



A CROSS-SECTIONAL, OBSERVATIONAL AND ANALYTICAL STUDY TO DETERMINE TOTAL MACULAR VOLUME AND FOVEAL RETINAL THICKNESS IN PREGNANT WOMEN

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ABSTRACT **INTRODUCTION:** Owing to the hemodynamic changes due to hormones during pregnancy, multiple anatomical, physiological and biochemical changes occur in all systems. These changes are transient in nature but may cause permanent damage if not caught early. **PURPOSE:** To evaluate Total Macular Volume and Foveal Retinal Thickness in 3rd trimester Pregnancy between (Normal Pregnant, Pregnancy Induced Hypertensives, Gestational Diabetics) and to compare these values with healthy non-pregnant females of the same age matched group. **METHODOLOGY:** A total of 140 eyes of 70 patients were evaluated for Total macular volume and foveal retinal thickness changes using OCT (3D Macula scan) and the results were compared by ANOVA and Paired-T test (SPSS software, version-26.0). **RESULTS:** Notable difference was noted in Total macular volume and Foveal retinal thickness between pregnant and non-pregnant. Also, notable difference noted between 3rd trimester healthy pregnant, gestational diabetics and pregnancy induced hypertensives (p value <0.05). **CONCLUSION:** Pregnancy summated with Diabetes / Hypertension may lead to permanent damage. Hence awareness and screening of pregnant females' post-partum is necessary.

KEYWORDS : Pregnancy, Foveal Retinal Thickness, Total Macular Volume.

INTRODUCTION:

All organs undergo progressive anatomical, physiological and biochemical changes during pregnancy, these alterations could be pathological or physiological, could be linked to the emergence of a brand-new disease, or could change the course of an already-existing disease. [1,2]

The well-known hypervolemia linked to pregnancy typically exceeds the blood volume of women who are not pregnant by 40 to 45 percent. The cardiac volume, which rises by about 40–45% above the baseline level, is another crucial parameter. Water retention in the body may result from these significant haemodynamic changes brought on by hormonal changes.[3]

The following are possible physiological changes in the eyes: [4,5]

- Cornea: Reduced corneal sensitivity, increase in thickness.
- A temporary loss of accommodation.
- Reduced intraocular pressure (IOP) as a result of greater outflow
- Retina: Changes in retinal thickness, volume have been reported.

Pregnancy when associated with comorbidities could lead to further alterations at the cellular level.

Following comorbidities have been considered in the study:

1) Pregnancy associated with Gestational diabetes mellitus (GDM):

Pregnancy-induced glucose intolerance, or GDM, is a condition that may or may not go away after the pregnancy. The most common condition affecting pregnant women is gestational diabetes mellitus (GDM), which can occur in up to 15%–25% of pregnancies worldwide.[6,7,8]

2) Pregnancy Induced Hypertension (PIH):

One of the main causes of maternal and perinatal mortality, PIH is a difficult stigma in the field of obstetrics. There are three stages to the fundus changes.

- Spastic stage: Characterized by spasm of retinal arterioles.
- The stage of sclerosis: when already-existing organic sclerotic changes in the vessels are combined with pregnancy-induced hypertensive changes.
- The stage of retinopathy characterized by disc oedema, cotton wool spots, micro aneurysms, flame- and splinter-shaped haemorrhages, and hard exudates.

The purpose of the current study is to assess the retinal changes in pregnant women with GDM and PIH in their third trimester and to compare the results to those of healthy third-trimester pregnant women and non-pregnant women using the Optical Coherence Tomography.[9,10,11]

1) Foveal Retinal Thickness (FRT) – Defined as the central foveal thickness corresponding to 1mm diameter of the ETDRS chart.

2) Total Macular Volume (TMV)- Defined as the volume corresponding to the 6mm x 6mm cube of the 3D Macular scan of OCT.

In normal, healthy, non-pregnant females, the average TMV ranges from 6.486 0.560 mm³ i.e. (5.926 – 7.046) and the average FRT ranges from (147.10 ± 19.41) micrometre or (127.69-166.51). [12,13] The TMV and FRT were found to increase more in the second trimester compared to the first and more so in the third trimester compared to the second, as per a study. [8]

Similar findings were found in other studies on macular changes during pregnancy. After childbirth, the changes usually go away. [14,15]

MATERIALS AND METHODS:

PLACE OF STUDY: Department of Ophthalmology and Department of Obstetrics and Gynaecology, Bharati Hospital and Research Centre.

STUDY DESIGN: Prospective - Cross-sectional and Observational study

SAMPLE SIZE: Total 140 eyes of pregnant females: (healthy-48, GDM-46, PIH-46) and 50 eyes of age matched non pregnant.

INCLUSION CRITERIA:

- Age group: 20-40 years
- Pregnant 3rd trimester:
 - Healthy pregnant women.
 - Pregnant women with gestational diabetes.
 - Pregnant women with pregnancy induced hypertension.
- Age matched non-pregnant.

EXCLUSION CRITERIA:

1. Patients unwilling to participate
2. Pregnancies associated with complications except DM and PIH
3. Diagnosed GDM and PIH with established retinopathy
4. History of previous ocular conditions like macular lesions, infections, tumors etc
5. Cases with poor OCT image reliability.

STUDY DURATION: October 2020 – August 2022

VARIABLES OF THE STUDY: Pregnancy, TMV and FRT

ANTICIPATED RISK FACTORS (IF ANY): NIL

METHODOLGY OF STUDY

Pregnant females were recruited from the Gynaecology and Obstetrics department. The entire procedure (including non-invasive examination) was explained to the participants in the language best understood by them. Prior permission was taken from all the participants in the form of written informed consent.

All the subjects were subjected to a complete ophthalmic examination

- Best corrected visual acuity
- Slit lamp examination of Anterior segment
- Examination of Posterior segment with +90D lens and Indirect ophthalmoscopy
- IOP measurement using NCT (Non-Contact Tonometry)
- Amsler's grid for central macular field assessment
- Optical Coherence Tomography (TOPCON- Spectral domain) – using 3D Macula scan for measuring macular volume and foveal retinal thickness.

STATISTICAL ANALYSIS: Compared by ANOVA and Paired-T test (SPSS software, version-26.0).

RESULTS: A total of 140 eyes of pregnant women and 50 eyes of non-pregnant women were evaluated, the overall mean of age of the patients was 26.34 ± 3.61 years, FRT in micrometres was 181.22 ± 8.76, and TMV was 7.21 ± 0.08 mm³.

Table 1: Comparison of mean of age between groups

	N	Mean	SD
Non-pregnant	50	24.24	2.40
Healthy pregnant	48	26.83	3.82
GDM	46	27.61	3.72
PIH	46	26.87	3.40

Table 2: Association of FRT between groups

		GDM	Healthy	Non-pregnant	PIH
GDM	r		-0.405	0.052	0.470
	p		0.0052*	0.7304	0.0010*
Healthy	r	-0.405		0.103	-0.627
	p	0.0052*		0.4869	<0.0001*
Non-pregnant	r	0.052	0.103		0.057
	p	0.7304	0.4869		0.7090
PIH	r	0.470	-0.627	0.057	
	p	0.0010*	<0.0001*	0.7090	

Table 3: Association of TMV between groups

		GDM	Healthy	Non-pregnant	PIH
GDM	r		0.032	-0.163	0.225
	p		0.8330	0.2796	0.1324
Healthy	r	0.032		-0.310	-0.001
	p	0.8330		0.0321*	0.9953
Non-pregnant	r	-0.163	-0.310		-0.439
	p	0.2796	0.0321*		0.0023*
PIH	r	0.225	-0.001	-0.439	
	p	0.1324	0.9953	0.0023*	

OCT Report of a Pregnant Female:

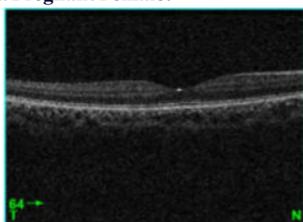


Figure: Bscan image (OCT)

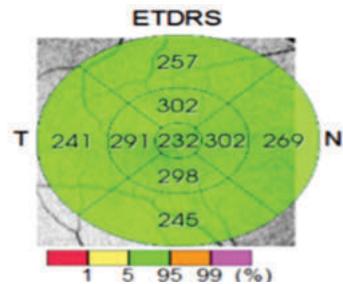


FIGURE: ETDRS Grid showing

Average Thickness (µm)	262.0
Center Thickness (µm)	179
Total Volume (mm ³)	7.42
ILM - OS/RPE Map	OS/RPE Surface

Figure: Showing TMV of the same female

DISCUSSION:

Evaluation of retinal parameters is essential for diagnosing, treatment and prognosis of various ocular manifestations during pregnancy. Microscopic assessment of these parameters is done by a non-invasive method- OCT.

FRT

As compared to non-pregnant group the FRT values were significantly increased in healthy pregnant, GDM and PIH groups, similarly FRT was also significantly higher in GDM and PIH group than healthy pregnant women. The difference was also significant between GDM and PIH.

- There was significant positive association regarding FRT values between GDM with PIH groups only.
- Negative association was reported between healthy pregnant vs GDM, healthy pregnant Vs PIH.

TMV

As compared to non-pregnant group the TMV values were significantly increased in healthy pregnant, GDM and PIH groups, similarly TMV was also significantly higher in GDM and PIH group than healthy pregnant women.

- There was a significant negative association reported between healthy pregnant vs PIH, healthy pregnant Vs non-pregnant women.

The study group by Can kaya C [4] et al. included 20 healthy nonpregnant women in the control group and 60 eyes from 60 healthy pregnant women in Groups 1 through 3 (first, second, and third trimesters). In groups 1, 2, 3, and 4, the mean age was 26.3 ± 3.1, 26.4 ± 4.2, 25.9 ± 2.9, and 25.8 ± 4.1 years, respectively. Regarding age, there was no discernible difference between the groups (p = 0.76).

According to Akpolat C [16] et al, the mean ages of the GDM, DM2, and control groups were 32.2 ± 6.68, 34.15 ± 6.59, and 33.1 ± 8.12 years, respectively. The three groups' ages were evenly distributed and ranged from 19 to 45.

The mean gestational age of the study group, which consisted of 89 subjects, was 35.09 ± 2.44 weeks, and the average age was 32.24 ± 3.75 years. The control group's average age was 34.04 ± 7.19 years old.

99 people were enrolled by Liu G. [17] et al., who divided them into three groups: normal controls (NC), pregnant controls (PC), and the GDM group, which included 31 women with GDM. The normal controls group consisted of 38 non-pregnant women. The three groups' average ages were 30.6 ± 4.9 years, ranging from 24 to 41 years for the NC group, 30.7 ± 4.9 years, ranging from 20 to 43 years for the PC group, and 30.6 ± 2.8 years, ranging from 25 to 41 years for the GDM group.

GDM

In the present study, there was a significant difference in FRT between

all groups. As compared to the non-pregnant group, the FRT values were significantly increased in the healthy pregnant and GDM groups; similarly, the FRT was also significantly higher in GDM than in healthy pregnant women. As compared to the non-pregnant group, the TMV values were significantly increased in the healthy pregnant and GDM groups; the TMV was also significantly higher in GDM than in healthy pregnant women.

Because patients are asymptomatic until macular oedema or proliferative diabetic retinopathy symptoms appear, screening for diabetic retinopathy during pregnancy is essential. Diabetic macular oedema, which can cause vision loss and is the most common cause of vision loss in diabetic retinopathy, can appear during pregnancy. There aren't many studies on how the maternal retinal microvasculature changes during pregnancy, especially with GDM. All over the world, it is more prevalent among women who are of childbearing age.

Average foveal thickness and volume were significantly higher in the first, second, and third trimesters compared to controls, according to Fahmy R et al. The mean FT for groups 2, 3, and 4 was 226.57 ± 23.3 m, 231.37 ± 19.21 m, and 240.3 ± 21.76 m, respectively, as opposed to the control mean of 214.2 ± 19.73 m. In groups 2, 3, and 4, the mean FV was, respectively, 0.259 ± 0.07 mm³, 0.241 ± 0.05 mm³, and 0.300 ± 0.11 mm³, as opposed to the control mean of 0.169 ± 0.015 mm³. When compared to the second trimester, the third trimester was connected to a significantly higher FV.

Liu G. [18] et al. found no other microvascular changes associated with diabetic retinopathy in GDM eyes, such as microaneurysm, hemorrhagic spot, or exudate changes on both OCT-A and fundus photographs. Instead, they found a significant decrease of vascular density and capillary dropout in the superficial vascular layer in both the PC and GDM groups.

PIH

We also found that the PIH group had a significantly higher FRT than the non-pregnant and healthy pregnant groups. Similar results were reported for TMV. As compared to the non-pregnant group, the TMV values were significantly increased in the healthy pregnant and PIH groups, with significantly higher values of TMV in the PIH group.

Wang Z [19] et al., found 148 abnormal eyes among the 196 eyes of the 98 patients with PIHS (Pregnancy induced hypertension syndrome). A serous detachment of the retinal neuroepithelium layer was present in 84 eyes (56.76 percent), including 50 in the central fovea of the macula and 34 in other areas of the eye (mainly around the optic disk). 26 eyes (17.56 percent) had additional changes like optic disc oedema and retinal haemorrhage, while 38 eyes (25.68 percent) had changes in the pigment epithelium layer and ellipsoid layer (previously known as the IS/OS layers). Only 2 of the 100 eyes of the 50 pregnant women in the control group displayed slight changes in the ellipsoid layer and pigment epithelium, with a significant difference in OCT manifestations between the two groups.

The three groups—healthy pregnancy, pre-eclampsia, and healthy non-pregnant women—did not differ significantly in mean age, spherical equivalent, or central subfield retinal thickness (CSRT), according to Kim JW [20] et al.

Additionally, we reported significantly higher values of FRT and TMV in pregnant women with GDM than PIH.

There was a significant positive association regarding FRT values between GDM and PIH groups only. A link was found between healthy pregnant women and GDM or healthy pregnant women and PIH. While there was no significant difference noted between other group combinations, there was a significant negative association reported between healthy pregnant vs. PIH women and healthy pregnant vs. non-pregnant women. While there was no significant difference noted between other group combinations.

There are numerous other studies that have documented FRT and TMV in various pregnancy trimesters. Cankaya C [4] et al., suggested for both TMV and FT, there was statistical significance among the 20 healthy women in the second trimester (group 2), the 20 healthy women in the third trimester (group 3), the 20 healthy nonpregnant women (group 4), and the group of healthy women in the first trimester

(group 1). For both TMV and FT, there was no statistically significant difference between groups 2-3 and 1-4. In both the study group and the control group, the Pearson correlation analyses found a significant positive correlation between FT and TMV.

The Early Treatment Diabetic Retinopathy Study (ETDRS) area's average choroidal thickness, according to Rothwell RT et al., was 271.56 ± 37.65 m in the control group and 295.15 ± 42.40 m in the pregnant group, with no statistically significant difference. For the pregnant women's group, the average total choroidal volume of the entire ETDRS area was 8.05 ± 1.12 mm³, whereas for the control group, it was 7.46 ± 1.03 mm³. In this series, the choroidal thickness and volume were higher in the pregnant women than in the control group in all subfields, with the only differences being those that were statistically significant being those in the CSF and volume, minimum foveal thickness, and IIM thickness and volume. The entire macular area had a thickness and volume difference of $+23.59$ m and $+0.59$ mm³, respectively. Within the same patient, there were no statistically significant differences in the choroidal thickness and volume between the right and left eyes based on the total and subfield analyses.

SUMMARY AND CONCLUSION: The present study evaluated Total Macular Volume (TMV) and Foveal Retinal Thickness (FRT) in pregnancy. A total of 140 eyes of pregnant women and 50 eyes of non-pregnant women were evaluated. The overall mean age of the patients was 26.34 ± 3.61 years, Mean FRT in micrometers was 181.22 ± 8.76 , and Mean TMV was 7.21 ± 0.08 mm³.

FRT: There was significant difference in FRT between all groups. As compared to non-pregnant group the FRT values were significantly increased in healthy pregnant, GDM and PIH groups, similarly FRT was also significantly higher in GDM and PIH group than healthy pregnant women. The difference was also significant between GDM and PIH groups.

There was significant positive association regarding FRT values between GDM with PIH groups only. The negative association was reported between healthy pregnant vs GDM, healthy pregnant Vs PIH. While there was no significant difference was noted between other group combinations.

TMV: There was significant difference in TMV between all groups. As compared to non-pregnant group the TMV values were significantly increased in healthy pregnant, GDM and PIH groups, similarly TMV was also significantly higher in GDM and PIH group than healthy pregnant women. The difference was also significant between GDM and PIH groups.

There was a significant negative association in TMV reported between healthy pregnant vs PIH, healthy pregnant Vs non-pregnant women. While there was no significant difference noted between other group combinations.

To conclude:

- Pregnancy alters retinal parameters more so in the last trimester which may or may not be permanent.
- These parameters acquire more significance when associated with comorbidities.

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