



EVALUATION OF RETINAL THICKNESS IN PREGNANCY USING OPTICAL COHERENCE TOMOGRAPHY

Physiology

Dr. Deepa Sivaraj*	Assistant Professor, Department of Physiology, Amrita School of Medicine, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi- 682041, India.*Corresponding Author
Dr. Saraswathy L	Professor and HOD, Department of Physiology, Amrita School of Medicine, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi-682041, India.
Dr. Gopal S Pillai	Professor and HOD, Department of Ophthalmology, Amrita School of Medicine, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi- 682041, India.
Dr. Sarala Sreedhar	Professor, Department of Obstetrics and Gynaecology, Amrita School of Medicine, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi- 682041, India.

ABSTRACT

BACKGROUND: During pregnancy, the maternal eyes are exposed to various hormonal and haemodynamic alterations. The information regarding retinal thickness in healthy pregnant women in Indian population is limited. **AIM:** To measure retinal thickness in healthy pregnant women in the third trimester using Optical Coherence Tomography (OCT) and compare that with age matched healthy non-pregnant women. **METHODS:** 20 healthy pregnant women (40 eyes) in the third trimester and 20 age matched healthy non pregnant women (40 eyes) were recruited for this study. Macular and Retinal nerve fiber layer (RNFL) thickness were measured using OCT in both healthy pregnant and non pregnant women. **RESULT:** The mean macular thickness in pregnant women was $181.71 \pm 12.33 \mu\text{m}$ at foveal, $245.5 \pm 12.28 \mu\text{m}$ at superior quadrant, $220.21 \pm 14.41 \mu\text{m}$ at temporal quadrant, $234.46 \pm 14.87 \mu\text{m}$ at inferior quadrant and $263.96 \pm 16.4 \mu\text{m}$ at nasal quadrant. Those for non-pregnant women was foveal $177.58 \pm 10.96 \mu\text{m}$, superior quadrant $233.21 \pm 12.72 \mu\text{m}$, temporal quadrant $211.25 \pm 13.60 \mu\text{m}$, inferior quadrant $223.21 \pm 12.72 \mu\text{m}$, and nasal quadrant $252.13 \pm 13.01 \mu\text{m}$. $P < 0.05$ for superior, inferior and nasal quadrants. Mean peripapillary RNFL thickness was $113.15 \pm 8.81 \mu\text{m}$ in pregnant women and $109.29 \pm 7.14 \mu\text{m}$ in non-pregnant women respectively ($p > 0.05$). **CONCLUSION:** This study provides a normative database for the retinal thickness in healthy Indian pregnant women by optical coherence tomography.

KEYWORDS

Pregnancy, OCT, Macular Thickness, Retinal Nerve Fiber Layer Thickness.

INTRODUCTION

Pregnancy is a period of immense physiological changes. Changes in metabolism, hormone profile and blood circulation can affect normal functioning of the maternal eyes. Ocular changes may be associated with development of new conditions or the exacerbation of preexisting conditions^{1, 2}. Knowledge of these ocular changes will help us to differentiate the physiological changes from ocular manifestation of systemic diseases and diseases pertaining to the eye in a pregnant woman.

Though there are studies on retinal changes during pregnancy, all of them were done in pathological conditions like Diabetic Retinopathy (DR), Central Serous Chorioretinopathy (CSCR) and Pregnancy induced hypertension (PIH). There is limited data on retinal changes available in normal pregnancy of Indian population.

Moloney et al found out that pregnancy increased the rate of progression in DR³. Poor glycemic control before pregnancy is associated with worsening of retinopathy and good glycemic control should occur before conception. Robert B Dinn et al concluded that all diabetic women should see an ophthalmologist before or shortly after becoming pregnant⁴.

Pregnancy is considered as a risk factor for CSCR development in women. Two studies reported infrequent central serous chorioretinopathy in the third trimester in healthy pregnant women^{5, 6}. A recent study found that pregnant women were 7.1 times more likely to develop CSCR than an age matched group without pregnancy⁷.

Pregnancy induced hypertension (PIH) includes gestational hypertension, preeclampsia and eclampsia occurs after 20th week of pregnancy⁸. The study by Pankaj Shah et al noticed that retinal changes were seen in 12% of patients with PIH⁹.

In the above said conditions, the retinal thickness is found to be increased. The changes in normal pregnancy have likelihood to graduate into abnormal toxic findings. This suggests that there is no clear cut dividing line between true toxemia and normal pregnancy. The variations of retinal changes may be used to predict the

possibilities of disease processes and to further increase our understanding about retina in normal and abnormal pregnancy.

The increase of fluid in the body, especially in the last trimester, may cause an increase of retinal thickness¹⁰.

The introduction of Optical Coherence Tomography (OCT) has enabled clinicians to reliably detect and measure small changes in macular thickness and to quantitatively evaluate the efficacy of different therapeutic modalities.

Currently, we are using values of normal population for comparing macular thickness in pathological states of pregnancy. No normative data regarding macular thickness in pregnancy is available in Indian literature. It will be of immense help in obtaining valuable background data which can be used as control for further follow up and early detection of retinal abnormalities in pregnancy. As OCT is more widely used, normative data using the same technique is required in interpreting physiological/pathological features of the retina.

OBJECTIVE:

To measure retinal thickness in healthy pregnant women in the third trimester using Optical Coherence Tomography (OCT) and compare that with age matched healthy non-pregnant women.

MATERIALS AND METHODS

This cross sectional comparative study was conducted in the departments of Physiology, Ophthalmology and OBG at Amrita Institute of Medical Sciences (AIMS), Kochi for a period of 3 months. Approval was obtained from Institutional Ethics Committee. Written informed consent was obtained from all the participants.

Participants were recruited into two groups. The study group consisted of 20 healthy pregnant women (40 eyes) in their last trimester who attended for antenatal check up in the OBG department at AIMS, while the control group consisted of 20 age matched healthy non-pregnant women (40 eyes) who were staffs working at various departments of AIMS.

Exclusion criteria for this study included prior history of any significant ocular disease, history of systemic disease such as hypertension or diabetes mellitus and the development of complications such as gestational diabetes mellitus, and pregnancy-induced hypertension (PIH).

Visual acuity, intraocular pressure, and visual field examination with automated perimeter were performed in both groups. OCT imaging of both eyes were done after mydriasis with tropicamide 0.5%.

Optical Coherence Tomography (OCT)

OCT is a non-invasive, non contact, transpupillary imaging technology which can image retinal structures in vivo with a resolution of 10 to 17 microns. Cross-sectional images of the retina are produced using the optical backscattering of light. The anatomic layers within the retina can be differentiated and retinal thickness can be measured^{11, 12}.

Traditional methods for evaluating macular edema such as slit lamp bio microscopy, stereoscopic photography and fluorescein angiography are relatively insensitive to small changes in retinal thickness.

Central foveal thickness at 1 mm, parafoveal thickness at 3 mm diameter, and RNFL (peripapillary area) thickness were the retinal parameters measured by OCT in this study. The 6 mm macular map was used to evaluate foveal and parafoveal thickness. Parafoveal thickness was recorded for upper, temporal, inferior, and nasal quadrants.

Statistical analysis was carried out using IBM SPSS Statistics 20 windows software. The study evaluated data with descriptive statistical methods (mean, standard deviation) between the two groups were compared using Student's *t*-test. A *p* value of less than 0.05 was considered statistically significant.

RESULTS

In the present study, 40 eyes of 20 healthy pregnant women were studied and compared with the same number of control group which included healthy non-pregnant women.

Mean age for the study group was 27.58 ± 4.75 and for the control group was 28.36 ± 5.40 .

Mean gestational age of pregnant women was 33 weeks.

Mean foveal and parafoveal thicknesses (four quadrants) in the study group were: foveal $181.71 \pm 12.33 \mu\text{m}$, superior quadrant $245.5 \pm 12.28 \mu\text{m}$, temporal quadrant $220.21 \pm 14.41 \mu\text{m}$, inferior quadrant $234.46 \pm 10.58 \mu\text{m}$, and nasal quadrant $263.96 \pm 16.4 \mu\text{m}$.

Mean foveal and parafoveal thicknesses (four quadrants) in the control group were: foveal $177.58 \pm 10.96 \mu\text{m}$, superior quadrant $233.21 \pm 12.27 \mu\text{m}$, temporal quadrant $211.25 \pm 13.60 \mu\text{m}$, inferior quadrant $223.21 \pm 12.72 \mu\text{m}$, and nasal quadrant $252.13 \pm 13.01 \mu\text{m}$.

Mean peripapillary RNFL thickness was $113.15 \pm 8.81 \mu\text{m}$ in the study group and $109.29 \pm 7.14 \mu\text{m}$ in the control group respectively.

Table 1. Mean Foveal, Parafoveal (Superior, Inferior, Temporal and Nasal) and Retinal Nerve Fiber Layer (RNFL) thickness expressed in micro meters

Thickness	Mean (SD)		P value
	Study group (40 eyes)	Control group (40 eyes)	
Fovea	181.71(12.33)	177.58(10.96)	0.25
Superior	245.5(12.28)	233.21(12.27)	0.03
Inferior	234.46(14.87)	223.21(12.72)	0.04
Temporal	220.21(14.41)	211.25(13.60)	0.24
Nasal	263.96(16.4)	252.13(13.01)	0.03
RNFL	113.15(8.81)	109.29(7.14)	0.29

DISCUSSION

During pregnancy, several physiological changes take place in the human body. Mostly, cardiovascular changes develop before, during, and after the delivery. There is a slight increase in both the total fluid volume of the body and the intracellular fluid volume¹³. Studies have reported that, increased cardiac flow and volume result in an increase in ocular blood flow during pregnancy^{14,15}.

Macular edema is a common cause of visual loss. Abnormal fluid accumulation within the retina and a concomitant increase in macular thickness, usually result from the breakdown of the blood-retinal barrier. This can be found in those with diabetic retinopathy, preeclampsia, CSCR, which are the common pathological conditions of the eye occurring in pregnancy.

Very few studies have investigated macular thickness during normal pregnancy. We conducted a cross sectional study in forty eyes of twenty pregnant women in their third trimester by using OCT and compared the results with that of same number of age matched healthy non pregnant women. In this study, we established the normative data of macular and RNFL thickness in normal pregnant Indian women. Macula was thickest in the nasal quadrant, followed by superior quadrant and progressively less in inferior and temporal quadrants. Means of all measurements in foveal and parafoveal thickness were higher in pregnant women than the control group. However, the statistically significant difference in thickness was only found in superior, nasal and inferior parafoveal areas.

Our data showed fairly similar outcome with Demir et al , who measured macular thickness in 40 pregnant women and 37 non pregnant women in the Turkish population¹⁰. They reported an increase of macular thickness in superior, inferior, and temporal quadrants.

Cankaya et al , have reported an increase in macular thickness during the second and third trimesters and they concluded that the increase of fluid in the body, in particular in the second and last trimester, may cause an increase of foveal thickness¹⁶.

A recent prospective study by Farahat et al, in 26 healthy pregnant women during first, second and third trimesters showed that the central macular thickness increased in the second trimester than in the first and increased in the third trimester than in the second¹⁷.

Our study reaffirms the fact that fluid volume in the body increases during pregnancy secondary to hormonal changes. The increase of macular thickness may be secondary to the increase and accumulation of intraretinal cellular fluid and is in tune with the findings of other studies.

Regarding RNFL thickness, our study result showed no significant difference in pregnant women ($p > 0.05$). Similar findings have been reported by Demir et al also.

In contrast Entezari et al documented that the mean RNFL thickness was significantly more during pregnancy in comparison with the postpartum period. They conducted the study in 32 pregnant women of Iranian population. They compared the data with the same women in the postpartum period¹⁹. Almost similar findings were documented by M Atas et al in a comparative study including 25 healthy pregnant women and 26 healthy non- pregnant women²⁰.

In clinical practice, the finding of RNFL thickness in normal pregnancy might be helpful in diagnosis of retinopathy in some chronic diseases including diabetes and hypertension. Decreased RNFL thickness in these chronic diseases might be misdiagnosed in pregnancy due to pregnancy induced increased thickness^{21,22}.

CONCLUSION

Our study provides a normative database for human macular and peripapillary RNFL thickness as measured by OCT in healthy Indian pregnant women, from a statistical stand point. It is a useful data for interpreting features of retina in pathological conditions of pregnancy. Further longitudinal studies throughout pregnancy and into the postpartum period with a larger number of patients are required to confirm the changes.

REFERENCES

1. Stalnikiewicz L, Floriot M, Guerri B, Anqioi K. Progression of diabetic retinopathy during pregnancy: a retrospective analysis of a series of 77 consecutive patients. *J FrOphtalmol*. 2010;33(7):481–486.
2. Vestgaard M, Ringholm L, Laugesen CS, Rasmussen KL, Damm P, Mathiesen ER. Pregnancy-induced sight-threatening diabetic retinopathy in women with type 1 diabetes. *Diabet Med*. 2010;27(4):431–435.
3. Moloney JB, Drury MI. The effect of pregnancy on the natural course of diabetic retinopathy. *American journal of ophthalmology*. 1982 Jun 1;93(6):745–56.
4. Dinn RB, Harris A, Marcus PS. Ocular changes in pregnancy. *Obstetrical & gynecological survey*. 2003 Feb 1;58(2):137–44.
5. Gass JD. Central serous chorioretinopathy and white subretinal exudation during

- pregnancy. *Arch Ophthalmol*. 1991;109(5):677-681.
6. Fastenberg DM, Ober RR. Central serous chorioretinopathy in pregnancy. *Arch Ophthalmol*. 1983;101(7):1055-1058.
7. Schultz KL, Birnbaum AD, Goldstein DA. Ocular disease in pregnancy. *Curr Opin Ophthalmol* 2005; 16:308-314.
8. Sheth BP, Mieler WF. Ocular complications of pregnancy. *Current opinion in ophthalmology*. 2001 Dec 1;12(6):455-63.
9. Shah AP, Lune AA, Magdum RM, Deshpande H, Shah AP, Bhavsar D. Retinal changes in pregnancy-induced hypertension. *Medical Journal of Dr. DY Patil University*. 2015 May 1;8(3):304.
10. Demir M, Oba E, Can E, Odabasi M, Tiryaki S, Ozdal E, Sensoz H. Foveal and parafoveal retinal thickness in healthy pregnant women in their last trimester. *Clin Ophthalmol*. 2011;5:1397-1400.
11. Konno S, Akiba J, Yoshida A. Retinal thickness measurements with optical coherence tomography and the scanning retinal thickness analyzer. *Retina* 2001; 21:57-61.
12. Wexler A, Sand T, Elsas TB. Macular thickness measurements in healthy Norwegian volunteers: an optical coherence tomography study. *BMC Ophthalmol* 2010; 13:10-13.
13. Larciprete G, Valensise H, Vasapollo B, Altomare F, Sorge R, Casalino B, De Lorenzo A, Arduini D. Body composition during normal pregnancy: reference ranges. *Acta Diabetol*. 2003;40(1):225-232.
14. Centofanti M, Miquiardi R, Bonini S, Manni G, Bucci MG, Pesavento CB, Amin CS, Harris A. Pulsatile ocular blood flow during pregnancy. *Eur J Ophthalmol*. 2002;12(4):276-280.
15. Chen HC, Newsom RS, Patel V, Cassar J, Mather H, Kohner EM. Retinal blood flow changes during pregnancy in women with diabetes. *Invest Ophthalmol Vis Sci*. 1994;35(8):3199-3208.
16. Cankaya C, Bozkurt M, Ulutas O. Total macular volume and foveal retinal thickness alterations in healthy pregnant women. *Semin Ophthalmol*. 2013;28(2):103-111.
17. Farahat HG, Elsayy MF, Darrag AA. Evaluation of macular changes during pregnancy by optical coherence tomography. *Menoufia Medical Journal*. 2019 Apr 1;32(2):672.
18. Ulusoy DM, Duru N, Atas M, Altunkaynak H, Duru Z, Açmaz G. Measurement of choroidal thickness and macular thickness during and after pregnancy. *International Journal of Ophthalmology*. 2015;8(2):321.
19. Entezari M, Arab M, Barmachi AA, Ghamary H, Ghavami B, Saracian S. Comparison of Retinal Nerve Fiber Layer Thickness in Pregnancy and Postpartum Period. *Journal of Clinical & Diagnostic Research*. 2018 Jan 1;12(1).
20. Atas M, Açmaz G, Aksoy H, Demircan S, Atas F, Gülhan A, Zararsız G. Evaluation of the macula, retinal nerve fiber layer and choroid in preeclampsia, healthy pregnant and healthy non-pregnant women using spectral-domain optical coherence tomography. *Hypertension in Pregnancy*. 2014 Aug 1;33(3):299-310.
21. Gangwani RA, Lee JW, Mo HY, Sum R, Kwong AS, Wang JH, Tsui WW, Chan JC, Lai JS. The correlation of retinal nerve fiber layer thickness with blood pressure in a Chinese hypertensive population. *Medicine*. 2015 Jun;94(23).
22. Park HY, Kim IT, Park CK. Early diabetic changes in the nerve fibre layer at the macula detected by spectral domain optical coherence tomography. *British Journal of Ophthalmology*. 2011 Sep 1;95(9):1223-8.