

Does pregnancy influence eye parameters? Assessment of choroidal thickness using EDI-OCT before and after labour depending on the way of delivery method

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ABSTRACT

Objectives: The aim of this study is to assess the choroidal thickness (CT) with use of EDI-OCT in patients before and after delivery depending on the mode of delivery.

Material and methods: The study involved 146 eyes of 73 patients aged 20–34 years, after natural labour (66 eyes) and C-section (80 eyes). Main inclusion criteria: Informed consent to participate in the study, age 18–35 years, single pregnancy, spherical refraction error –4.00 to +4.00 D, no eye pathologies, no surgery and ophthalmic procedures-including refractive surgery, childbirth after 36 weeks of pregnancy, BCVA = 1.0. Patients were examined twice: in 36 WG and on 6th week after the birth. All examinations were carried out between 8:00 am and 10:00 am in order to avoid daily cycle fluctuations. CT measurements were made manually by two independent researchers at: subfoveal and 500 µm, 1000 µm, 1500 µm, 3000 µm temporally and nasally. The student's t-test was made.

Results: In C-section group CT differences before and after delivery were statistically significant in 7/9 of the analysed areas. Mean subfoveal choroidal thickness was 370.86 µm vs 388.71 µm in 36 WG and in 6th week postpartum respectively ($p = 0.0003$). In women after natural labour, differences were statistically significant in 3/9 of the analysed areas. Mean subfoveal choroidal thickness was 303.27 µm vs 308.34 µm in 36 WG and in 6th week postpartum respectively ($p = 0.4800$).

Conclusions: The thickness of the choroid was lower in women in 36 WG in comparison to 6th week after birth. Changes in the thickness of the choroid are particularly noticeable in women after caesarean section.

Key words: pregnancy; caesarean section; natural childbirth; choroid; optical coherence tomography

Ginekologia Polska 2020; 91, 11: 668–673

INTRODUCTION

Pregnancy, being a special physiological condition of a woman's organism, is characterized by a variety of changes in many systems and organs. In recent years there has been a growing trend in research to investigate the influence of pregnancy and labour on the visual system [1].

The choroid is one of the most vascularized tissues in our body. Despite its small size, it is the structure with the highest blood flow in relation to volume. Until recently, there were no diagnostic methods available to create clear image of the choroid, therefore its physiology has not yet been fully understood. Examination of the choroid became available after Spaide's et al. [2] introduction of EDI-OCT modification, which, thanks to its high resolution and great-

er depth of scanning, allowed to visualize the structure of the choroid. This discovery led to an increased interest in the choroid physiology and intensified clinical trials on the influence of numerous factors and pathological conditions on the morphology of *choriocapillaris*. Among the factors that correspond to the thickness of choroid (CT, *choroidal thickness*) the most important are: vascular diseases such as diabetic retinopathy, hypertension, AMD and also AL, CCT, IOP, age and refractive error [3–5] It has been shown that CT changes during the 24-hour cycle [6, 7]. Ulaş has also shown that CT fluctuates between phases of the menstrual cycle [8], which may indicate a hormonal background for described changes. This interpretation is supported by studies of Wickham et al. [9], who showed the presence of female

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sex hormone receptors mRNA in choroid cells. For a long time, it was believed that unlike retina and anterior vascular membrane, choroid has no autoregulatory mechanism and its physiology is controlled mainly by autonomic nervous system mediators and hormonal stimulation. Recent reports indicate that small vessels of the choroid can have some degree of its own blood flow regulation, but the mechanism of this phenomenon has not yet been fully explained [10].

Results of recent studies on the influence of pregnancy and childbirth on the anterior segment of the eye showed changes, such as the increase in central corneal thickness, temporary change in spherical refraction, increase of depth of anterior chamber [11, 12], and resulting indirect drop in intraocular pressure [13–16]. Mentioned changes are interpreted as hormonally related, which is supported by in vitro studies. The presence of estrogen and progesterone receptors mRNA in the stroma of cornea has been shown. Other changes, such as the change in endothelial cell density [17], the appearance of transient astigmatism [11], or changes in corneal biomechanical parameters [14, 15, 18, 19] are controversial and require further research. In recent years, several studies have been published, assessing the impact of pregnancy and childbirth on the thickness of the choroid. However, the results obtained by the researchers are divergent and the physiological background of these changes is still unclear.

This study aims to answer the following research questions: Is the thickness of the choroid different in patients in the third trimester of pregnancy compared to post-delivery period? Does the birth method affect the thickness of the choroid?

MATERIAL AND METHODS

This prospective research was carried out in accordance with the Helsinki Declaration. Patients who agreed to participate in the study gave their written, informed consent after explanation of the nature and possible consequences of the study. The research was conducted in the period from October 2016 to September 2019. The study involved 146 eyes of 73 patients aged 20–34 years. The study involved both pregnant women giving birth vaginally (66 eyes of 33 patients) and women who gave birth by caesarean section (80 eyes of 40 patients). The preliminary qualification procedure was carried out, as part of which the following tests were performed:

- interviews: ophthalmological and obstetrical,
- BCVA to far and near vision using standardized Snellen tables,
- assessment of the anterior and posterior segment of the eye in biomicroscopy,
- auto kerato-refractometer.

Patients who met the criteria for inclusion were recruited to the research group — Table 1.

Patients qualified to participate in the project were examined twice: in 36 WG and 6 weeks after the delivery. The tests were carried out on the SPECTRALIS[®]OCT (Heidelberg Engineering) device. Optical coherent tomography of the choroid was performed. The measurement of the choroidal thickness was performed according to the protocol presented below. Anatomical limitations of the choroid were determined as:

- upper limit: the boundary between the end of the retinal pigment epithelium and Bruch's membrane (the lower edge of the hyperreflex line),
- lower limit: border between sclera and choroid

Measurements were made manually each time by two independent researchers. Protocol included manual measurements at 9 spots: subfoveal, 500, 1000, 1500, 3000 μ m temporally and nasally from the fovea, respectively. The measurement diagram is illustrated in Figure 1.

The researchers were not informed about whether the result presents a measurement from the third trimester of pregnancy or from the period after childbirth. All examina-

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Informed consent to participate in the study	No informed consent to participate in the study
Age 18–35 years old	18 years > Age > 35 years old
Physiological delivery or cesarean section	Complicated pregnancy
Single pregnancy	Multiple pregnancy
Refraction error –4.00 to +4.00 D sph.	Operative vaginal delivery- OVD: vacuum and forceps delivery
Good cooperation during research	Pregestational diabetes melitus And gestational diabetes melitus
No eye diseases	Hypertension in pregnancy
No surgery and/or ophthalmic procedures in history	Preeclapsja
Childbirth after 36 weeks of gestation	<i>Intrauterine growth restriction — IUGR</i>
Distance BCVA: LogMAR = 0.0, (V= 20/20)	Defective spherical refraction outside of the scope of inclusion criteria
Near BCVA: Sn = 0.5/30 cm	Lack of cooperation from the patient
	Active disease of the anterior or posterior segment of the eye
	Condition after ophthalmic operations or surgeries, refractive procedure performed
	Premature delivery < 36 weeks gestation
	Distance BCVA: LogMAR > 0.0, (V < 20/20)
	Near BCVA: > 0.5 /30 cm

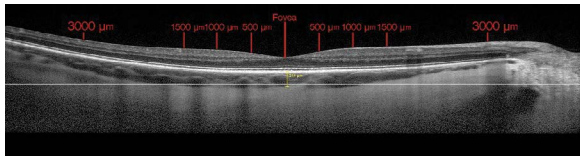


Figure 1. Measurements method

tions were carried out in the morning between 8:00 am and 10:00 am in order to avoid fluctuations related to the daily cycle.

For the analysis of the results, the values of parameters being the arithmetic mean of the measurements obtained by both researchers were used. The results were analysed statistically using StatSoft Statistica 13.1. All the results were presented as an average ± standard deviation. Before starting the analysis, the conditions for parametric tests were checked. The normality of decomposition was checked by the Shapiro-Wilk test and the homogeneity of variance by the Leaven test. Because the above assumptions were met, the analysis of significance of differences was carried out with the student’s t-test for dependent samples. The $p < 0.05$ was assumed to be statistically significant.

RESULTS

Table 2 presents detailed results of CT analysis in nine areas: subfoveal, 500, 1000, 1500, 3000 μm temporal and nasal from the fovea. The results are presented as mean and

standard deviation (μm). The table presents a comparison of CT between groups of women after natural labour and C-section with the level of significance p of the Student’s t-test.

Regardless of the delivery method and the analysed area of the choroid, the mean and standard deviation of choroid thickness were lower in women in 36 WG in comparison to 6th week after birth. However, these differences in CT before and after delivery were not statistically significant in all areas. In addition, a significant difference was observed depending on the delivery method of pregnancy. On the basis of t-Student’s analysis it was shown that in Caesarean section group CT changes before and after delivery are statistically significant ($p < 0.05$) in 7/9 of the analysed areas (subfoveal, Nasal: 500, 1000, 1500, 3000 μm, Temporal: 500, 1000 μm). In 2/9 areas (Temporal: 1500, 3000 μm), despite the observed trend, we did not observe significant differences ($p > 0.05$). Patients giving natural birth showed a similar trend as those giving birth with c-section, but the differences were not statistically significant in all regions of the choroid. In the group of women after natural labour, differences were statistically significant in 3/9 of the analysed areas (Nasal: 500, 1000, 1500 μm) and in 6/9 (Subfoveal, Nasal 3000 μm, Temporal: 500, 1000, 1500, 3000 μm) $p > 0.05$ was obtained. When measured at 3000 μm nasally, the choroid was slightly thicker before childbirth than after delivery, but the mean difference was only 1.02 μm and the difference was statistically insignificant ($p = 0.77$), so the difference is

Table 2. Results														
Location (μm from fovea)	CS — group before delivery		CS — group after delivery		Mean difference (μm)	SD (μm)	p-value (t-student)	NL — group before delivery		NL — group after delivery		Mean difference (μm)	SD (μm)	p-value (t-student)
	Mean (μm)	SD (μm)	Mean (μm)	SD (μm)				Mean (μm)	SD (μm)	Mean (μm)	SD (μm)			
SFCT	370.86	100.92	388.71	96.01	-17.86	40.95	0.0003	303.27	88.09	308.34	112.62	-5.07	47.51	0.4800
Nasal 500 μm	348.36	96.85	367.48	97.93	-19.12	32.73	0.0000	276.66	80.34	295.52	105.42	-18.86	47.62	0.0119
Nasal 1000 μm	325.25	92.73	340.6	95.27	-15.35	31.36	0.0001	256.52	78.69	275.2	100.67	-18.68	53.06	0.0243
Nasal 1500 μm	281.21	85.36	300.14	93.08	-18.94	92.07	0.0000	224.86	74.3	241.5	91.18	-16.64	35.14	0.0031
Nasal 3000 μm	156.75	56.92	171.68	79.11	-14.92	56.34	0.0228	130.61	53.09	129.59	49.14	1.02	22.96	0.7690
Temporal 500 μm	362.78	100.44	378.9	100.02	-16.12	53.87	0.0105	291.23	83.29	302.93	108.38	-11.7	47.08	0.1064
Temporal 1000 μm	352.58	96.54	363.97	99.448	-11.39	42.5	0.0213	293.32	79.95	299.07	105.83	-5.75	41.29	0.3607
Temporal 1500 μm	340.09	96.71	344.87	101.55	-4.78	39.92	0.3003	297.68	81.67	300.59	96.08	-2.91	41.26	0.6424
Temporal 3000 μm	294.04	84.61	298.73	92.32	-4.7	53.83	0.4492	268.73	51.96	277.75	75.97	-9.02	43.48	0.1758

CS: group (cesarean section group); NL: group (natural labour group)

within the limits of measurement error (SD for this measurement = 22.96 μm).

The results allow us to conclude that the decrease in the thickness of the choroid after delivery compared to the third trimester of pregnancy is significantly more noticeable in women after C-section than in women after vaginal delivery.

DISCUSSION

The lack of an unambiguous mechanism determining the character of changes in the thickness of choroid during pregnancy and after labour makes the subject controversial and worth taking an effort to conduct our own research project to clarify conflicting data [20].

Our study is the largest prospective study available in the literature (143 eyes), comparing the thickness of the choroid before and after childbirth. Our results are in opposition to the results of some researchers, but the methods of group selection and research schemes published in the literature are not identical. Choroid in pregnant patients was examined by many authors [1, 4, 11, 20, 27–33]. However, most of them [1, 11, 27–32] were clinical-control cohort examinations in which the thickness of choroid of pregnant women was compared to other, non-pregnant women. Such a study method does not allow obtaining objective results due to individual variation in the thickness of the choroid.

Dadaci et al. [28] examined 54 eyes of 27 patients in the first and third trimester of pregnancy. They showed that the choroid in the first trimester of pregnancy is thicker than in the third trimester. The authors did not perform postpartum tests, but instead used a control group of 50 eyes of 25 non-pregnant women. In this way, they found that the thickness of the choroid in the third trimester was higher than in non-pregnant patients (control group). Results [28] show the trend of CT changes during pregnancy, highlighting the differences between 1st and 3rd trimester, which is a great value of the work of these authors, but in our opinion those results do not allow to determine the direction of CT changes until the end of postpartum confinement, which was done in our work. In order to precisely trace changes in the thickness of the choroid during pregnancy, it is necessary to examine the same group of patients before and after childbirth as we have done in our study. Only such an examination scheme will allow to obtain objective results.

Goktas et al. [30] conducted a study in which they compared the thickness of the choroid in four groups of 30 eyes each, respectively in: 1st, 2nd and 3rd trimester of pregnancy and control group. They found that the thickness of the choroid was highest in the 2nd trimester with no increase of this parameter in the 1st and 3rd trimester of pregnancy compared to the control group. CT is a parameter of high individual volatility and in our opinion more reliable results would bring prospective studies.

Kara et al. [27] conducted a large study of 100 pregnant women, which they compared with the control group — non pregnant women. CT was measured only in subfoveal region, and the study group consisted of pregnant women with no distinction between trimesters. Considering the results of other researchers such as Goktas et al. [30] there is a clear difference in CT measured at different stages of pregnancy. The paper provides some information about mean CT values in particular trimesters of pregnancy, but it does not allow to determine the direction and dynamics of changes of this parameter.

Takahashi et al. [4, 20] and Ulusoy et al. [33] were the only ones who have done prospective study and examine the same group of women during pregnancy and after childbirth, so their results deserve special attention in this discussion.

Takahashi et al. [20] recruited patients in the 1st trimester of pregnancy and conducted long-term observation based on four measurements: in the 1st, 3rd trimester, shortly after childbirth and one month after childbirth. By examining 62 eyes they showed that the CT was highest in the 1st trimester, decreased in the 3rd trimester and remained at a similar level to the first month after birth. This is a remarkably interesting study due to the fact that the authors have traced the changes in CT from the initial period of pregnancy to the first month after birth. It should be noted, that in comparison to our work, in which we examined 146 eyes in total, Takahashi et al. [20] have examined a relatively small group. In contrast to our study, they did not show any significant differences between CT in the 3rd trimester and the first month after childbirth ($p > 0.05$). While our team showed that the choroid is thinner in the third trimester of pregnancy compared to the period after delivery ($p < 0.05$). Takahashi et al. [20] performed the last CT measurement 4 weeks after birth, and our team-6 weeks. This may be of clinical importance as the regression of postpartum physiological changes usually occurs 6–7 weeks after birth. Takahashi et al. [20] provide valuable information on the direction of CT changes from the 1st trimester of pregnancy to the 4th week after birth, but do not determine the nature of the changes at a later stage. Our research shows that the CT may increase in relation to the values in the 3rd trimester after the end of the postpartum period, as a result of a natural regression of postpartum changes in the woman's body, leading to the return of the pre-pregnancy choroid morphology.

The study of Ulusoy et al. [33] is the second of three prospective studies so far available in the literature, in which the same patients were examined before and after labour. The same study scheme was used in our work and by Takahashi et al. [20] Like us, he also examined women in 36 WG, but carried out a follow-up 3 months after the birth. SFCT was higher in the third trimester of pregnancy than three months

after the birth ($p < 0.05$), which does not agree with the results of our studies, which show that SFCT is lower before labour in comparison to period after delivery. It should be noted, however, that statistically significant differences were obtained in women giving birth by C-section ($p < 0.05$). In case of vaginal delivery, despite the preserved tendency, the differences were not statistically significant ($p > 0.05$). Ulusoy et al. [33] did not specify in their methodology the type of birth, which, according to our research, is important for measuring CT. In the remaining regions results [33] were the same as ours — the choroid was thinner in 36 WG than after childbirth, but differences were not statistically significant ($p > 0.05$). If we do not consider the method of delivery, our research shows that the choroid is thinner in 36 WG than on 6th week after birth. However, after two separate analyses, depending on the method of delivery, these differences are most clearly seen and statistically significant, particularly in the group of women after C-sections. Perhaps the timing of the follow-up by Ulusoy et al. [33], which was carried out twice as late (12 weeks) as in the case of our follow-up (6 weeks), affects the CT value after birth.

We are the only team in the world to measure women's choroid before and after childbirth, differentiating the results according to the method of delivery. We decided that the prospective study of the same patients have greater scientific value, due to the fluctuation of individual thickness of the choroid. It is known that as soon as the 1st trimester of pregnancy, the peripheral resistance of vessels decreases and the blood flow in the choroid increases during the 1st–2nd trimester of pregnancy [34]. As pregnancy progresses, the volume of circulating blood increases steadily, increasing by 40% in the 3rd trimester in comparison to pre-pregnancy levels. As can be seen from the work of Thornburg et al. [35], blood especially at the end of pregnancy is redistributed to important organs, such as the uterus, breast glands and kidneys. Moreover, as it results from the work of Dahle et al. [36], in the third trimester of pregnancy, mainly between 37 and 39WG, the number of adrenergic alpha-1 receptors in a woman's body increases, which is supposed to prepare for the initiation of childbirth. As reported by Dadaci et al. [28] it is the increase in the activity of these receptors that may affect the redistribution of blood from the vascular system to other organs and the constriction of choriocapillaris, which may explain reduction of thickness of the choroid demonstrated in our study with use of OCT in the 3rd trimester of pregnancy. Current knowledge does not allow us to explain why in the case of a caesarean section, there is a more pronounced increase in the thickness of the choroid after birth than in the case of natural childbirth. This is the most interesting conclusion from our work — that C-section may influence the visual organ. It is possible that future research will clarify the exact mechanism of this phenomenon.

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