

Evaluation of choroidal thickness and choroidal vascularity index during pregnancy



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Objective: To assess the choroidal structural characteristics in the first and third trimesters in pregnant women using enhanced depth imaging optical coherence tomography and binarization method.

Design: Prospective study.

Participants: Twenty-five eyes of 25 pregnant women in the first trimester (group 1) and 25 eyes of 25 pregnant women in the third trimester (group 2) were examined. Healthy age-matched 25 participants were enrolled as a control group (group 3).

Methods: The choroidal thickness (CT) was measured at 3 points; subfoveal, 1500 μm nasal to the fovea, and 1500 μm temporal to the fovea. Total choroidal area, luminal area, stromal area, stroma/lumen ratio, and choroidal vascularity index (CVI) were measured by Image-J software.

Results: The mean subfoveal and nasal CT were statistically significantly increased in group 1 compared with controls ($p = 0.005$ and $p = 0.004$, respectively). The mean temporal CT was statistically significantly increased in group 1 compared with groups 2 and 3 (group 1 vs group 2, $p = 0.043$; group 1 vs group 3, $p = 0.011$). The mean total choroidal area, stromal area, and luminal area were significantly increased in groups 1 and 2 compared with control group ($p < 0.001$, $p < 0.001$, $p < 0.001$, and $p < 0.001$, $p = 0.002$, $p = 0.002$, respectively). There were no statistically significant differences among groups in terms of mean stroma/lumen ratio and CVI ($p = 0.148$ and $p = 0.312$, respectively).

Conclusions: There was a significant increase in subfoveal, temporal, and nasal CT in the first trimester. Total choroidal, stromal, and luminal areas were significantly increased in the first and third trimesters.

Objectif: Évaluer les caractéristiques de la structure de la choroïde pendant le premier et le troisième trimestre de la grossesse à l'aide de la tomographie par cohérence optique à l'imagerie à profondeur améliorée et d'une stratégie de binarisation.

Nature: Étude prospective.

Participants: Ont été examinés 25 yeux de 25 femmes au premier trimestre de la grossesse (groupe 1) et 25 yeux de 25 femmes au troisième trimestre de la grossesse (groupe 2). Le groupe témoin (groupe 3) était formé de 25 participantes appariées pour l'âge et en bonne santé (groupe 3).

Méthodes: On a mesuré l'épaisseur de la choroïde (EC) à 3 endroits : dans la sous-fovéa, à 1500 μm en nasal de la fovéa et à 1500 μm en temporal de la fovéa. On a eu recours au logiciel ImageJ pour mesurer la surface totale de la choroïde, la zone luminale, la zone stromale, le rapport stroma/lumen et l'indice de vascularisation choroïdienne (CVI, pour *choroidal vascularity index*).

Résultats: L'EC sous-fovéale et nasale moyenne était significativement plus élevée dans le groupe 1, comparativement au groupe témoin ($p = 0,005$ et $p = 0,004$, respectivement). De même, l'EC temporale moyenne était significativement plus élevée dans le groupe 1, comparativement aux groupes 2 et 3 (groupe 1 vs groupe 2, $p = 0,043$; groupe 1 vs groupe 3, $p = 0,011$). La surface totale de la choroïde, la zone stromale et la zone luminale moyenne étaient significativement plus élevées dans les groupes 1 et 2, comparativement au groupe témoin ($p < 0,001$; $p < 0,001$; $p < 0,001$ et $p < 0,001$; $p = 0,002$; $p = 0,002$, respectivement). On n'a noté aucune différence statistiquement significative entre les groupes quant au rapport stroma/lumen ni au CVI moyen ($p = 0,148$ et $p = 0,312$, respectivement).

Conclusions: On a enregistré une hausse significative de l'EC sous-fovéale, temporale et nasale pendant le premier trimestre de la grossesse. La surface totale de la choroïde, la zone stromale et la zone luminale moyenne, quant à elles, étaient significativement plus élevées pendant le premier et le troisième trimestre de la grossesse.

It is known that pregnancy can cause alterations in cardiovascular, hematologic, pulmonary, renal, and visual systems.¹ The cornea, meibomian glands, and choroidal structures may show structural alterations that might lead to alterations of the tear film, refraction, intraocular pressure, and ocular blood flow.²⁻⁴

In particular, the choroid seems to be more susceptible to hemodynamic and hormonal alterations taking place during pregnancy. The influence of pregnancy on the choroid is still under investigation. The association of central serous chorioretinopathy and pregnancy has been documented previously.^{5,6}

Before the use of enhanced depth imaging optical coherence tomography (EDI-OCT), imaging options for evaluating the choroid were limited. Imaging techniques like ultrasonography or fluorescein/indocyanine green angiography did not provide enough data as those offered by the EDI-OCT.^{7,8} Moreover, fundus angiography is of limited use in pregnant women owing to its invasive nature and concerns about complications for the women and for the fetus.⁹

The EDI-OCT technique is noninvasive, repeatable, and quick. The development of this technique has allowed sufficient analysis of choroidal structures.^{10–12} The aim of the present study was to assess the structural characteristics of the choroid in pregnant women in the first and third trimesters using EDI-OCT and binarization method.

Materials and Methods

The study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board at the Kırşehir Ahi Evran University (2020-13/100). Each patient was informed about the aims and methods of the study and informed consent was obtained from all participants.

This study was conducted on otherwise healthy pregnant women in the first trimester (group 1) and in the third trimester (group 2) who were followed up at the Department of Obstetrics and Gynecology. Healthy women compatible with age and sex were included in the study as a control group (group 3). All of the participants belonged to Turkish ethnicity. The pregnancies were singleton and it was the first pregnancy for all participants. None of the participants had previously given birth or had undergone an abortion in the past.

Women with a history of ocular surgical intervention, any ocular pathology, refractive disorders with a spherical equivalent greater than ± 1 D, or intraocular pressure > 21 mmHg were excluded from the study. Systolic and diastolic blood pressures of all participants were at normal levels. Participants with systemic hypertension, pregestational or gestational diabetes, asthma, or obstructive sleep apnea syndrome or other oxygen-related conditions were also excluded. None of the women participating in the study were current smokers.

The women underwent ophthalmologic examination including best-corrected visual acuity, intraocular pressure measurement, and slit-lamp biomicroscopy.

All participants underwent EDI-OCT imaging (Spectralis, Heidelberg Engineering Inc., Heidelberg, Germany). Choroidal thickness (CT) was measured from the posterior edge of the retinal pigment epithelium to the choroid/sclera junction. The CT was measured at the following 3 points; subfoveal, 1500 μm nasal to the fovea, and 1500 μm temporal to the fovea. Only the right eye per participant was selected. All measurements were made by the same blinded physicians. EDI-OCT imaging was recorded at the same time of the day (9:00 AM to 12:00 PM) to avoid the influence of diurnal variations.

Binarization was performed with Image-J software (Version 1.50a; National Institutes of Health, Bethesda, MD; Fig. 1). The subfoveal B scan was exported for binarization and choroidal vascularity index (CVI) analysis. We selected 3000 μm wide area with the margins of 1500 μm nasal and 1500 μm temporal from the foveal center. The choroidal area was identified from the retina pigment epithelium to the choroid/sclera junction, and the borders were set manually with the Image-J ROI Manager. Then, the image was converted to 8 bits and adjusted by the Niblack auto local threshold. The choroidal, luminal, and stromal areas were automatically calculated for both groups. The light pixels were accepted as the stromal area, and the dark pixels were accepted as the luminal area.¹³ The CVI was calculated as the ratio between the luminal area and the total choroidal area.

SPSS 11.5 (SPSS Inc., Chicago, IL) was used for all between-group comparisons. The normality of all data was tested by the Kolmogorov–Smirnov test. The significance of the difference among all groups was evaluated by one-way analysis of variance and the Kruskal–Wallis test. Pairwise comparisons with the Tukey honestly significant difference and Bonferroni tests were used to assess which groups differed. $p < 0.05$ was set for statistical significance.

Results

This study was conducted on 25 eyes of 25 pregnant women in group 1, 25 eyes of 25 pregnant women in group 2, and 25 eyes of 25 healthy age-matched controls in group 3. Mean age was 28 ± 6 years (range, 18–44) in group 1, 28 ± 5 years (range, 18–39) in group 2, and 29 ± 6 years

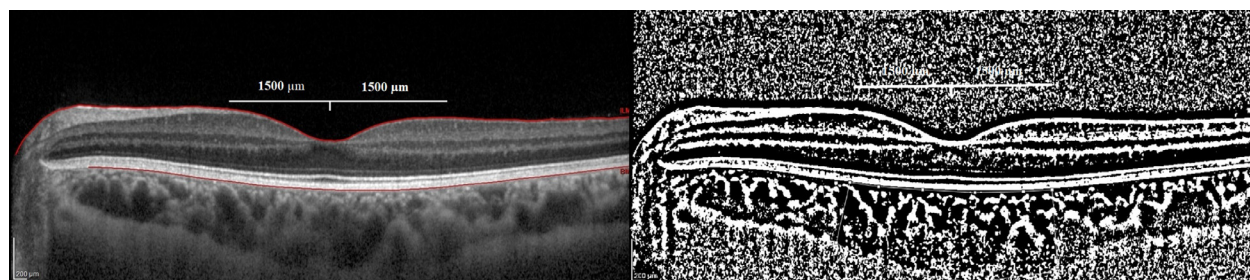


Fig. 1—(A) Enhanced depth imaging optical coherence tomography image of a pregnant woman in the first trimester. **(B)** Converted binary image using ImageJ with the area of interest in the choroid demarcated with a white line. The choroidal area was measured at approximately 3000 μm wide with the margins of 1500 μm nasal and 1500 μm temporal from the foveal center.

Table 1—Demographic and clinical characteristics of patients included in the study

	Pregnant women first trimester	Pregnant women third trimester	Controls
Number of eyes/ participants	25/25	25/25	25/25
Age (y)	28 ± 6	28 ± 5	29 ± 6
mean ± SD (range)	(18–44)	(18–39)	(19–37)
Gestational age (wk)	9.1 ± 2.6	35.4 ± 2.8	
mean ± SD (range)	(6–12)	(30–39)	

(range, 19–37) in group 3. There was no significant difference between the 3 groups in terms of age ($p = 0.842$).

The mean best-corrected visual acuity was 0.0 on the log-MAR scale. Intraocular pressure measurements were within the normal range in all patients. Demographic and clinical characteristics for all groups are shown in Table 1.

The mean subfoveal and nasal CT were statistically significantly increased in group 1 compared with controls ($p = 0.005$ and $p = 0.004$, respectively). The mean temporal CT was statistically significantly increased in group 1 compared with groups 2 and 3 (group 1 vs group 2, $p = 0.043$; group 1 vs group 3, $p = 0.011$).

The p values of the comparisons are shown in Table 2. Box plots showing CT measured in pregnant women and control groups are shown in Figure 2.

According to measurements made with Image-J, the mean total choroidal, stromal, and luminal areas were significantly increased in groups 1 and 2 compared with control group ($p < 0.001$, $p < 0.001$, $p < 0.001$, and $p < 0.001$, $p = 0.002$, $p = 0.002$, respectively). There were no statistically significant differences among groups in terms of mean stroma/lumen ratio and CVI ($p = 0.148$ and $p = 0.312$, respectively). The p values of these comparisons are shown in Table 3. Box plots showing choroidal parameters measured by Image-J in pregnant women and control groups are shown in Figure 3.

Discussion

The choroid is the layer that supplies nutrients for the retinal pigment epithelium and outer retinal layers. It is responsible for the majority of intraocular blood flow and it can be

influenced by hemodynamic factors like blood flow and perfusion pressure.^{14,15}

Pregnancy promotes metabolic, hormonal, and hemodynamic alterations that could cause changes in choroidal blood flow. As a result of the influence on the hemodynamics of the cardiovascular system in pregnancy, the effect of a decrease in vascular resistance prevails over the effect of an increase in blood volume, resulting in a decrease in systolic and diastolic blood pressures. Decreased vascular resistance might result in increased blood flow through many organs.¹⁶

It has been reported previously that the prevalence of central serous chorioretinopathy increases during pregnancy.^{17,18} Also, a retrospective clinical control trial¹⁹ showed that pregnancy is a significant risk factor for central serous chorioretinopathy. It can be assumed that choroidal vasodilation and increased hydrostatic pressure can lead to increased choroidal vascular permeability and choroidal vascular leakage in pregnancy.

Previous studies have evaluated CT during the pregnancy period, with contradictory results. Certainly, there may be many factors affecting the CT during pregnancy such as age, different trimesters, and blood pressure. Takahashi et al.²⁰ and Kim et al.²¹ demonstrated that CT was not significantly different when comparing pregnant women in their third trimester with healthy nonpregnant women. However, Kara et al.²² and Sayin et al.²³ conducted studies comparing the CT of pregnant women at different gestational ages with nonpregnant women and concluded that subfoveal choroid was significantly thicker in pregnant women compared with the control group. Dadaci et al.²⁴ reported that CT was found to be significantly decreased in healthy pregnant women in the third trimester compared with those in the first trimester. Rothwell et al.²⁵ compared the CT of healthy pregnant women in the third trimester with healthy nonpregnant women. They reported that pregnant women had increased CT compared with healthy nonpregnant women. Greene et al.²⁶ showed a significant decrease in CT in the third trimester compared with the first trimester.

Current results showed a significant increase in subfoveal, temporal, and nasal choroid thickness in the first trimester compared with the controls. Subfoveal and nasal choroid thickness was found to be thicker in pregnant women in the first trimester than in the third, but the difference was not statistically significant. Also, we showed that subfoveal,

Table 2—Choroidal thickness measurements (μm) for each group and statistical comparisons

Variables	Pregnant women first trimester	Pregnant women third trimester	Controls	p values			
				ANOVA/ Kruskal–Wallis test	Pairwise comparisons		
					1 vs 3	2 vs 3	1 vs 2
Subfoveal	400.1 ± 82.3	344.4 ± 87.2	304.9 ± 80.9	0.007*	0.005*	0.361	0.137
Nasal	345.8 ± 71.5	289.1 ± 81.7	259.9 ± 68.7	0.005*	0.004*	0.491	0.076
Temporal	371.8 ± 73.1	301.4 ± 68.1	286.2 ± 93.5	0.009*	0.011*	0.854	0.043*

ANOVA, analysis of variance.

*Statistically significant p values

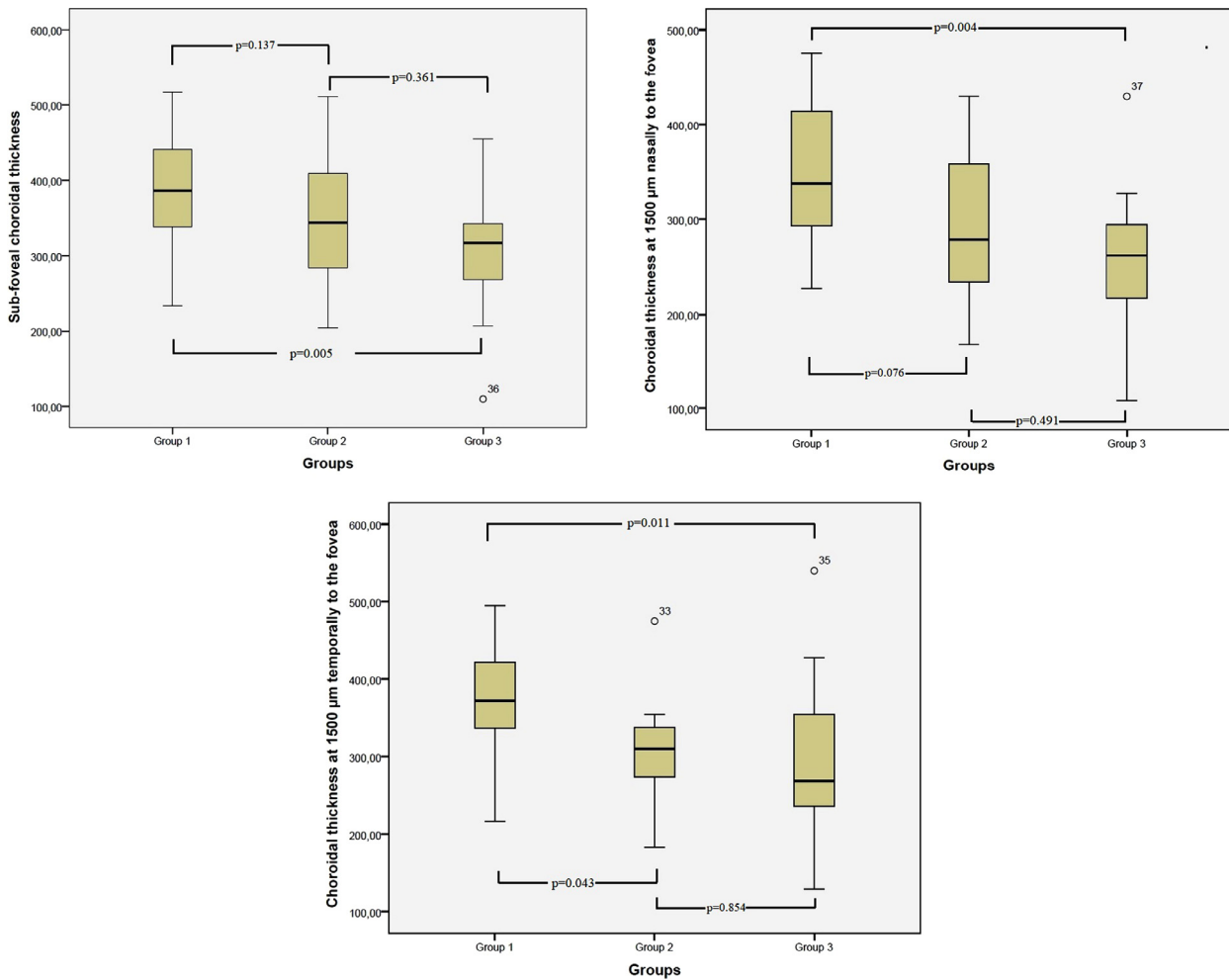


Fig. 2—Box plots showing choroidal thickness measured in the pregnant women and the control group.

Table 3—Choroidal structural characteristics evaluated with Image-J and statistical comparisons

Variables	Pregnant women first trimester	Pregnant women third trimester	Controls	p values		
				ANOVA/Kruskal-Wallis test	Pairwise comparisons	
					1 vs 3	2 vs 3
TCA (mm ²)	1.32 ± 0.1	1.21 ± 0.1	0.93 ± 0.1	<0.001*	<0.001*	0.155
SA (mm ²)	0.39 ± 0.05	0.37 ± 0.05	0.30 ± 0.07	<0.001*	<0.001*	0.688
LA (mm ²)	0.93 ± 0.1	0.83 ± 0.1	0.63 ± 0.1	<0.001*	0.002*	0.191
SLR	0.42 ± 0.1	0.45 ± 0.1	0.52 ± 0.2	0.148	0.143	0.866
CVI (%)	70.2 ± 3.9	68.9 ± 3.3	66.8 ± 4.3	0.312	0.285	0.819

ANOVA, analysis of variance; TCA, Total choroidal area; SA, Stromal area; LA, Luminal area; SLR, Stroma/lumen ratio; CVI, choroidal vascularity index.

*Statistically significant p values.

temporal, and nasal CT were increased in the third trimester compared with the controls. Only the difference between temporal CT was statistically significant.

During pregnancy, blood flow increases in many organ systems, including the kidneys, extremities, and skin.^{27–29} One study³⁰ reported increased ocular blood flow during pregnancy caused by vasodilation owing to changes in estrogen levels. Increased CT may be secondary to increased blood flow during pregnancy.

To the best of our knowledge, this was the first study to evaluate choroidal vascular structures in pregnant women using the EDI-OCT and binarization method. According to the results, the healthy pregnant women in the first and third trimesters had significantly thicker total choroidal, stromal, and luminal areas than controls. In terms of total choroidal, luminal, and stromal areas, there was no significant difference between pregnant women in the first and third trimesters.

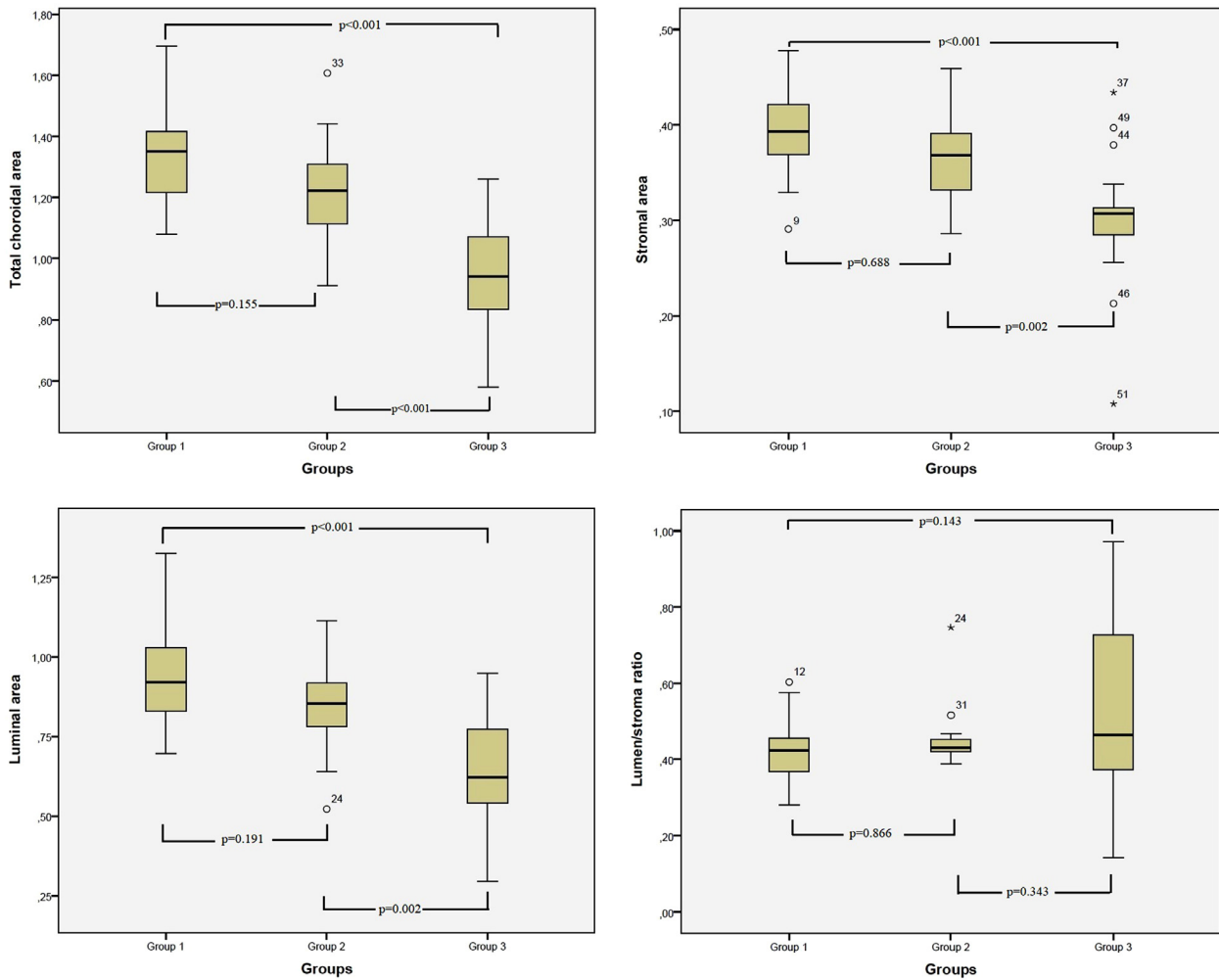


Fig. 3—Box plots showing choroidal parameters measured by Image-J in the pregnant women and the control group.

In the present study, we measured the stroma/lumen ratio for each group. According to the results, although there was no statistically significant difference, this ratio was lower in the first trimester than in the third trimester and the control group. Similarly, the mean stroma/lumen ratio was lower in women in the third trimester group compared with the control group. But there was no statistically significant difference. The lower stroma/lumen ratio in pregnant women can be explained by the prominence of enlargement in the lumen region and therefore the increase in the vascular component in these eyes.

CVI is a relatively new imaging tool for the measurement and analysis of the choroidal vascular system by quantifying both luminal and stromal choroidal components. Some reports^{31–35} have been published regarding CVI and its applications in the assessment, diagnosis, and treatment of diseases of the retina and the choroid like central serous chorioretinopathy, polypoidal choroidal vasculopathy, panuveitis, and diabetic retinopathy. Agrawal et al.³¹ appraised CVI in eyes with central serous chorioretinopathy and reported that eyes with acute central serous chorioretinopathy had significantly higher CVI compared with their fellow eyes. They suggested that

increased CVI suggests increased vascular component compared with the stromal component in acute central serous chorioretinopathy.³¹ Agrawal et al.³³ evaluated CVI in posterior uveitis and panuveitis, reporting an increased CVI, which decreased after 3 months of follow-up.

In the present study, we observed that the mean CVI was increased in the first and third trimesters of pregnant women compared with healthy controls, but the difference was not significant. Considering that the CVI was defined as the ratio of luminal area to total choroidal area, increased CVI measurements in the first and third trimesters compared with controls can be explained by the fact that the choroidal luminal area has shown greater increase than the stromal area. This may explain the corresponding decrease in CVI.

The data in the present study indicated a consistent trend of increased CT and increased choroidal stromal and luminal area in the first versus the third trimester, although the differences were not significant. Normal pregnancy is dynamic process that is accompanied by numerous changes in the maternal vascular system to provide adequate blood and nutrient supply to gradually increasing demands of the fetus and the maternal organs and systems. Increased vascular compliance has been

shown in normal human pregnancy starting in the first trimester and decreasing up to the third trimester. In the first trimester, there is also a substantial decrease in peripheral vascular resistance. As the choroid is primarily a vascular complex, a number of adaptations may be expected to occur during pregnancy leading to choroidal structural changes. Therefore, pregnancy-induced vascular changes including expansion of systemic blood volume and reduction of systemic vascular resistance may have an effect on the choroidal circulation and structural parameters in different trimesters of pregnancy.

This study had some limitations, such as a small number of participants. The cross-sectional design allowed us to analyze choroid characteristics merely in the first and third trimesters of pregnancy. More consistent results could be achieved with a longitudinal study of CT during the 3 trimesters of pregnancy and the postpartum period with a large number of participants.

Conclusions

The current study showed a significant increase in subfoveal, temporal, and nasal CT in the first trimester compared with the control group. The otherwise healthy pregnant women in the first and third trimesters had significantly thicker total choroidal, stromal, and luminal areas. There was no significant difference between groups in terms of CVI values. Whether the physiologic hemodynamic and hormonal adaptations in pregnancy are responsible for the choroidal structural and vascular alterations in healthy pregnant women remain to be answered in future studies.

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Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

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Originally received Aug. 23, 2020. Final revision Nov. 1, 2020. Accepted Dec. 4, 2020.

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