ocular complications can provide guidance for clinical practice.

In conclusion, our study showed significant change in choroidal thickness at seven locations measured with EDI OCT throughout pregnancy and 6 weeks after delivery. We showed that 6 weeks after delivery, choroidal thickness remains significantly higher than nonpregnant subjects.

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Conflicts of interest

There are no conflicts of interest.

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