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Changes In Biomechanical Parameters Of Eye, Corneal Sensitivity, Central Corneal Thickness And Intraocular Pressure In Second And Third Trimister Of Pregnancy

Shreya Soni[1], Atul Mishra[2]
Department of Ophthalmology, Katihar medical college, Al Karim university, India
Department of Ophthalmology, Katihar medical college, Al Karim university, India

Abstract :
Background: *Pregnant women have a variety of physiological changes, including adjustments to their immunological, haematological, cardiovascular, and hormone systems. Previous studies have documented some physiological ocular changes such as in CCT, corneal curvature, IOP, corneal sensitivity, aqueous humour outflow, refractive changes, and allergies. Corneal sensitivity, IOP and CCT during pregnancy have been the subject of studies, however the information is localised and limited, and no meta-analysis has been recently published in Indian population, therefore this study was conducted.*
Materials and methods: *In a prospective longitudinal study, 60 pregnant women aged 18-35 years were examined for changes in CCT, corneal sensitivity and IOP during the second or third trimester of pregnancy followed by 6 weeks postpartum. Data were analyzed using SPSS version 23.0.*
Results: *CCT values varied directly and significantly by trimester ($p < 0.001$). Duration of pregnancy varied inversely and significantly with corneal sensitivity ($p <0.05$) and intraocular pressure ($p < 0.001$).*
Conclusion: *A decrease in intraocular pressure and corneal sensitivity was observed in late pregnancy with an increase in central corneal thickness, which was reversible at 6 weeks postpartum, suggesting a likely change in variables due to factors such as hormonal changes and body fluid accumulation during pregnancy.*
Key words **:** *Central corneal thickness, intraocular pressure, corneal sensitivity, pregnancy, hormonal changes*

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I. INTRODUCTION

Pregnancy is a physiological state of a woman's body, when she is carrying a foetus in her womb.[1] It is associated with various other changes in other systems and organs. Glaucoma is a group of diseases that can cause vision loss and blindness by damaging the optic nerve. One of the criteria for glaucoma diagnosis and treatment is intraocular pressure (IOP). The normal IOP range, as determined by the Goldman applanation tonometer (GAT), is between 10 and 21 mmhg. IOP value varies during the day and is influenced by water intake. The trabecular outflow channel, corneal curvature, central corneal thickness (CCT), and sclera stiffness are local factors that affect IOP.[2] Systemic factors that affect IOP include age, gender, race, heredity, cardiovascular conditions, movement or a change in posture, hormones, diet, and medicines. The corneal resistance will be affected by an excessively thick or thin CCT. The measured IOP will be greater than its true value if CCT is lesser than the average value (520µm), but if CCT is lower than the average value, the measured IOP will be greater than its true value.[3] As a result, the CCT is a crucial signal for the glaucoma diagnosis and treatment. Cornea has abundant sensory nerve supply. Corneal sensitivity (CS) can be another parameter for checking upon the health of cornea. Pregnant women have a variety of physiological changes, including adjustments to their immunological, haematological, cardiovascular, and hormone systems. Previous studies have documented some physiological ocular changes such as in CCT, corneal curvature, IOP, corneal sensitivity, aqueous humour outflow, refractive changes, and allergies. Corneal sensitivity, IOP and CCT during pregnancy have been the subject of studies, however the information is localised and limited, and no meta-analysis has been recently published in Indian population. To summarise the alterations in IOP and CCT throughout pregnancy, we conducted a systematic review and meta-analysis in this study.

II. MATERIAL AND METHODS

The study design is a hospital based prospective longitudinal study that includes patients visiting Obstetric Clinic of Katihar Medical College at Katihar, Bihar. The study period was 1 year. The study was mildly affected by the 3rd wave of COVID-19 due to which follow-ups and clinic visits had reduced; hence the sample size initially taken had to be altered. Pregnant women who agreed to participate in the study and had no known ocular diseases in their second and third trimesters of pregnancy were eligible for inclusion. Patients with systemic comorbidities such as diabetes and hypertension, those with ocular pathologies such as glaucoma and past ocular surgeries such as glaucoma surgeries and cornea refractive surgeries, those using any topical medications 3 months before recruitment, and those refused to give their consent were excluded from the study.[4]

Study Design: hospital based prospective longitudinal study

Study Location: This was a tertiary care teaching hospital based study done in Department of Ophthalmology, at Katihar Medical College at Katihar, Bihar.

Study Duration: Aug 2021 to July 2022

Sample size : 60

Sample size calculation: The sample size was estimated according to single proportion design. The target population from which we randomly selected our sample was considered 50,000. Sample size was calculated at 10% margin of error and 95% confidence interval which was 60.

Subjects & selection method: The study had the 60 healthy pregnant women who were selected at random. Women who agreed to participate in the study at the obstetrics and gynaecology department were sent to the ophthalmology outpatient department, where the patient's eyes were examined.

Criteria of inclusion :

1. Pregnant women who agreed to participate in the study
2. Singleton pregnancy
3. No known ocular disorder

Criteria of exclusion :

1. Pregnant women with systemic diseases like hypertention, diabetes mellitus, bronchial asthama, thyroid disorder or haematological, cardiovascular or neuronal disorder
2. History of refractive or any ocular surgeries
3. History of use of any topical drugs until 3 months before recruitment
4. Failed to follow up on the second visit post delivery

Procedure:

Corneal sensitivity(CS), intraocular pressure (IOP), and central corneal thickness (CCT) were added as biomechanical factors. As this was a prospective study, examinations were completed over the course of two visits. The first visit occurred in the second or third trimester of pregnancy, and the second one occurred in the sixth week after delivery. Due to patient dropouts and failure to return for a second visit, the final analysis group taken into account only included 60 pregnant females. All the tests were carried out without the use of mydriatics and cycloplegics with the clearance from ethical Committee.

Corneal sensitivity - tested by touching a cotton ball to the cornea to elicit a blink response. Results - The presence of a brisk blink response indicated normal corneal sensation. The test was repeated in 4 quadrants and other corneas were compared**.**

Intraocular pressure - recorded with a Goldmann applanation tonometer (GAT). It was recorded thrice and average was taken. The test was repeated with the other eye. IOP was measured over a specific time range (10:00am-2:00pm) to avoid circadian variation errors in IOP.

Central corneal thickness- Pachymetry (CCT evaluation) was done using the Ophthalmic A scan Biometer Matrix model: SP-1000 series. Subjects were appropriately positioned and given a target to see. The pachymeter was advanced toward the central cornea. It was held in this position for a few seconds until a beep was heard. The test was repeated three times. Average of the values was considered as final to avoid error.

III. DATA ANALYSIS

All data collected were entered into a Microsoft XP EXCEL spreadsheet and converted to SPSS version 23. For descriptive analytics: Means, standard deviations and percentages were calculated. For inferential statistics, parametric and nonparametric tests were performed to find significant differences between pregnant women both during and 6 weeks after delivery with 95% confidence, and p-values ≤ 0.05 were considered statistically significant. 95% confidence intervals were used to calculate the standard error of the mean.

IV. RESULTS

Participants ranged from 18 to 35 years of age. At the first visit, 42 pregnant women in their 3rd trimester and 18 pregnant women in their second trimester were observed and were followed up for their second visit at 6 weeks postpartum. The majority of participants were unaware that pregnancy affects their eyes. Those who knew (n = 9) obtained information primarily from ophthalmologists, obstetricians, and the Internet. The majority of pregnant women did not have eye problems before the index pregnancy. Among those with a history of eye problems, the most common symptoms identified as bothersome were itching and visual disturbance. Most participants had never worn eyeglasses before their index pregnancies. The majority of participants did not undergo an eye check as part of the prenatal screening of the index pregnancy. The majority of those who noticed eye changes were unable to associate it with pregnancy.

The cornea was the least sensitive in both eyes of most pregnant women in the third trimester (35; 72.9%) compared with the second trimester (11; 61.1%) and most at second visit 6 weeks postpartum (24; 24.4%). Pregnant Women in third trimester (39; 81.25%) were more likely to have higher CCT than in second trimester (11; 61.1%) compared with postpartum (27; 36.6%) observed . In the majority of pregnant women in third trimester (32; 66.7%), intraocular pressure in both eyes fell below normal, compared to (7; 38.9%) women in the second trimester who had decreased intraocular pressure compared with postpartum values (17;28.3%). Gestational age influenced the participant's CS, CCT, and IOP scores. Gestational duration varied inversely with her CS and IOP, with the lowest value recorded in the third trimester, whereas CCT varied directly, with the highest value recorded in the third trimester. Simple linear regression with gestational age as the independent variable showed that CS ($P < 0.05$) and her IOP ($P < 0.001$) were significantly decreased, but CCT was significantly increased ($P < 0.001$) showed an inverse relationship was found between CCT and IOPi.e. Increased CCT was associated with decreased IOP. This association was statistically significant in the third trimester ($P<0.05$). An increase in CCT was associated with a statistically significant decrease in corneal sensitivity in the third stage ($P < 0.05$).

Table 1 : Mean, standard deviation and P value of IOP in various duration of pregnancy

PERIOD OF PREGNANCY	Mean IOP (mmhg)	Standard deviation	P value
2nd trimester	14.56	3.14	<0.001
3rd trimester	11.87	3.29	<0.001
6 weeks post partum	13.4	2.86	<0.001

Table 2 : : Mean, standard deviation and P value of CCT in various duration of pregnancy

Period of pregnancy	Mean CCT value (in µm)	Standard deviation	P value
2nd trimister	549.5	42.52	P<0.001
3rd trimister	554.7	41.82	P<0.001
6 weeks post partum	538.2	42.91	P<0.001

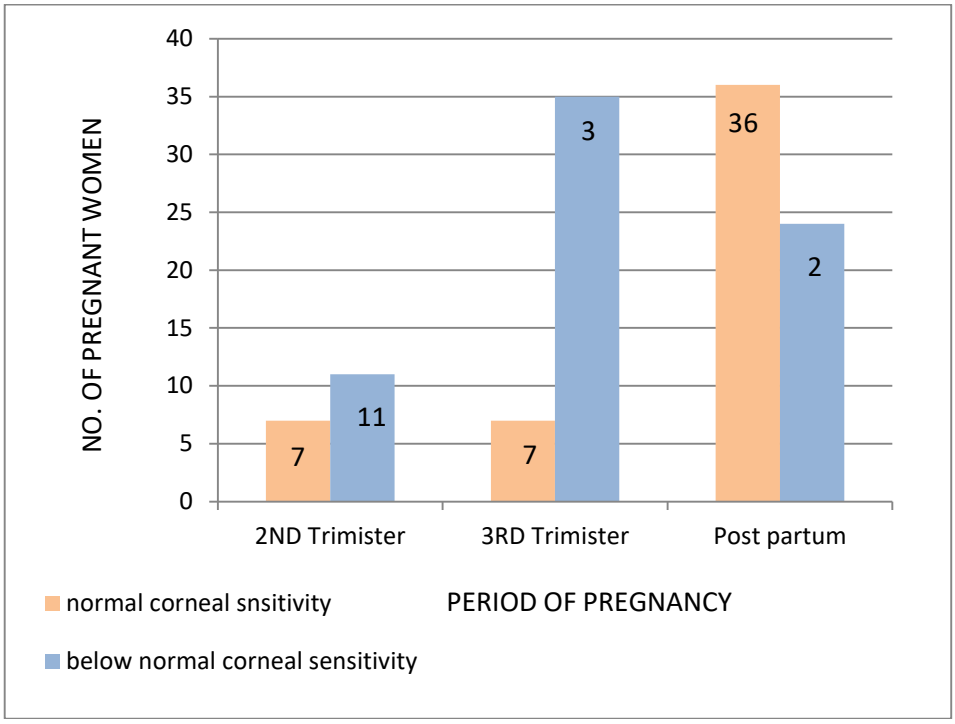

FIGURE 1. Histogram describing no. of pregnant women in various durations of pregnancy with normal and below normal corneal sensitivity

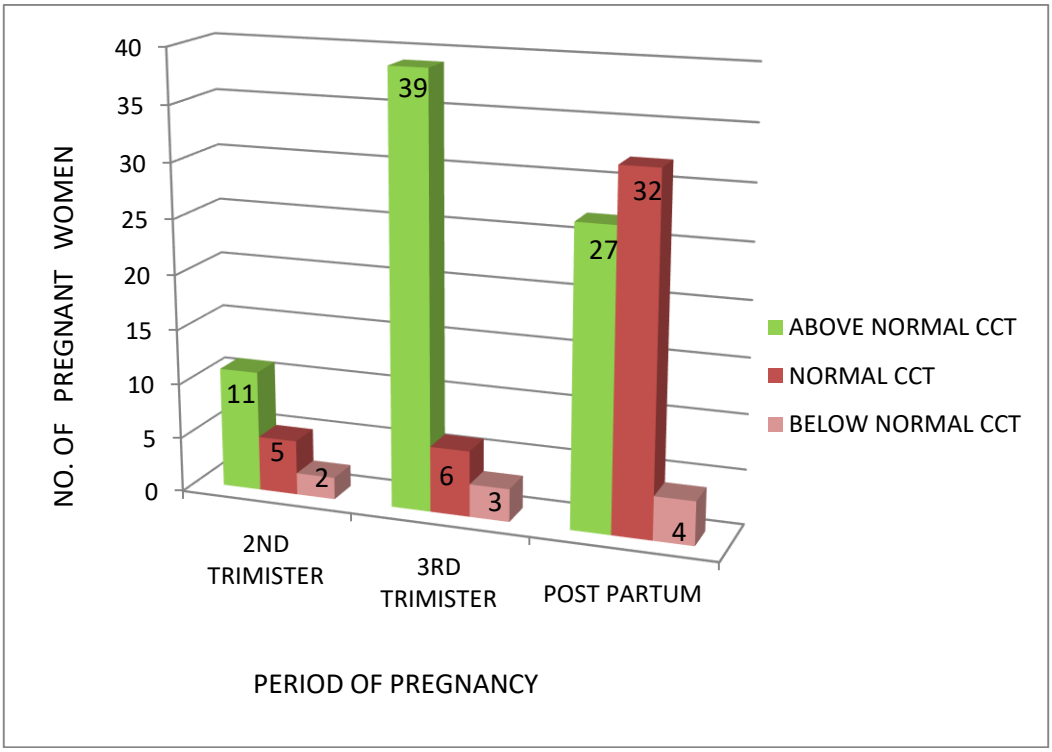

Figure 2: 3D bar graph describing no. of pregnant women in various durations of pregnancy with below normal, normal and above normal central corneal thickness.

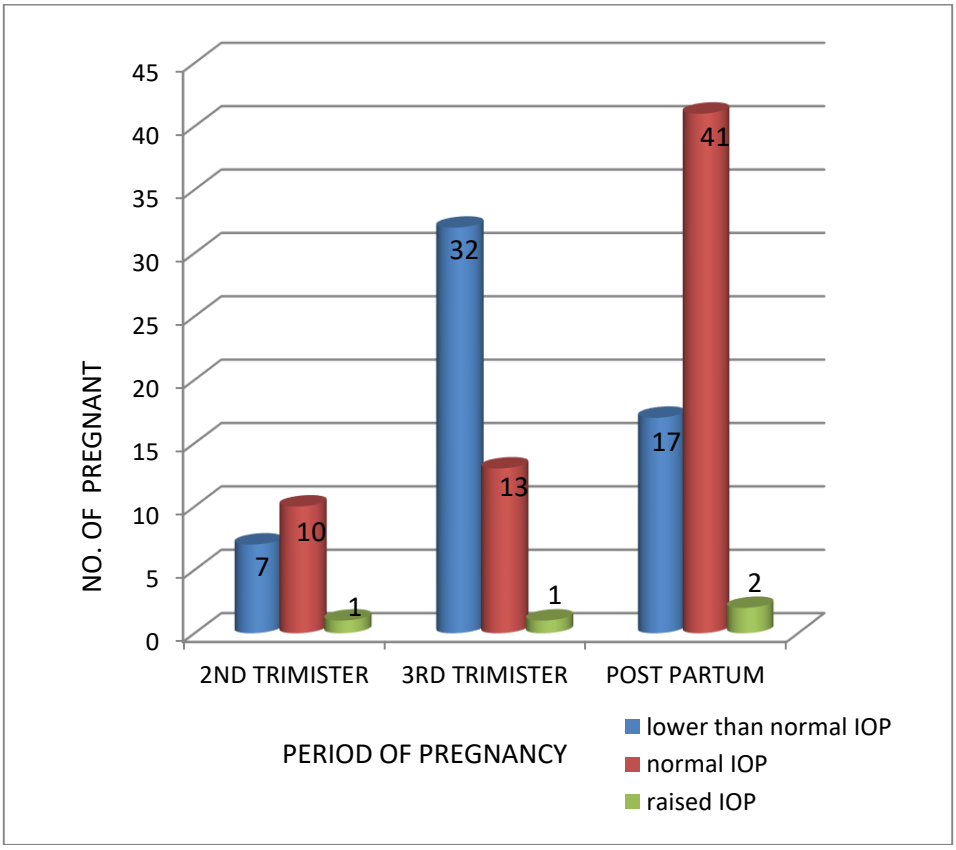

FIGURE 3 : Clustered cylinder chart shows the no.of pregnant women with normal, raised and lower than normal IOP which is seen in various period of pregnancy

Table 3. Simple linear regression analysis was used with IOP as dependent variable and CCT being an independent variable representing relationship between CCT and IOP which is most significant in third trimester of pregnancy (p<0.05)

	Regression coefficient ($R^{2)}$	P value
2nd trimister	0.01	0.86
3rd trimister	-0.026	0.02
6 weeks post partum	-0.001	0.62

V. DISCUSSION

The physiology of pregnancy is one of the most fascinating topics in medicine. Until today, despite numerous studies, not all the mechanisms that cause changes in all tissues and organs during pregnancy have been precisely determined. The visual system remains inevitable in this area, in contrast to the numerous studies known to be the result of and detailing the effects of pregnancy on most organs. In this study, we have tried to explain the effect of uncomplicated pregnancy and physiological delivery over corneal morphology, sensitivity and intraocular pressure. Our research was done during period of one year August 2021 to July 2022, which initially included 100 pregnant women in the first visit but approximately 40 pregnant women failed to followup probably due to rise of COVID-19 cases (3rd wave of COVID-19). Therefore, our final analysis is based on the research on the eyes of 60 healthy pregnant women. The age mean±SD was 29.56±5.21. The mean age of our study was similar to previous studies in Iran[5] and Malaysia[6]. The study looked at some physiological changes eyes during late trimisters of pregnancy and at 6 weeks post partum and tried to establish baseline differences during the two. In this study, we could establish that late trimisters of pregnancy had a huge impact on the corneal biomechanical properties and the best effect observed was in the third semester. This may be due to hormonal changes during pregnancy that peak during late trimisters.[4][5] CCT increased almost 2 times among the participants from 3rd trimesters that reduced in the postpartum period. Increase may be caused by fluid retention through hormonal changes. Hormonal changes that occur during pregnancy were reported to peak in the third trimester.[7] In current study, similar to reports from other previous . A decrease in corneal sensitivity was observed in participants of this study. Also reported in a previous study by Millodot[8]. CS declined during pregnancy. This allows the patient lack of awareness of the presence of a foreign object or trauma to the eye, resulting in possible injury in eye. Reduced CS in these pregnant women may be as a result of fluid retention, a

view supported by the increased CCT observed. CS correlated inversely with the increase in CCT in this study and increase in CCT caused a corresponding decrease in CS which was significant in the third trimester. A progressive decrease in IOP was observed among the participants in this study across the trimesters. This is similar to findings from several other studies where IOP was reported to fall during pregnancy.[5][9][10] The decrease in IOP could be due to an increase in the hormonal level of progesterone and estrogen which lead to dilatation of the circulatory system vessels and reduction in aqueous humour production.[5][11] A woman's progesterone level begins to increase at approximately 20 weeks of gestation and continues to increase until the end of the third trimester.[12] In addition, estrogen levels first increase at 9 weeks and peak at 31–35 weeks of gestation.[10][12] Another considered mechanism could be the result of relaxin hormone which causes relaxation of the pelvic ligament in pregnancy and this effect is believed to be extended to the corneoscleral envelope to produce decreased ocular rigidity and cause a reduction in IOP.[11][12] Pilas-Pomykalska et al. [11] reported 19.8% decrease in IOP during pregnancy which agreed with our findings. This is shown by conflicting studies like Qureshi[13] in which it was explained that the drop in intraocular pressure can be falsely low, which results in reduced corneoscleral rigidity.

An inverse correlation was found between CCTs and the IOP in this study was the increase in CCT associated with reduced IOP. This is similar to another study by Wang [14] Studies in India by Shruthi[15] that observed a 3.13% increase in CCT associated with it. The intraocular pressure had risen to 9.33 and was similar. The results of this study were CCT increased with duration, whereas CS and the IOP decreased as the pregnancy progressed. Our results are consistent with those from a previous study by Wang et al.[14] Taradaj et al[16] and Nwachukwu et al [4] that reported significant reduction in intraocular pressure and increased CCT in the 2nd and 3rd trimester of pregnancy. These researchers reported negative changes in intraocular pressure that correlates with progesterone, estrogen, and relaxin. Similarly CCT level changes are positively correlated are to the levels of these three female hormones. [4][5]

VI. CONCLUSION:

In India, there is a dearth of knowledge about ocular changes during pregnancy among pregnant women. The Aim of this study was to determine whether uncomplicated pregnancy with natural labour exerted influence on the cornea and intraocular pressure. In this study population, it is seen that, pregnancy significantly altered CCT, CS, and IOP. Over the trimesters, there was a gradual rise in CCT and a commensurate fall in CS and IOP. Six weeks after delivery, these physiological changes were reversed. When compared to the postpartum period, the cornea's morphology in third trimester of pregnancy changes more as compared to second trimester of pregnancy and so does IOP as both CCT and IOP have a significant inverse relationship with each other. Reduced corneal sensitivity knowledge is an important awareness to be spread in pregnant women to reduce ocular pathologies and better the healthcare. By being aware of these changes, needless pregnancy interventions can be avoided.

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