Article

Evaluation of the Choroid in Women with Uncomplicated Pregnancy

Li Su[1,2], Wongsiri Taweebanjongsin[1], Stephanie L. Gaw[3], Gilad Rabina[4], SriniVas R. Sadda[1], and Irena Tsui[1,5]

[1] Doheny Eye Institute, Department of Ophthalmology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA
[2] Department of Ophthalmology, Shanghai General Hospital (Shanghai First People's Hospital), Shanghai Jiao Tong University School of medicine, Shanghai, China
[3] Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco, San Francisco, CA, USA
[4] Department of Ophthalmology, Tel Aviv Sourasky medical Center, affiliated with Sackler School of Medicine, Tel Aviv University, Israel
[5] Stein Eye Institute, Department of Ophthalmology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Purpose: To study the choroid in uncomplicated pregnant women using advanced optical coherence tomography (OCT) imaging and analysis.

Methods: Women with uncomplicated pregnancy in the third trimester ($>$28 weeks gestational age) and age-matched nonpregnant women were enrolled in this prospective study. All subjects underwent spectral-domain OCT with enhanced depth imaging mode and spectral-domain optical coherent tomography angiography (OCTA). Main outcomes were subfoveal choroidal thickness (SFCT), choroidal vascularity index (CVI), and choriocapillaris flow deficits (CC FD).

Results: Twenty-two eyes of 12 uncomplicated pregnant women and 23 eyes of 15 nonpregnant, female controls were included. The mean age was 32.27 ± 6.96 years for the pregnant group and 30.08 ± 5.49 years for control group ($P > 0.05$). Mean SFCT was 238.70 ± 82.96 μm in the pregnant group, and 277.40 ± 61.79 μm in the control group. CVI was $67.58\% \pm 2.45\%$ in the pregnant group and $67.31\% \pm 2.62\%$ in the control group. The CC FD% was 54.06 ± 3.95 in the pregnant group, and 55.02 ± 3.78 in the control group. There was no significant difference between the pregnant and control groups ($P > 0.05$) in SFCT, CVI or CC FD.

Conclusions: Although extensive hemodynamic changes occurred with pregnancy, choroidal measurements by OCT and OCTA demonstrated no differences in uncomplicated third-trimester pregnant women compared with nonpregnant controls.

Translational Relevance: The unaltered choroid in uncomplicated third-trimester pregnancy we described allows clinicians to determine whether abnormal choroidal measurements could be used as a biomarker for complications of pregnancy.

Introduction

Significant physiological changes occur in every system during pregnancy. Hematological, vascular, endocrine, metabolic, and immunological system changes occur to accommodate the developing fetus and prepare the mother for labor and delivery.[1–3] The various systemic changes during pregnancy also affect the eye.[4] An increase in the central corneal thickness, change in its curvature, decrease in corneal sensitivity, and a decrease in intraocular pressure are transitional and physiological, and these changes resolve after pregnancy with minimal residual effects. Pathological conditions during pregnancy, such as preeclampsia and central serous chorioretinopathy (CSC), may lead to severe retinal and choroidal complications and visual disturbances, including serous retinal detachments, Purtscher's-like retinopathy, and retinal and vitreous hemorrhages.[5] So it is important to understand the

normal retinal and choroidal changes occurring in normal pregnancy because this will help differentiate abnormalities from adaptations.

The choroid, which provides nutrients and removes metabolic wastes from retinal pigment epithelium (RPE) and the outer retina, plays a key role in maintaining retinal function and vision acuity. The choroidal circulation status is influenced by age, axial length, oxygenation, perfusion pressure, various ocular pathological conditions, and systemic diseases.[6,7] Optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) are important breakthrough imaging technologies of the past decade. OCT provides rapid, noninvasive, high-resolution, cross-sectional images of the retina, and RPE. Enhanced depth imaging optical coherence tomography (EDI-OCT), which enables the visualization and measurement of the choroid, facilitates a comprehensive understanding of choroidal behavior in physiological and pathological conditions. OCTA can provide unprecedented three-dimensional images of not only the retinal microcirculation, but also the inner choroidal circulation.

Considering the significant systemic changes and the structural and functional features of the choroid, a number of transformations may be anticipated to occur in the choroidal circulation during pregnancy, subsequently leading to structural changes. To date, little was known about the choroidal vascular changes during pregnancy. Several studies have explored the association between subfoveal choroidal thickness (SFCT) and pregnancy using EDI-OCT. Some studies show the SFCT increases during pregnancy,[8–11] whereas others suggest that the pregnancy itself does not increase SFCT.[12,13] The choroid, however, is composed of various elements, including blood vessels, stromal tissue, and nerves, and evaluations focused on alterations in the SFCT alone do not provide information regarding which tissue components in the choroid are changing. Choroidal vascularity index (CVI) is a novel biomarker for assessing the choroidal vascular status in ocular diseases.[14,15] CVI appears to be less variable and less impacted by other physiological factors compared with CT, which makes it a relatively stable index for studying choroidal alterations due to pathology. Until now, little is known about the CVI changes during pregnancy. In addition, although the choriocapillaris (CC) has been thought to play a central role in many retinal and choroidal disorders, it has not been well studied until the development of OCTA and processing strategies to manage the artifacts commonly associated with OCTA. The purpose of this study was to quantitatively assess the SFCT, CVI, and CC changes in a cohort of women with uncomplicated pregnancy compared with age-matched controls.

Materials and Methods

Setting and Participants

This study was a prospective, case-control study, which was approved by the Institutional Review Board of the University of California–Los Angeles and was conducted in accordance with the ethical standards stated in the Declaration of Helsinki. Written informed consent was obtained from all subjects before imaging.

Consecutive subjects meeting eligibility criteria were recruited from the Fair Oaks Women's Center (Pasadena, CA, USA) and imaged at the Doheny UCLA Eye Center (Pasadena, CA, USA) between June 2018 and January 2019. Inclusion criteria for the pregnancy group included uncomplicated pregnancy in the third trimester (>28 weeks gestational age) in healthy females. Subjects were excluded if they had any history of previous ocular or systemic diseases, such as diabetes mellitus or hypertension, or complications of pregnancy, such as gestational diabetes or preeclampsia at the time of imaging. A control group of age-matched nonpregnant women without systemic or ocular history were also recruited. Additional exclusion criteria for either the uncomplicated pregnancy or control group included the presence of refractive error greater than −6.0 diopters spherical equivalent (SE).

Image Acquisition and Scanning Protocols

All subjects underwent spectral-domain OCT (SD-OCT) with the EDI mode (Spectralis; Heidelberg Engineering, Heidelberg, Germany). The macular region was scanned using a horizontal raster scan (30° × 5°) centered on the fovea, with 7 B-scans and 100 frames averaged in each B-scan. The raster scan passing through the foveal center was selected for CVI and CT analysis.

OCTA images were captured without pharmacologic dilation using the spectral-domain OCTA (SD-OCTA) device (Spectralis, Heidelberg Engineering, Heidelberg, Germany). A 10° × 10° (512 × 512 A-scans) OCTA scan was acquired centered on the fovea. OCTA scans were repeated until a sufficient quality scan (Q ≥ 30, no evidence of motion artifact) was obtained. The instrument software's automatic segmentation boundaries were inspected on all B-scans, and manual correction was performed on any B-scans

demonstrating segmentation errors. A slab spanning from 20 to 30 μm deep to the RPE band was used to isolate the CC. The manufacturer's projection artifact removal function was used to remove residual artifact from the overlying retinal circulation.

Image Processing

Choroidal scleral interface was defined as the hyper-reflective border at the outer aspect of the vascular structure of the choroid. CT was analyzed using the Spectralis EDI-OCT B-scan and measured from Bruch's membrane to the choroid-sclera interface at the foveal center using the caliper tool in the instrument software.

For the measurement of CVI, image binarization was carried out using the approach described by Agrawal et al.[15,16] Briefly, the FIJI software (an expanded version of ImageJ version 1.51a; fiji.sc) was used for image processing. The entire 10 degree OCT B scan passing through the fovea was first converted to 8-bit images using the Default setting. Subsequently, the Niblack's auto local threshold tool was applied to allow segmentation of the luminal area (LA) and stromal area (SA). Then total choroidal area (TCA) was selected using polygonal tool by manual plotting of the choroidal upper border at the RPE and the lower border marked at the choroid-sclera junction. Then the image was converted back to an RGB (red, green, blue) image to allow computation of size of LA by the color threshold tool. Finally, CVI was calculated as a proportion of LA to TCA.

For the measurement of the CC flow deficit (FD), the en face images of the custom CC slab were exported from the Spectralis software after confirmation of proper segmentation, and then imported into the FIJI software. The CC images were binarized using a modified version of the previously reported method.[17–19] Briefly, the images were duplicated to apply two binarization methods. One image was processed first by a Hessian filter, followed by global thresholding using Huang's fuzzy thresholding method. The other (duplicate) image was binarized using median local thresholding. Finally, the two different binarized images were combined to generate the final binarized image in which only pixels that existed on both binarized images were included. CC FD was measured using the Phansalkar method (radius: 23.44 μm) as described previously.[20] The percentage of CC FD was calculated as percentage of the resulting area using the "Analyse Particles" command.

Statistical Analysis

All measurements were performed by two masked, independent, certified Doheny Image Reading Center OCT/OCTA graders (L.S., W.T.), and intergrader analysis was performed to assess repeatability. Statistical analyses were performed using SPSS Statistics version 20 (IBM, Armonk, NY, USA). To detect differences in CT, CVI, and CC FD between two groups, linear mixed model analysis was used to adjust for correlations between two eyes of the same subject. The inter-grader reproducibility was assessed using intraclass correlation coefficient (ICC). A *P* value < 0.05 was considered statistically significant.

Results

Twenty-two eyes of 12 uncomplicated pregnant women were included in this study. The mean age was 32.27 ± 6.96 years, and the mean gestational age was 33 ± 3.59 weeks (range 29–39). All pregnant subjects were singleton pregnancies. All eyes had 20/20 visual acuity. Twenty-three eyes of 15 nonpregnant, healthy female controls were also enrolled. The mean age was 30.08 ± 5.49 years. The demographic data for the two groups are shown in Table 1. There was no significant difference in age or spherical equivalent refractive error between these groups ($P > 0.05$). The OCT image quality was 35.30 ± 3.34 dB in the pregnant group and 35.35 ± 4.25 dB in the control group. The OCTA image quality was 37.14 ± 2.62 dB in the pregnant group and 36.00 ± 2.26 dB in the control group. There was no significant difference in OCT or OCTA image quality between the pregnant group and the control group ($P > 0.05$, Table 1).

For SFCT and CVI analysis, 20 eyes from 10 uncomplicated pregnant women and 20 eyes from 10 nonpregnant normal controls were included after excluding eyes without sufficient image quality (<30 dB). The mean SFCT thickness was 238.70 ± 82.96 μm (range 140–422 μm) in the uncomplicated pregnancy group, and 277.40 ± 61.79 μm (range 161–402 μm) in the control group. There was no significant difference between these two groups ($P > 0.05$, Table 2) in SFCT. The ICC between the two graders was 0.97 (95% confidence interval [CI]: 0.94–0.98) for SFCT measurement.

For the CVI, the total subfoveal choroidal area was 3.63 ± 1.10 mm^2 in the uncomplicated pregnant group and 3.93 ± 0.62 mm^2 in the control group, respectively. The subfoveal luminal area was 2.44 ± 0.69 mm^2 in the uncomplicated pregnant group and 2.64 ± 0.43 mm^2

Table 1. Cohort Demographics

	Pregnant Group	Control Group	*P*
Eyes	22 eyes (12 subjects)	23 eyes (15 subjects)	/
Age (years)	32.27 ± 6.96	30.08 ± 5.49	0.384
Gestational Age (weeks)	33 ± 3.59	/	/
Spherical Equivalent (D)	−1.41 ± 1.83	−1.76 ± 1.79	0.170
OCT Image Quality	35.30 ± 3.34	35.35 ± 4.25	0.890
OCTA Image Quality	37.14 ± 2.62	36.00 ± 2.26	0.113

Table 2. SFCT, CVI, and CC in Uncomplicated Pregnant Group and Control Group

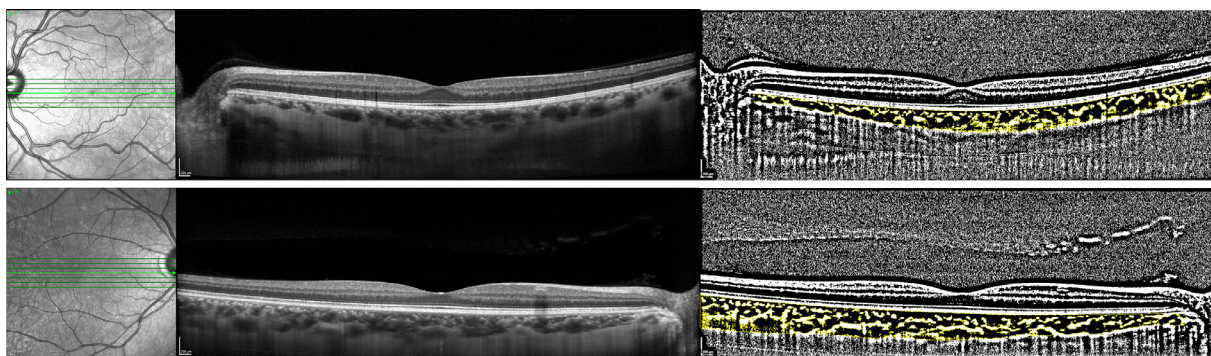|	Pregnant Group	Control Group	*P*
Choroidal thickness (µm)	238.70 ± 82.96	277.40 ± 61.79	0.283
Total area (mm^2)	3.63 ± 1.10	3.93 ± 0.62	0.059
Luminal area (mm^2)	2.44 ± 0.69	2.64 ± 0.43	0.069
Stromal area (mm^2)	1.19 ± 0.42	1.28 ± 0.23	0.105
CVI (%)	67.58 ± 2.45	67.31 ± 2.62	0.927
CC FD (%)	54.06 ± 3.95	55.02 ± 3.78	0.694

Figure 1. Examples of CVI measurement. Upper row: images from an uncomplicated pregnant woman, lower row: images from a healthy control. Left: IR images, middle: EDI-OCT B-scan images centered on the fovea, right: binarized EDI-OCT B-scan images using Niblack auto local threshold on Fiji. After binarization, region of interest was overlaid on the scan illustrating luminal (dark region) and stromal (light region) area. The CVI in the upper row is 71.39% and the CVI in the lower row is 69.90%.

in the control group. The subfoveal stromal area was 1.19 ± 0.42 mm^2 in the uncomplicated pregnant group and 1.28 ± 0.23 mm^2 in the control group. The CVI was 67.58% ± 2.45% in the uncomplicated pregnant group and 67.31% ± 2.62% in the control group. There was no significant difference in subfoveal total, luminal, or stromal choroidal area or CVI between the uncomplicated pregnant group and the control group ($P > 0.05$, Fig. 1, Table 2). The ICC between the two graders was 0.95 (95% CI: 0.81–0.98) for CVI.

For the CC analysis, the percentage of CC FD (%) was 54.06 ± 3.95 in the uncomplicated pregnancy group, and 55.02 ± 3.78 in the control group (Table 2, Fig. 2). There was also no significant difference between these two groups ($P > 0.05$) in the CC

FD percentage. The ICC between the two graders was 0.99 (95% CI: 0.98–0.99) for CC FD.

Discussion

In this study, we observed that there was no significant difference in SFCT, CVI, or CC in women with uncomplicated pregnancy compared with age-matched nonpregnant women. To our knowledge, our study was the first investigation to compare CVI between uncomplicated pregnancy and age-matched nonpregnant controls. It is important to investigate physiological changes associated with pregnancy to improve our understanding of pregnancy-related disorders
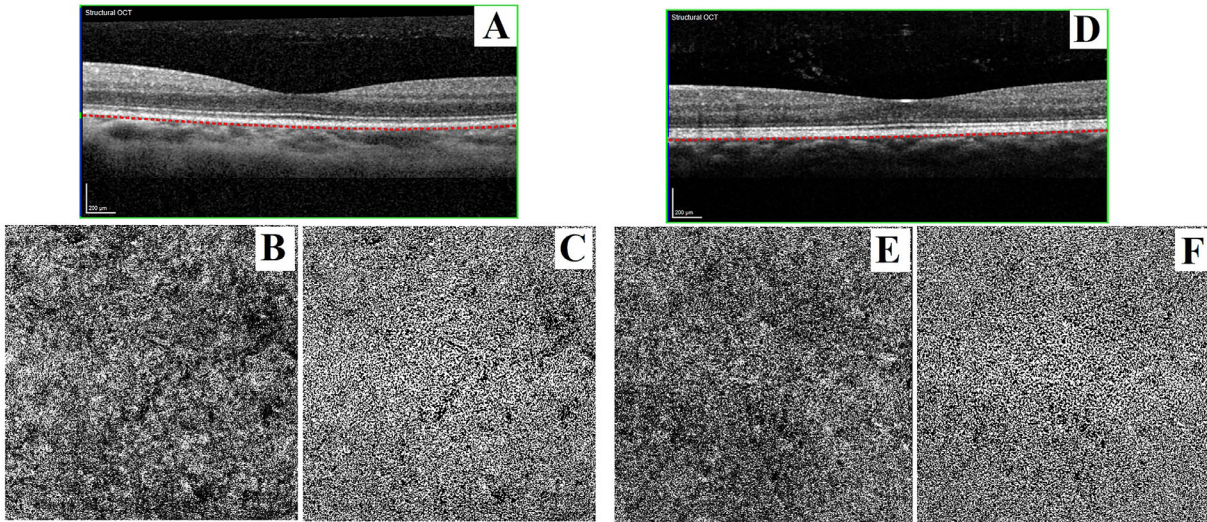
translational vision science & technology

Figure 2. Two cases (one from each group) illustrating the CC measurement. A and D were single structural B-scan images centered on the fovea showing the CC segmentation. B and E were en-face OCTA images of CC (20-30μm deep to the RPE band). C and F were final binarized CC images used to calculate the percentage of CC FD. A-C: the image of an uncomplicated pregnant woman. The CC FD was 51.83%; D-F: the image of a healthy control woman. The CC FD was 53.51%.

pertaining to both the mother's eye and the fetus's overall health. In our study, the OCT and OCTA image quality (without dilation) in the pregnant group was as good as in the control group, which validated our ability to use OCT and OCTA as quantitative research tools in pregnant subjects.

Using EDI-OCT, several studies have investigated the association between SFCT and pregnancy. Some studies have noted that pregnancy itself does not appear to increase CT,[13] which was in agreement with the findings of our study. Goktas et al.[21] found that choroidal thickening could occur in the second trimester, but there was no significant difference in choroid thickness between the first or third trimester and normal controls. Dadaci et al.[12] also confirmed that there was no significant difference in CT between the first or third trimester and control eyes, but the CT significantly decreased in healthy pregnant women during the third trimester. In contrast, Ulusoy et al.[22] found that CT increased in the third trimester and returned to a normal range in the three months after delivery. The changes in CT during pregnancy and after delivery might be a dynamic process, which is related to the marked physiological changes in the metabolic, hormonal, and hemodynamic systems. Of note, the CT is influenced by age, sex, systemic/local diseases and their treatment, drug use, intraocular pressure, refractive error, and many other factors.[23, 24] The somewhat inconsistent results pertaining to CT changes during pregnancy reported in the literature may derive from measurements taken at different times

of day, variable ages of subjects, and measurement error. Future studies evaluating CT changes during pregnancy should take these biases into consideration, and future studies with more subjects and data from multiple trimesters will be helpful to provide further clarity on this issue.

The choroid is a complex tissue consisting of vascular and stromal components. Measurement of CVI takes into account both the vascular and interstitial components of the choroid, which provides complimentary information to the SFCT.[17] In addition, CVI is a two-dimensional measurement, whereas CT is a single-dimensional measurement.[17] Therefore CVI is considered to be a more-reliable marker for studying choroidal changes than CT. Indeed, CVI (but not CT) was shown to be less affected by confounding factors such as axial length, intraocular pressure, age, and systolic blood pressure.[16,17] Our study was the first one to investigate CVI in pregnant subjects. In our study, there was no significant difference in CVI in uncomplicated pregnant women compared with eyes of age-matched normal controls. The utility of CVI to evaluate the choroidal vasculature has also been studied in other ocular and systemic diseases.[25] Wei et al.[25] found that eyes with exudative age-related macular degeneration (AMD) had a reduction in CVI but no significant changes in CT compared with fellow eyes. Agrawal et al.[15] found that CVI increased in both acute CSC eyes and fellow eyes. Tan et al.[26] reported that patients with retinitis pigmentosa showed reduced CVI when compared with normal eyes. Thus CVI has evolved

into a noninvasive tool for studying structural changes in the choroid and monitoring retinal and choroidal diseases.[25,26] Larger studies with multiple times points are required, however, to better elucidate CVI adaptations during the course of pregnancy and in the setting of ocular disorders associated with pregnancy.

In contrast to fluorescein angiography (FFA) and indocyanine green angiography (ICGA), OCTA is noncontact, noninvasive, easy to perform, and capable of providing depth-resolved, high-resolution, three-dimensional images of the retinal and inner choroidal vasculature without dye injection.[27] This safety consideration is particularly important in the setting of pregnancy when the use of invasive dyes should generally be avoided. Using OCTA, our previous studies found that perfusion density in superficial retinal capillary plexus (SCP) significantly decreased and perfusion density in deep retinal capillary plexus (DCP) significantly increased in the third trimester of pregnant women compared with nonpregnant controls.[28] We hypothesized that the retinal microvasculature adapts by vasodilation during pregnancy due to hematological, vascular, and endocrine changes. Ciloglu et al.[27] found that retinal microvascular structure changed in pregnant women with preeclampsia compared with uncomplicated pregnant women and nonpregnant controls. Despite these reported changes in the retinal microvasculature in normal pregnancy and preeclampsia, our present study found that CC FD showed no significant difference in uncomplicated pregnancy women compared with age-matched controls. The retinal and choroidal circulations, however, have separate and different autoregulatory mechanisms, so it is perhaps not surprising that they would behave differently in pregnancy. Saito et al.[29] reported that OCTA was able to detect ischemic changes in the choriocapillaris in pregnant women with hypertensive eye changes. CC changes in other ocular disorders associated with pregnancy, such as pre-eclampsia, need further investigation.

Our study does have limitations inherent to studying a vulnerable population such as pregnancy that should be considered in assessing our results. First, our sample size is relatively small, but we rationalize that it may be adequately powered to detect significant changes. Ulusoy et al.[22] found that SFCT increased more than 20% in the third trimester compared with normal healthy control women. If we assume a 20% change in choroidal thickness as clinically relevant, a sample size of 26 is needed to detect differences in groups at $\alpha = 0.05$ and power $= 80\%$. Moreover, highly choroid-relevant diseases, such as central serous chorioretinopathy, show that macular choroidal thickness has the potential to change up to 40% compared

with normal controls.[30] CVI, even more sensitive than CT, has been shown in prior studies to detect differences as small as 3%, lending further credence to our negative study.[17] Second, because of having only one timepoint, we are not able to assess dynamic alterations in SFCT, CVI, and CC FD that may occur during the course of pregnancy. This may be addressed by future longitudinal studies that may extend from before pregnancy through the postpartum process to capture earlier changes in pregnancy that may return to baseline by third trimester. Despite these shortcomings, we were able to demonstrate proof of concept that the choroid of pregnant women can be evaluated reliably without the need for dilation. Our study also has several strengths that our group has leveraged before, including the use of EDI-OCT and OCTA, which are ideal for evaluation of the choroid, prospective imaging protocols, analysis of the entire foveal 10 degree scan, and the use of independent, certified image reading center graders.

In summary, using EDI-OCT and OCTA we observed that SFCT, CVI, and CC FD in uncomplicated third-trimester pregnant women showed no significant difference compared with eyes of age-matched controls. The knowledge that normal pregnancy leaves the choroid unaltered allows clinicians to determine whether abnormal choroidal measurements could be used as a biomarker for diseases such as gestational hypertension, preeclampsia, or other complications of pregnancy. Future studies with larger samples imaged in both the second and third trimester of pregnancy can confirm our results and determine whether pregnancy complications cause significant changes in SFCT, CVI, or CC FD. These findings may provide a useful foundation for future studies aimed at better understanding the etiology of ocular and systemic diseases associated with pregnancy.

Acknowledgments

References

1. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. *Cardiovasc J Afr*. 2016;27:89–94.

2. Lockitch G. Clinical biochemistry of pregnancy. *Crit Rev Clin Lab Sci*. 1997;34:67–139.

3. Ouzounian JG, Elkayam U. Physiologic changes during normal pregnancy and delivery. *Cardiol Clin*. 2012; 30:317–329.

4. Mackensen F, Paulus WE, Max R, Ness T. Ocular changes during pregnancy. *Dtsch Arztebl Int*. 2014;111:567–575.

5. Roos NM, Wiegman MJ, Jansonius NM, Zeeman GG. Visual disturbances in (pre)eclampsia. *Obstet Gynecol Surv*. 2012;67:242–250.

6. Pongsachareonnont P, Somkijrungroj T, Assavapongpaiboon B, Chitamara T, Chuntarapas M, Suwajanakorn D. Foveal and parafoveal choroidal thickness pattern measuring by swept source optical coherence tomography. *Eye (Lond)*. 2019;33:1443–1451.

7. Abbey AM, Kuriyan AE, Modi YS, et al. Optical coherence tomography measurements of choroidal thickness in healthy eyes: correlation with age and axial length. *Ophthalmic Surg Lasers Imaging Retina*. 2015;46:18–24.

8. Ataş M Açmaz G, Aksoy H, et al. Evaluation of the macula, retinal nerve fiber layer and choroid in preeclampsia, healthy pregnant and healthy non-pregnant women using spectraldomain optical coherence tomography. *Hypertens Pregnancy*. 2014;33:299–310.

9. Rothwell RT, Meira DM, Oliveira MA, Ribeiro LF, Fonseca SL. Evaluation of choroidal thickness and volume during the third trimester of pregnancy using enhanced depth imaging optical coherence tomography: a pilot study. *J Clin Diag Res*. 2015;9:NC08–NC11.

10. Duru N, Ulusoy DM, Özköse A, et al. Choroidal changes in pre-eclampsia during pregnancy and the postpartum period:comparison with healthy pregnancy. *Arq Bras Oftalmol*. 2016;79:143–146.

11. Kara N, Sayin N, Pirhan d, et al. Evaluation of subfoveal choroidal thickness in pregnant women using enhanced depth imaging optical coherence tomography. *Curr Eye Res*. 2014;39:642–647.

12. Dadaci Z, Alptekin H, Oncel Acir N, Borazan M. Changes in choroidal thickness during pregnancy detected by enhanced depth imaging optical coherence tomography. *Br J Ophthalmol*. 2015;99:1255–1259.

13. Kim JW, Park MH, Kim YJ, Kim YT. Comparison of subfoveal choroidal thickness in healthy pregnancy and preeclampsia. *Eye(Lond)*. 2015;30:349–354.

14 Velaga SB, Nittala MG, Vupparaboina KK, et al. Choroidal vascularity index and choroidal thickness in eyes with reticular pseudodrusen. *Retina*. 2020;40:612–617.

15 Agrawal R, Chhablani J, Tan KA, Shah S, Sarvaiya C, Banker A. Choroidal vascularity index in central serous chorioretinopathy. *Retina*. 2016;36:1646–1651.

16 Agrawal R, Gupta P, Tan KA, Cheung CM, Wong TY, Cheng CY. Choroidal vascularity index as a measure of vascular status of the choroid: Measurements in healthy eyes from a population-based study. *Sci Rep*. 2016;6:21090.

17. Wei X, Kumar S, Ding J, Khandelwal N, Agarwal M, Agrawal R. Choroidal structural changes in smokers measured using choroidal vascularity index. *Invest Ophthalmol Vis Sci*. 2019;60:1316–1320.

18. Borrelli E, Uji A, Sarraf D, Sadda SR. Alterations in the choriocapillaris in intermediate age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2017;58:4792–4798.

19. Su L, Ji YS, Tong N, et al. Quantitative assessment of the retinal microvasculature and choriocapillaris in myopic patients using swept-source optical coherence tomography angiography. *Graefes Arch Clin Exp Ophthalmol*. 2020;258:1173–1180.

20. Uji A, Balasubramanian S, Lei J, Baghdasaryan E, Al-Sheikh M, Sadda SR. Choriocapillaris imaging using multiple en face optical coherence tomography angiography image averaging. *JAMA Ophthalmol*. 2017;135:1197–1204.

21. Goktas S, Basaran A, Sakarya Y, et al. Measurement of choroid thickness in pregnant women using enhanced depth imaging optical coherence tomography. *Arq Bras Oftalmol*. 2014;77:148–151.

22. Ulusoy DM, Duru N, Ataş M, Altınkaynak H, Duru Z, Açmaz G. Measurement of choroidal thickness and macular thickness during and after pregnancy. *Int J Ophthalmol*. 2015;8:321–325.

23. Pongsachareonnont P, Somkijrungroj T, Assavapongpaiboon B, Chitamara T, Chuntarapas M, Suwajanakorn D. Foveal and parafoveal choroidal thickness pattern measuring by swept source optical coherence tomography. *Eye (Lond)*. 2019;33:1443–1451.

24. Abbey AM, Kuriyan AE, Modi YS, et al. Optical coherence tomography measurements of choroidal thickness in healthy eyes: correlation with age

and axial length. *Ophthalmic Surg Lasers Imaging Retina*. 2015;46:18–24.

25. Wei X, Ting DSW, Ng WY, Khandelwal N, Agrawal R, Cheung CMG. Choroidal vascularity index : a novel optical coherence tomography based parameter in patients with exudative age-related macular degeneration. *Retina*. 2017;37:1120–1125.

26. Tan R, Agrawal R, Taduru S, Gupta A, Vupparaboina K, Chhablani J.Choroidal vascularity index in retinitis pigmentosa: an OCT study. *Ophthalmic Surg Lasers Imaging Retina*. 2018;49:191–197.

27. Ciloglu E, Okcu NT, NÇ Dogan. Optical coherence tomography angiography findings in preeclampsia. *Eye (Lond)*. 2019;33:1946–1951.

28. Chanwimol K, Balasubramanian S, Nassisi M, et al. Retinal vascular changes during pregnancy detected with optical coherence tomography angiography. *Invest Ophthalmol Vis Sci*. 2019;60:2726–2732.

29. Saito M, Ishibazawa A, Kinouchi R, Yoshida A. Reperfusion of the choriocapillaris observed using optical coherence tomography angiography in hypertensive choroidopathy. *Int Ophthalmol*. 2018;38:2205–2210.

30. Jirarattanasopa P, Ooto S, Tsujikawa A, et al. Assessment of macular choroidal thickness by optical coherence tomography and angiographic changes in central serous chorioretinopathy. *Ophthalmology*. 2012;119:1666–1678.