Original Article

Variations in the central corneal thickness during the menstrual cycle in Indian women

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Purpose: To determine the changes in central corneal thickness (CCT) during the menstrual cycle in Indian women. **Methods:** A prospective observational clinical study at a tertiary care center between December 2015 and December 2018. One hundred and twenty sixty women between 18 and 45 years were included. The CCT was measured using an ultrasound pachymeter at three specific timelines of the menstrual cycle: at the beginning (1st to 3rd day), during ovulation time (14th to 16th day), and at the end of the cycle (28th to 33rd day). Phases of the cycle were confirmed by the urine luteinizing hormone level. **Results:** The mean CCT of both eyes was 541.76 ± 4.21 µm, 559.21 ± 4.50 µm, and 544.52 ± 8.06 µm at the beginning, mid, and end of cycle, respectively. The mean CCT of the right eye was 541.68 ± 4.15 µm, 559.08 ± 4.50 µm, and 544.44 ± 8.06 µm and of the left eye was 541.84 ± 4.27 µm, 559.35 ± 4.50 µm, and 544.61 ± 8.06 µm at the beginning, mid, and end of cycle, respectively. **Conclusion:** The CCT value was significantly ($P < 0.001$) higher during ovulation compared to the beginning and end of the menstrual cycle. Our study recommends adding menstrual history in the workup of women undergoing refractive surgery as physiological variations in the CCT may result in unexpected surgical outcomes.

Key words: Central corneal thickness, LH surge, menstrual cycle, refractive surgery, ultrasound pachymeter

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Refractive procedures have evolved over the years, from radial keratotomy to the modern-day laser-assisted surgeries. The corneal thickness is an important consideration for these surgeries.[1] In women, fluctuating hormone levels due to menstruation, pregnancy, and menopause can influence the corneal thickness.[2] The menstrual cycle and its effects have been a subject of discussion for many researchers. Varying women hormone levels cause various cyclical changes in the reproductive system, the most significant of which are ovulation and endometrial changes. With time and research, it has been elucidated that these hormones have receptors beyond the reproductive system, influencing different tissues, organs, and biochemical processes.[3]

Gonadal hormone receptors have been observed in human ocular tissues such as the cornea, iris, ciliary body, lens, conjunctiva, and lacrimal and meibomian glands.[4] Physiological changes in the hormone milieu, oral contraceptive use, or hormonal replacement therapy[5] can influence the management of glaucoma[6] and dry eyes[7] and are important in contact lens users as well.[8] Noninvasive methods to monitor these physiological events such as identifying the time of ovulation include basal body temperature monitoring[9] and urinary luteinizing hormone (LH) levels.[10] In a multicentric trial, Leiva *et al*. found that the urinary LH values of 25–30 IU/L was the best predictive values for ovulation within 24 h.[11] Previous studies have shown that these hormones can increase the central corneal thickness (CCT) by 5.6% on days 15 and 16,[12] increase in the intraocular pressure (IOP) during the menstrual phase,[13] and influence tear film production and stability during the menstrual cycle.[14] Along with corneal topography and tomography, the CCT or pachymetry is an important consideration for planning the ablation zone in refractive surgery. A literature review on PubMed did not reveal any studies in the Indian population on the variations in CCT during the menstrual cycle, which, therefore, is the aim of our study.

Methods

This is a prospective, observational study done at a tertiary care center in north India between December 2015 and December 2018. The study was approved by the Institutional Review Board and Ethics Committee and complied with the Tenets of the Declaration of Helsinki. Of the 735 women who were screened, 163 subjects fulfilled the study criteria, but 37 of them refused to participate. A total of 126 patients were included in the study after taking an informed consent. Inclusion criteria were women between 18 and 45 years of age with normal menstrual cycles. For the purpose of this study, a normal menstrual cycle was defined as that lasting between

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21 and 35 days, with 2–6 days of flow. There were both ocular and gynecological exclusion criteria. Those with a previous history of eye surgery, conditions that can affect the CCT such as keratoconus, prolonged topical medications, scarred corneas, infectious corneal diseases, dry eye, and contact lens users were excluded**.** In addition, women with a history of infertility, polycystic ovarian diseases, pelvic inflammatory diseases, current use of contraceptives, breastfeeding mothers, and diabetic patients were excluded. Self-reported dates of the menstrual cycle by the participants were noted, but the ovulation time was confirmed by the urine LH level.

A complete ocular examination, including slit-lamp examination and fundus examination, was done to rule out any ocular abnormality. The CCT was measured by an ultrasound pachymeter (Tomey SP-300 Pachymeter) by a single experienced investigator under topical anesthesia. An average of three readings was taken at the beginning (1st to 3rd day), during ovulation time (14th to 16th day), and at the end of the cycle (last three days). All measurements were taken between 8 am and 10 am to avoid the possibility of diurnal fluctuation.

The paired t-test was used to compare the CCT between the different phases of the cycle. The independent-samples t-test was utilized to compare parameters between the right and left eye of each patient. Intergroup variation was studied by the analysis of variance (ANOVA) test. The data was analyzed by SPSS Version 20.0 (IBM Corp, Chicago, USA).

Results

Out of the 126 subjects, in 19 subjects, the CCT measurements for all three-time points in the cycle were unavailable. Hence, readings of 105 women were taken for the analysis. The mean age of the participants was 26.6 + 2.6 years (range: 18–45 years). The mean duration of the cycle was 27.9 + 2.9 days (range: 24–34 days). The mean CCT of both eyes was 541.76 ± 4.21 µm, 559.21 ± 4.50 µm, and 544.52 ± 8.06 µm at the beginning, during ovulation, and end of cycle, respectively. The CCT values were significantly ($P < 0.001$) higher during ovulation compared to the beginning and end of the menstrual cycle. The CCT at the end of the cycle was significantly higher compared to the beginning of cycle ($P < 0.002$). Results of the paired t-test applied on the change in mean CCT during different phases are described in Table 1.

The mean CCT of the right eye was 541.68 ± 4.15 µm, 559.08 ± 4.50 µm, and 544.44 ± 8.06 µm and of the left eye was 541.84 ± 4.27 µm, 559.35 ± 4.50 µm, and 544.61 ± 8.06 µm at the beginning, mid, and end of cycle, respectively. The unpaired t-test showed no difference between the mean CCT values in any phase of the menstrual cycle [Table 2]. The mean CCT in all phases was 548.40 ± 9.61 and 548.61 ± 9.66 µm in the right and left eyes, respectively. In 97 women (92%), CCT changes were seen, while in seven, there was no difference between any phases of the cycle.

Discussion

The effect of the menstrual cycle and fluctuating levels of hormones on the eye are multifold. They can affect the corneal hydration and tear film and thence, the corneal thickness.[15] It is also associated with variations in the corneal biomechanics.[16] In addition, the pituitary gland is hyperactive during ovulation leading to a higher secretion of antidiuretic hormone. This can increase the IOP and cause hydration of the cornea, thereby increasing the CCT.[17] Such variations may be important in potential candidates for refractive surgery, and also influence the IOP measurements and contact lens compliance.

In our study, the cornea was thickest at mid cycle followed by the end and beginning of the cycle. Feldman *et al*. and Soni reported the lowest CCT just before ovulation and maximum at the beginning of the cycle.[16,18] Giuffre *et al*. reported that the cornea was thickest at the end of the cycle and thinnest at the beginning.[19] Kiely *et al*. studied a group of six women and reported that the cornea was thickest at the time of ovulation.[20] Ghahfarokhi *et al*. found that the cornea was thickest during ovulation time and the thinnest at the end of the cycle.[21] In another study, the CCT and biomechanical parameters significantly varied throughout the menstrual cycle.[22] Studies on the variation of the CCT during the menstrual cycle are fraught with inconsistent results and findings. Reasons include the number of participants, use of different types of pachymeters, and subjective methods to determine the time of ovulation. We used an ultrasonic pachymeter for CCT measurement and urine LH levels for the confirmation of ovulation time. This allowed for a more accurate comparison between different subjects and correlation with the menstrual cycle.

Conclusion

Based on our findings of the CCT being significantly higher during ovulation, menstrual history seems to be an important

Table 1: Comparison of the mean central corneal thickness (CCT) of the right and left eye (in µm) during the different phases

Eye	Comparison of different phases of measurements of CCT	Means of paired differences of CCT	Paired *t*-test	Degree of freedom (df)	*P*
Left	Between beginning and middle	−17.40	28.30	97	<0.001
	Between middle and end	14.64	15.44	97	<0.001
	Between beginning and end	−2.76	3.21	97	<0.002
Right	Between beginning and middle	−17.51	28.36	97	<0.001
	Between middle and end	14.69	15.53	97	<0.001
	Between beginning and end	−2.81	3.20	97	<0.002
Overall	Between beginning and middle	−17.45	40.17	194	<0.001
	Between middle and end	14.67	21.96	194	<0.001
	Between beginning and end	−2.78	4.54	194	<0.002

Table 2: Mean central corneal thickness of the right and left eye (in µm) during the different phases and the entire menstrual cycle

Phases of the menstrual cycle	Eye		*t*	*P*
	Right (*n*=97)	Left (*n*=97)		
Beginning	541.68±4.15	541.84±4.27	0.26	0.796
Middle	559.08±4.50	559.35±4.50	0.40	0.688
End	544.44±8.06	544.65±8.06	0.18	0.857
Entire cycle	548.40±9.61	548.61±9.66	0.26	0.794

consideration during refractive surgery workup, for contact lens fitting and glaucoma evaluation in women. One limitation of our study is that the stages of the menstrual cycle and follicular maturation were not verified by an abdominal ultrasound since we relied on the history and urine LH levels. Since the LH levels during all the phases of the menstrual cycle were not measured, a correlation between CCT and LH levels was not possible. Studies with a larger number of subjects taking into consideration the above factors may further confirm our findings.

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Conflicts of interest

There are no conflicts of interest.

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