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PROSPECTIVE OBSERVATIONAL STUDY TO ESTIMATE PREGNANCY INDUCED CHANGES IN CENTRAL CORNEAL THICKNESS AND INTRAOCULAR PRESSURE

Ophthalmology

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ABSTRACT

PURPOSE: To estimate concurrent changes in Central Corneal Thickness (CCT) and Intraocular pressure (IOP) during normal pregnancy.

METHODS

DESIGN: Prospective cohort study of changes in Central Corneal thickness and Intraocular pressure in 45 pregnant women during third trimester and six weeks postpartum in a tertiary care hospital in Western Maharashtra, India. The change in Central Corneal thickness was measured by AS-OCT in third trimester of pregnancy and six weeks postpartum. The change in Intraocular pressure was measured by Noncontact tonometer in units of mm of Hg in third trimester of pregnancy and six weeks postpartum. Correlation analysis was performed between the change in CCT and IOP.

RESULTS: Results of our study suggest a significant increase in CCT accompanied by a decrease in IOP in the same eyes during the third trimesters of normal pregnancy compared to six weeks postpartum.

CONCLUSION: Due consideration should be given while diagnosing glaucoma during pregnancy and initiating treatment in view of physiological variance in IOP. Novel spectacle prescription and refractive surgeries must be circumvented during pregnancy owing to erroneous results due to these physiological changes in pregnancy.

KEYWORDS

Pregnancy, Central corneal thickness, Intraocular pressure

INTRODUCTION

Pregnancy is a distinct physiological state, which is characterized by a diversity of changes. An enormous number of hormonal, metabolic, immunologic, hematologic and cardiovascular changes occur in pregnancy [(1)]. All tissues including the eye are affected during this period. Thorough knowledge on physiological ocular changes in pregnancy has paramount significance in differentiating certain features from pathological processes and also laying down the management protocols. Amongst the various ocular changes in pregnancy, changes in Central Corneal thickness (CCT) and Intraocular pressure carry their own significance. Corneal thickness is vital because it can mask an accurate reading of intraocular pressure as thicker cornea overestimate and thinner cornea underestimate the Intraocular pressure.

Previous studies have claimed that, as pregnancy advances there is an increase in Central Corneal thickness and decrease in Intra ocular pressure [(1,2,3,4)]. These changes are thought to be due to both intracellular and extracellular fluid retention, as well as the interaction of hormone receptors in ocular structures with the sex steroids and usually resolve in postpartum period [(5)]. Some studies claim that the increased thickness is due to corneal edema which may lead to alteration in refractive power [(5)]. Also, ocular changes in pregnancy are influenced by general acidosis during the period [(2)]. Third trimester of pregnancy is the state at which the influence of pregnancy hormones is at the peak followed by a decreased effect almost reaching to pre-pregnant state at about six weeks postpartum[(6,7)].

In this study we will be focussing on impact of these factors on Central corneal thickness and Intraocular pressure during third trimester compared to six weeks postpartum. Optimum treatment for glaucoma in pregnancy must not be withheld so as to prevent any further deterioration and results from this study might help in setting useful guidelines to manage glaucoma during pregnancy. Results might also help in proclaiming the avoidance of refractive surgery and spectacle prescription during pregnancy as the results may not be accurate owing to the physiological change in Central Corneal thickness.

METHODOLOGY

Study design and subjects

This prospective study included 50 eyes (right eye) of 50 consecutive pregnant women undergoing routine antenatal care at a tertiary care centre who presented between October 2019 and October 2020. Out of the 50 subjects 2 were not included in the study due to preterm delivery and 3 were lost to follow up. The study adhered to the tenets of the Declaration of Helsinki and was approved by institutional review board. Written informed consent was taken from all patients involved in this study.

The inclusion criteria of this study were, pregnant women between age of 18 to 35 years, uncomplicated singleton pregnancy and delivery after 36 weeks. The exclusion criteria were complicated pregnancy, multiple pregnancy, premature delivery (< 36 weeks) and previous history of ophthalmic surgery including refractive surgery.

Complete ophthalmologic examination, including the recording of best corrected visual acuity, refraction, anterior and posterior segment examinations, IOP and CCT measurements were performed at third trimester and six weeks postpartum period. Both eyes were measured, however only the measured values in right eye were taken for computation of result as there were no statistically significant differences found between right and left eyes.

Visual acuity assessment along with refraction was done using standard Snellen's chart. Non-contact tonometer and Anterior segment Optical coherence tomography (AS-OCT) were used to measure the intraocular pressure and central corneal thickness respectively. While calculating the intraocular pressure and Central corneal thickness values, average of 3 consecutive readings was used for the data analysis. No anterior segment or fundus pathology was observed

during the study period.

Statistical Analysis

Data analysis was performed by using SPSS (Statistical Package for Social sciences) software Version 25:0. Qualitative data variables were expressed by using frequency and percentage (%) The numerical data values were expressed as mean and standard deviation. Paired t-test was used to compare the CCT and IOP values of 3rd trimester and 6 weeks postpartum periods. P-value of < 0.05 was considered statistically significant.

RESULTS

The average age of the pregnant subjects in the study is 27.75 ± 2.33 years (Range 24 to 34 years). Of the 45 pregnant women, 33 (73.33%) were emmetropic and 12 (26.67%) were having refractive error. The Best corrected visual acuity was 6/6 during third trimester and remained same in all the subjects till six weeks postpartum. However, refractive power changed in 4 subjects at six weeks postpartum compared to third trimester. The Anterior and posterior segment findings of all subjects were normal and consistent during the entire study period.

With respect to gravidity, 25 subjects (55.6%) are primi gravida and 20 subjects (44.4%) are multigravida in this study. No statistically significant difference in IOP and CCT change is noted when both the groups are compared and the mean change of IOP and CCT remained consistent in both the groups.

Most of the women in the study were found in the IOP range of 12.1 to 14 mm Hg in both the groups (Table 1). The mean IOP measurements in third trimester and six weeks postpartum were 12.62 ± 1.22 mm Hg and 14.26 ± 1.43 mm Hg respectively (Table 2).

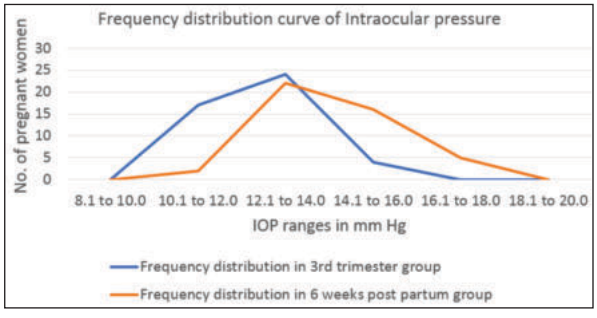
Table 1: IOP frequency distribution comparison between third trimester and six weeks postpartum:

IOP range (mm Hg)	No. of women in their 3rd trimester	No. of women at 6 weeks postpartum
≤ 10.0	0 (0%)	0 (0%)
10.1 to 12.0	17 (37.77%)	2 (4.44%)
12.1 to 14.0	24 (53.33%)	22 (48.88%)
14.1 to 16	4 (8.88%)	16 (35.55%)
16.1 to 18	0 (0%)	5 (11.11%)
Total	**45 (100%)**	**45 (100%)**

Table 2. Comparison of Intraocular pressure and Central corneal thickness values between Third trimester and six weeks postpartum.

	Intraocular pressure (IOP) in mm of Hg	
	3rd trimester	6 weeks postpartum
Min	10.33	12
Max	16	17.67
Mean	12.62	14.26
SD	1.22	1.43
Median	12.67	14
Paired t test	p value < 0.001	

A statistically significant difference was found in IOP in the third trimester compared to the six weeks postpartum measurements (p<0.001). The Intraocular pressure was found to be lowest in the third trimester. Area under the frequency distribution curves of IOP in both groups are shown in Graph 1.



Graph 1: Comparison of frequency distribution curves and area under curves of IOP at third trimester and six weeks postpartum:

With respect to CCT most of the women in the study were found in the CCT range of 560 to 580 µm in both the groups (Table 3). The Central corneal thickness (CCT) measurements in the third trimester and six weeks postpartum were 569.53 ± 14.37 µm and 554.56 ± 13.44 µm (Table 4).

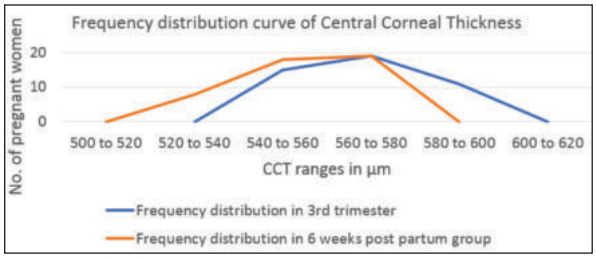
Table 3: CCT frequency distribution comparison between third trimester and 6 weeks postpartum:

CCT range (µm)	No. of women in their 3rd trimester	No. of women 6 weeks postpartum
≤ 540	0 (0%)	8 (17.77%)
541 to 560	15 (33.33%)	18 (40.00%)
561 to 580	19 (42.22%)	19 (42.22%)
580 to 600	11 (24.44%)	0 (0%)
Total	**45 (100%)**	**45 (100%)**

Table 4. Comparison of Intraocular pressure and Central corneal thickness values between Third trimester and six weeks postpartum.

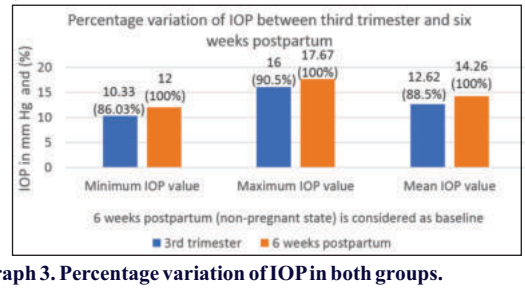
	Central corneal thickness (CCT) in µm	
	3rd trimester	6 weeks postpartum
Min	545	532
Max	595	577
Mean	569.53	554.56
SD	14.37	13.44
Median	570	554
Paired t test	p value < 0.001	

There was a statistically significant difference found in CCT in the third trimester compared to six weeks postpartum (p<0.001). Mean CCT was observed to be highest in the third trimester compared to six weeks postpartum. Area under the frequency distribution curves of IOP in both groups are shown in Graph 2.

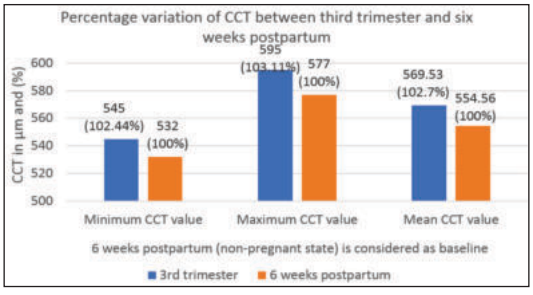


Graph 2: Comparison of frequency distribution curves and area under curves of CCT at third trimester and six weeks postpartum:

Percent changes of IOP and CCT during the third trimester compared to six weeks postpartum are shown in Graph 3 and Graph 4 respectively considering the six weeks postpartum (non-pregnant state) measurement as baseline.



Graph 3. Percentage variation of IOP in both groups.



Graph 4. Percentage variation of Central corneal thickness in both groups.

DISCUSSION

Pregnancy is a state influenced by hormones leading to many physiological changes. During the third trimester, it was found that the hormonal influence is at the peak followed by a decreased effect almost reaching to pre-pregnant state at about six weeks postpartum [6,7]. In this study, Intraocular pressure (IOP) and Central corneal thickness (CCT) were measured in third trimester and six weeks postpartum and were compared.

Previous studies and individual reports that have studied either IOP changes or CCT changes alone during pregnancy have revealed that IOP decreases and CCT increases during pregnancy [1]. Our results show that there was a significant decrease in IOP during the third trimester of pregnancy compared to six weeks postpartum, coupled with a significant reciprocal increase in CCT during the same time frame. Weinreb et al, in their study observed that the increase in corneal thickness during the gestation period returned to baseline level within a few weeks after delivery [8]. They hypothesized that pregnancy-related fluid retention may be a cause of increased corneal thickness as well as alteration in corneal topography [8].

More recently Estrogen, Progesterone, and Androgen receptors have been identified in nuclei of stromal and endothelial cells of human cornea [9]. The increased retention of water is a normal, physiologic alteration of pregnancy, which is under the influence of ovarian, placental, and steroid hormones. After delivery, the corneal thickness return to baseline due to the mobilization and excretion of water [8]. In another study, an association between corneal thickness and estrogen levels was demonstrated [10]. Hormones have been suggested to have direct effects or secondary effects, such as systemic water retention due to estrogen induced upregulation of the Renin-aldosterone system, on the cornea. Spoerl et al. showed that estrogen hormone is a potentially modulating factor in the biomechanical properties of the cornea. In their study, porcine eyes incubated with estrogen had increased thickness and reduced stiffness, as determined based on stress-strain curves [11]. Corneal thickness, corneal hysteresis, and corneal resistance factor have also been shown to vary during the menstrual cycle of healthy women.

Table 1 shows the comparative IOP frequency distribution between third trimester and 6 weeks postpartum. Our study exhibited that in both the groups maximum women were found in the IOP range of 12.1 to 14 mm Hg. Graph 1 shows a comparative display of the frequency distribution curves of Intraocular pressure in third trimester and six weeks postpartum. It was observed that the area under curve of six weeks postpartum IOP readings, shifted proportionately towards right (higher side of IOP) compared to third trimester readings. From this it can be implied that there is a uniform rise in mean IOP after third trimester reaching normal pre-pregnant values in few weeks postpartum. Table 2 depicts the comparison between Intraocular pressure of Third trimester and six weeks postpartum. It was observed in this study that the mean Intraocular pressure is less by 1.64 mm Hg (11.5%) in the third trimester compared to six weeks postpartum as depicted in graph 3.

The various proposed mechanisms to explain pregnancy-related IOP reduction are increased aqueous outflow, lower episcleral venous pressure due to decreased systemic vascular resistance, lower scleral rigidity as a result of increased tissue elasticity, and general acidosis during pregnancy [12]. As per the previous studies, a 9.5% decrease in intraocular pressure during third trimester of pregnancy has been seen followed by its return to baseline pressure shortly after delivery [1]. The ocular hypotensive effect of pregnancy has been reported by many authors, and improvement in pre-existing glaucoma in pregnant subjects has also been documented [1].

All the IOP measurements in this study were recorded using a Non-contact tonometer (NCT). Though Goldmann applanation tonometer (GAT) is believed to be the most reliable and preferred method of measuring IOP, NCT was used in this study due to its advantages. Main advantages of the NCT over the GAT are, it is rapid, does not cause epithelial damage and there is no need to use fluorescein or local anesthetics during the procedure avoiding exposure of the fetus to any dye or drugs. Other benefits of the NCT include its ease of use and the decreased risk for infection (Herpes, Adenovirus, or transmissible agents causing Creutzfeldt Jacob disease). However, NCT is having its own disadvantage in the form of inferior accuracy and reliability compared to the GAT readings. This could be a possible limitation in this study. Despite its limitation, NCT was chosen to be the method of IOP measurement in this study as it is more acceptable for pregnant women due to aforementioned advantages. Further, one study examined the intraobserver agreement among the GAT, the NCT, and the Schiotz tonometry, particularly in pregnant women, and found the NCT to be the most stable and reproducible method [13].

Green et al. studied aqueous humor formation and found that it remained stable, whereas IOP decreased throughout the trimesters and returned to normal levels at 3 months postpartum [14]. The majority of proposed mechanisms underlying the decrease in IOP during pregnancy indicate an association between female hormones and increased outflow. Paterson and Miller observed a marked increase in aqueous outflow facility associated with progesterone levels in pregnancy [15]. The decrease in IOP with the use of progesterone or the combination of progesterone and estrogen at pharmacologic doses is also reported [1,16].

Another hypothesis suggests that surplus progesterone during pregnancy acts as a glucocorticoid receptor antagonist and that it wedges the ocular hypertensive effect of endogenous steroids [17].

Glucocorticoid receptors are known to exist in the outflow apparatus and their inhibition would thus have an IOP-lowering effect. Intramuscularly administered relaxin, another pregnancy-associated hormone, was shown to decrease IOP via increased outflow facility in both male and female patients with glaucoma [15]. The outcome of relaxin on outflow facility is assumed to be interceded by collagen changes, which in turn affect the rigidity of Schlemm's canal and the trabecular meshwork. Episcleral venous pressure has been stated to decrease in pregnant women and this decrease might be associated with a diminution in general peripheral vascular resistance during pregnancy [1,18].

Table 3 shows the CCT frequency distribution comparison between third trimester and 6 weeks postpartum. Most of the women in the study were found in the CCT range of 560 to 580 µm in both the groups. Graph 2 shows a comparative display of the frequency distribution curves of Central corneal thickness in third trimester and six weeks postpartum. It can be observed that the area under curve of six weeks postpartum CCT readings, shifted proportionately towards left (lower side of CCT) compared to third trimester readings. From this it can be implied that there is a uniform reduction in mean CCT during the post-partum period reaching the normal pre-pregnant values. Table 4 depicts the comparison between Central corneal thickness of Third trimester and six weeks postpartum. Our study demonstrated that the mean Central corneal thickness is higher by 14.97 µm (2.7%) in the third trimester compared to six weeks postpartum as depicted in graph 4. The increased corneal thickness in pregnant subjects may be the result of the generalized, physiologic increase in water retention during the pregnant state or may be secondary to lowered intraocular pressure [16]. As per the previous studies, a 3% increase in corneal thickness with insignificant fluctuation through each trimester of pregnancy has been seen and its return to baseline thickness shortly after delivery suggests a hormonal influence on corneal fluid retention [19].

During this study change in refraction is noticed in four pregnants and rest of the subjects maintained a same refraction. Agrawal N et al [20] reported that the corneal curvature was significantly increased as pregnancy advanced, i.e., Vertical keratometry (KV) and horizontal keratometry (KH) of third trimester were steeper in comparison to that of second and first trimester. Apart from change in curvature, corneal edema associated increase in pachymetry values may also be a cause for the change in refractive index of the cornea, thus changing the refraction temporarily. Hence, new spectacle prescription and refractive surgeries may be avoided in pregnancy, particularly during the third trimester owing to the possibility of erroneous results due to physiological changes in refraction.

CONCLUSION

Results of our study suggest a significant increase in CCT accompanied by a decrease in IOP in the same eyes during the third trimesters of normal pregnancy compared to six weeks postpartum. Due consideration should be given while diagnosing glaucoma during pregnancy and initiating treatment in view of physiological variance in IOP. Women found with IOP values near to upper limit (21 mm Hg) during pregnancy should be followed up for any rise in IOP after the completion of pregnancy. Further, this study also accentuates that novel spectacle prescription and refractive surgeries must be circumvented during pregnancy owing to erroneous results due to physiological changes in pregnancy. Contact lens intolerance may develop in pregnancy due to corneal edema and change in curvature.

Further studies may be required to determine a direct cause and effect relationship between sex hormones and Intraocular pressure.

REFERENCES

1. Efe, Y. K., Ugurbas, S. C., Alpay, A., & Ugurbas, S. H. (2012). The course of corneal and intraocular pressure changes during pregnancy. Canadian journal of ophthalmology. Journal canadien d'ophtalmologie, 47(2), 150–154. https:// doi. org/ 10. 1016/ j. jcjo. 2012. 01.004.
2. Salim S. (2014). Glaucoma in pregnancy. Current opinion in ophthalmology, 25(2), 93–97. https://doi.org/10.1097/ICU.0000000000000029.
3. Mackensen, F., Paulus, W. E., Max, R., & Ness, T. (2014). Ocular changes during pregnancy. Deutsches Arzteblatt international, 111(33-34), 567–576. https:// doi. org/ 10. 3238/arztebl.2014.0567.
4. Taradaj, K., Ginda, T., Ciechanowicz, P., Maciejewicz, P., Suchońska, B., Szymusik, I., Kociszewska-Najman, B., Wielgoś, M., & Kęcik, D. (2018). Changes in the parameters of the anterior segment of the eye in pregnant women - literature review. Ginekologia polska, 89(3), 169–173. https://doi.org/10.5603/GP.a2018.0028.
5. Ataş, M., Duru, N., Ulusoy, D. M., Altınkaynak, H., Duru, Z., Açmaz, G., Ataş, F. K., & Zararsız, G. (2014). Evaluation of anterior segment parameters during and after pregnancy. Contact lens & anterior eye : the journal of the British Contact Lens Association, 37(6), 447–450. https://doi.org/10.1016/j.clae.2014.07.013.
6. Belkin, A., Chen, T., DeOliveria, A. R., Johnson, S. M., Ramulu, P. Y., Buys, Y. M., & American Glaucoma Society and the Canadian Glaucoma Society (2020). A Practical Guide to the Pregnant and Breastfeeding Patient with Glaucoma. *Ophthalmology. Glaucoma*, *3*(2), 79–89. https://doi.org/10.1016/j.ogla.2019.12.004.
7. Nwachukwu, N. Z., Okoye, O. I., Okoye, O., Eze, C. C., Nwachukwu, D. C., Nwagha, U. I., & Umeh, R. E. (2018). Relationship between corneal biomechanical properties among pregnant women in a tertiary hospital in Nigeria. Nigerian journal of clinical practice, 21(8), 993–999. https://doi.org/10.4103/njcp.njcp_381_17.
8. Weinreb, R. N., Lu, A., & Beeson, C. (1988). Maternal corneal thickness during pregnancy. American journal of ophthalmology, 105(3), 258–260. https:// doi. org/ 10. 1016/ 0002-9394(88)90006-2.
9. Gupta, P. D., Johar, K., Sr, Nagpal, K., & Vasavada, A. R. (2005). Sex hormone receptors in the human eye. Survey of ophthalmology, 50(3), 274–284. https:// doi. org/ 10. 1016/ j. survophthal.2005.02.005.
10. Giuffrè, G., Di Rosa, L., Fiorino, F., Bubella, D. M., & Lodato, G. (2007). Variations in central corneal thickness during the menstrual cycle in women. *Cornea*, *26*(2), 144–146. https:// doi.org/10.1097/01.ico.0000244873.08127.3c
11. Spoerl, E., Zubaty, V., Raiskup-Wolf, F., & Pillunat, L. E. (2007). Oestrogen-induced changes in biomechanics in the cornea as a possible reason for keratectasia. The British journal of ophthalmology, 91(11), 1547–1550. https:// doi. org/ 10. 1136/ bjo. 2007. 124388
12. Yenerel, N. M., & Küçümen, R. B. (2015). Pregnancy and the Eye. Turkish journal of ophthalmology, 45(5), 213–219. https://doi.org/10.4274/tjo.43815.
13. Akar, Y., Yucel, I., Akar, M. E., Zorlu, G., & Ari, E. S. (2005). Effect of pregnancy on intraobserver and intertechnique agreement in intraocular pressure measurements. Ophthalmologica. Journal international d'ophtalmologie. International journal of ophthalmology. Zeitschrift fur Augenheilkunde, 219(1), 36–42. https:// doi. org/ 10. 1159/ 000081781
14. Green, K., Phillips, C. I., Cheeks, L., & Slagle, T. (1988). Aqueous humor flow rate and intraocular pressure during and after pregnancy. *Ophthalmic research*, *20*(6), 353–357. https:// doi.org/10.1159/000266751.
15. PATERSON, G. D., & MILLER, S. J. (1963). HORMONAL INFLUENCE IN SIMPLE GLAUCOMA. A PRELIMINARY REPORT. *The British journal of ophthalmology*, *47*(3), 129–137. https://doi.org/10.1136/bjo.47.3.129.
16. Treister, G., & Mannor, S. (1970). Intraocular pressure and outflow facility. Effect of estrogen and combined estrogen-progestin treatment in normal human eyes. Archives of ophthalmology (Chicago, Ill. : 1960), 83(3), 311–318. https:// doi. org/ 10. 1001/ archopht. 970.00990030313008.
17. Ziai, N., Ory, S. J., Khan, A. R., & Brubaker, R. F. (1994). Beta-human chorionic gonadotropin, progesterone, and aqueous dynamics during pregnancy. Archives of ophthalmology (Chicago, Ill. : 1960), 112(6), 801–806. https:// doi. org/ 10. 1001/ archopht. 994.01090180099043.
18. Wilke K. (1975). Episcleral venous pressure and pregnancy [proceedings]. Acta ophthalmologica. Supplementum, (125), 40–41. https://doi.org/10.1111/j.1755-3768.1975.tb01228.x.
19. Chawla, S., Chaudhary, T., Aggarwal, S., Maiti, G. D., Jaiswal, K., & Yadav, J. (2013). Ophthalmic considerations in pregnancy. Medical journal, Armed Forces India, 69(3), 278–284. https://doi.org/10.1016/j.mjafi.2013.03.006.
20. Agrawal, N., Agarwal, L. T., Lavaju, P., & Chaudhary, S. K. (2018). Physiological Ocular Changes in Various Trimesters of Pregnancy. Nepalese journal of ophthalmology :a biannual peer-reviewed academic journal of the Nepal Ophthalmic Society : NEPJOPH, 10(19), 16–22. https://doi.org/10.3126/nepjoph.v10i1.21685