Original Article

Association Of Menstrual Phase With Central Corneal Thickness And Corneal Topography

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Abstract

Introduction: The development of corneal refractive surgery requires precision calculations, and it is known that female hormonal changes contribute to the corneal condition. Some previous studies found that sex steroid hormone receptors presence in the human corneal tissues.
Methods: A prospective observational study conducted on 44 healthy women of productive ages with regular menstrual cycles using a purposive sampling technique. Central corneal thickness and corneal topography were measured three times using optical biometry, according to menstrual phases (follicular, ovulation, and luteal phase). The ovulation phase is confirmed by determining a peak of luteinizing hormone levels in the urine.
Results: The mean central corneal thickness of both eyes was 537.5 ± 37.3 µm, 537.9 ± 36.1 µm, and 536 ± 37.4 µm, at the follicular, ovulation, and luteal phase, respectively. The mean corneal topography of both eyes was -1.19 ± 0.60 D, -1.09 ± 0.55 D, and -1.14 ± 0.62 D, at the follicular, ovulation, and luteal phase, respectively. The difference of central corneal thickness was statistically significant ($p<0.05$) relating to the different stages of menstrual cycle, meanwhile the difference of corneal topography was not statistically significant ($p>0.05$)
Conclusion: Central corneal thickness fluctuated during menstrual cycle; the thickest cornea was at ovulation phase ($p<0.05$). These corneal changes could be secondary to hormonal changes associated with menstrual cycles. These conditions should be considered for decision-making of corneal refractive surgery in women.

Keywords: central corneal thickness, corneal topography, menstrual cycle

INTRODUCTION

The menstrual cycle is an important life rhythm in women that is regulated by the level of interaction of progesterone, estradiol, follicular stimulation, and luteinizing hormone. The menstrual cycle is generally around 28 days, and consists of 3 phases, namely the follicular phase (before the ovum is released) which occurs at the beginning of the menstrual period, the ovulation phase (release of the ovum) on the 14th day, and the luteal phase (after the ovum is released) on the 14th day. period before menstruation. It is known that the peak of estrogen levels occurs twice, namely just before ovulation (it is highest) and during the luteal phase. During the ovulation phase, there is an increase in estrogen from the dominant follicle and triggers a surge in Lutenizing Hormone (LH) resulting in ovulation.[1].

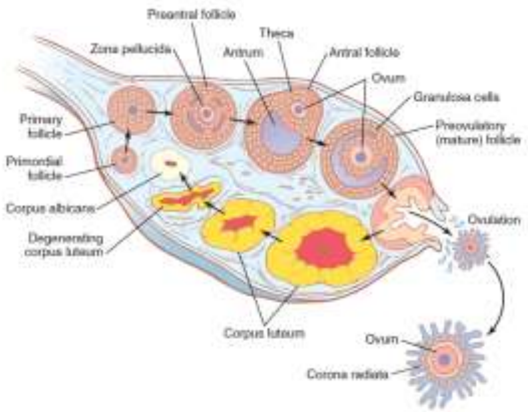

Figure 1. Stages of follicular growth in the menstrual cycle
Source:Hall, John E..Guyton and Hall: Textbook of Medical Physiology. 13th ed. Philadelphia, PA: Elsevier, 2016. Text.

Several epidemiological studies have reported that estrogen also regulates ocular tissue, although the exact mechanism is still unclear. In many studies it is said that progesterone receptors and estrogen receptors are found in the cornea in epithelial cells, stromal cells and endothelial cells[2]. In addition to the cornea, estrogen receptors were also found in the conjunctiva, lens, retina and other ocular tissues.

Sex steroid hormones are found in all body tissues and circulate in the blood circulation. However, not all tissues can be involved in the action of these hormones, only in tissues that have hormone receptors that can correspond. In the ocular tissue, estrogen receptors, progesterone receptors, and androgen receptors are found in various ocular tissues, such as lens, retina, choroid, cornea, iris, ciliary body, lacrimal gland, meibomian gland, lids, and conjunctiva.[3].

Eye disorders can be experienced by everyone. Compared to other diseases, eye disorders are considered to have a milder impact. This is probably the reason why there is not much publication on sex differences in disease in ophthalmology. However, a small eye disorder can have a big impact on a person's quality of life. A routine examination is needed regarding the condition of the corneal morphology through corneal topography[4].

The aim of a topographic examination of the cornea is to obtain detailed and accurate information about the contour of the cornea and present it in a format that is clinically useful. The raw images captured by the topographic system often provide only gross relative values for structural abnormalities of the cornea, which are then computerized to analyze so that they can display the data in a much more accurate and sensitive format.[5].

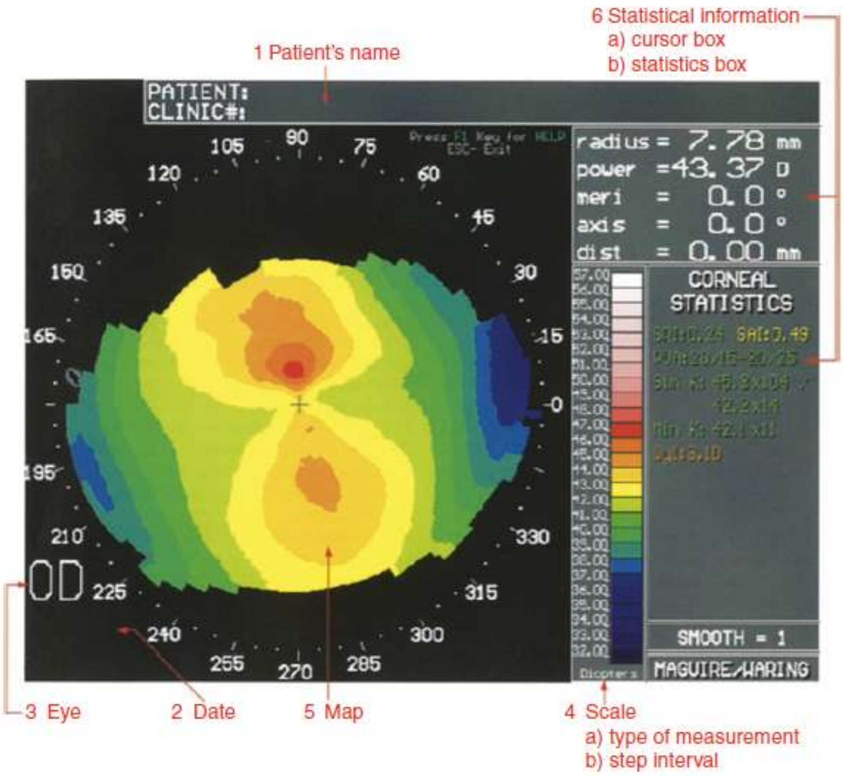

Figure 2. Topographical view of the cornea. In general, the topography of the cornea displays several parts, which are arranged systematically

Source : Corbett M, Maycock N, Rosen E, O'Brart D. Corneal Topography Principles and Applications. 2nd edition. Switzerland: Springer; 2019. P.3-94.

Corneal topography is a non-invasive technique for qualitatively and quantitatively analyzing corneal morphology. Developments in science and technology in corneal surgery, refractive surgery, and contact lenses have increased the need for precise and accurate examination of the corneal surface.

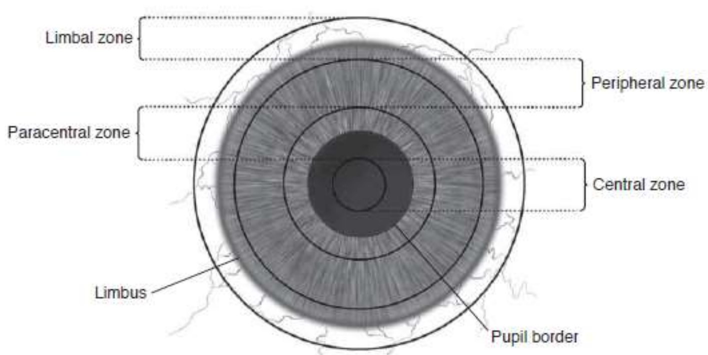

Figure 3.**Corneal topographical zone**[6]

Source: Weisenthal RW, Daly MK, Feder RS, et al. External Disease and Cornea. In : Basic and Clinical Science Course. San Francisco: American Academy of Ophthalmology; 2019.

In recent years, there has been much research on the presence of sex hormone receptors on the cornea. Fluctuations in sex hormones in a woman occur during the menstrual cycle, pregnancy, and post menopause[3].

In a study of the menstrual cycle in relation to the cornea, involving 5 healthy young women, the results were that the central corneal thickness increased in 4 women in the days before and on the day of ovulation.[7]. Other studies have shown a slight decrease in corneal thickness at the end of menstruation, and an increase at ovulation compared to before ovulation. And in addition, this increase also occurs in the early luteal phase [8]. Another study on a larger scale, in which 60 healthy women of reproductive age, found the thickest cornea at ovulation and the thinnest at the end of the menstrual cycle [9].

A woman's cornea can be affected by the hormonal changes that occur during the monthly menstrual cycle. Indeed, cyclic variations in corneal topography and corneal thickness have been described. These changes may be driven by the direct interaction of sex hormones with sex hormone receptors located on the human cornea[3].

Estrogen and progesterone are the key hormones involved in menstruation and their levels rise and fall twice during the cycle. While estrogen is responsible for growing and maturing the uterine lining and egg before ovulation, progesterone, also called the relaxing hormone, balances the effects of estrogen by controlling the formation of the uterine lining. Estrogen is most abundant in the first half of the menstrual cycle and progesterone predominates in the second half of the cycle. Thus, the menstrual cycle has three key phases, after menstruation, which are associated with hormonal changes[10].

There are risk factors for central corneal thickening and changes in corneal topography which are associated with estrogen levels during the menstrual cycle, which can be considered by ophthalmologists and help make decisions in female patients who need therapy or actions related to the cornea so as to minimize complications that may occur. This study aims to analyze the relationship between the phases of the menstrual cycle with central corneal thickness and corneal topography. With specific objectives which include (a) knowing the value of central corneal thickness during the follicular, ovulation, and luteal phases; (b) to analyze changes in central corneal thickness values between follicular, ovulation, and luteal phases. (c) knowing the value of corneal topography during the follicular, ovulation, and luteal phases; (d) analyzing changes in corneal topography values between follicular, ovulation, and luteal phases. Based on this description, this research is important to add to the research-based literature on eye health in Indonesia.

MATERIALS AND METHODS

Research Design and Sample

The design of this study is an observational prospective study to evaluate and analyze the relationship between menstrual cycle phase and central corneal thickness and corneal topography. The targeted population in this study were women of childbearing age who were on duty at the Hasanuddin University Hospital during the time the research was taking place. The sampling technique used in this research is probability sampling with purposive sampling. The number of samples in this study were 44 people, with a total population of 48 people.

Research Inclusion and Exclusion Criteria

The inclusion criteria set out in this study include: a)Individual women aged 18-35 years, with regular menstrual cycles of 21-35 days; b) Individuals with a normal ocular surface (no signs of infection, inflammation, trauma or degenerative disease); c) Individuals with Spherical Equivalent in the range of ±2.50 D; d) Individuals without contact lens use in the past 2 weeks; e) Individuals without hormonal and steroid treatment; f) Individuals without chronic systemic disorders, autoimmune, hormonal disease, or malignancy; g) Individuals who are willing to be respondents.

Exclusion criteria set in this study include: a)Individuals with irregular astigmatism; b) Individuals who have had eye surgery; c) Individuals declared pregnant during the sampling period; d) Individuals post partum and breastfeeding less than 3 months; e) Uncooperative individuals; f) Individuals who do not complete the inspection process.

Research Variables

The variables used in this study include: a) Independent variables: the menstrual cycle phase, which consists of the follicular phase, the ovulation phase, and the luteal phase; b) Dependent variables: central corneal thickness and corneal topography and ; c) Control variables: age, education, nutritional status and conditions of the menstrual cycle.

RESULTS

Respondent Characteristics

The number of respondents in this study was as much as the characteristics of the respondents in this study including occupation, marital status, age, body mass index (BMI), nutritional status, refractive disorders, menstrual cycle duration and menstrual duration.

Table 1. Characteristics of respondents

Variable	Frequency N (%)	Mean ± SD
Work		
MPPDS	31 (70.5)	
MPPD	9 (20.5)	
Nurse	4 (9)	
Marital status		
Not married yet	24 (54.5)	
Marry	20 (45.5)	
Age (years)	29.6 ± 4.1	
BMI (kg/m2)	23.4 ± 3.4	
Nutritional status		
Slender weight	1 (2.3)	
Light thin weight	1 (2.3)	
Normal weight	29 (65.9)	
Light fat weight	5 (11.4)	
Heavy fat weight	8 (18.2)	
Refractive disorders (glasses)		
Emetrop	20 (45.5)	
myopia	24 (54.5)	
Hypermetropia	0 (0)	
Cycle duration (days)	28.9 ± 2.2	
Menstrual duration (days)	6.3 ± 1.3	

Source : SPSS data processing, 2023

Based on table 1 above, the characteristics of the respondents in this study showed that the majority of respondents were Specialist Medical Education Program Students (MPPDS), namely 31 people (70.5%), then Medical Education Program Students (MPPD) as many as 9 people (6.8%)) and 4 nurses (3.0%). As many as 24 respondents (54.5%) were single, with an average age of 29.6 years. The average score of the respondent's Body Mass Index (BMI) is 23.4 or within the normal range (18-25). Most of the respondents also had normal nutritional status, namely 29 people (22.0%) followed by 13 people (29.6%) who were overweight and 2 people (4.6%) who were thin. The average duration of the menstrual cycle of all respondents was also in the normal range (28 days), namely 28.9 days. The average duration of menstruation is 6.

Central Corneal Thickness

The results of research regarding central corneal thickness based on research data processing showed the following findings:

Table 2. Central corneal thickness description

Menstrual phase	Average Central Corneal Thickness	
	Right Eye (µm)	Left Eye (µm)
Follicular Phase	536.7 ± 36.9	528.3 ± 37.8
Ovulation Phase	538.1 ± 35.4	537.6 ± 37.2
Luteal phase	535.8 ± 37.4	537.4 ± 38.1

Source : SPSS data processing, 2023

Based on table 2 above, shows the average thickness of the central cornea in both the right and left eyes. The results of this study showed that in the right eye, the highest average central corneal thickness was in the ovulation phase with an average thickness of 538.1 µm. In the left eye, the highest value was during the ovulation phase with an average thickness of 537.6 µm. The mean thickness values of the left eye were similar in the ovulatory and luteal phases. The results of research data processing regarding differences in central corn thickness in the three menstrual phases can be seen in the table below:

Table 3. Differences in central corneal thickness in the three menstrual phases

Menstrual phase	Mean ± SD	Median (Minimum-Maximum, µm)	p value
Follicular Phase	537.5 ± 37.2	533.0 (466-638)	
Ovulation Phase	537.9 ± 36.1	536.0 (464-628)	0.05
Luteal phase	536.6 ± 37.4	533.5 (459-632)	

Source : SPSS data processing, 2023

Based on table 3 above, it shows the difference in central corneal thickness in the three menstrual phases. The normality test shows that the data is not normally distributed, so the Friedman test is used. These results show that there is a significant change in one of these phases with a p value of 0.05. Figure 4 shows a box plot diagram showing the mean, median, standard deviation of central corneal thickness in each phase.

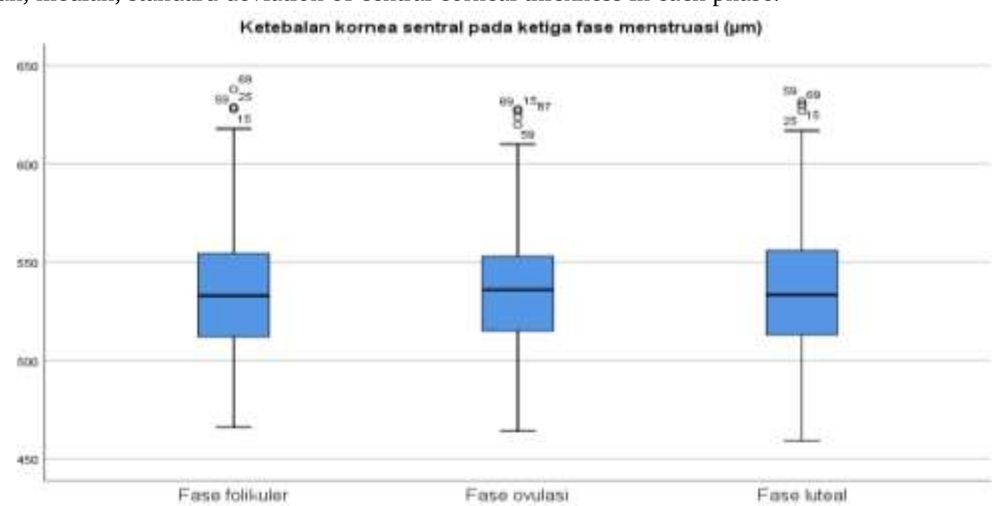

Figure 4. Box-plot diagram showing the quartile and median distribution of central corneal thickness values at each phase of the menstrual cycle

Based on the results of follow-up tests using the Wilcoxon post hoc test to find out more specifically about the differences in central corneal thickness in the follicular phase and the ovulation phase, the ovulation phase and the luteal phase, as well as the luteal phase and the follicular phase show the following results.

Table 4. Results of the Wilcoxon post hoc test for central corneal thickness in the three menstrual phases

Differences in menstrual phases	p value (Wilcoxon test)
Follicular phase and ovulation phase	0.18
The ovulation phase and the luteal phase	0.02
Luteal phase and follicular phase	0.18

Source : SPSS data processing, 2023

Based on table 4 above, shows a follow-up test using the Wilcoxon post hoc test to find out more specifically about differences in central corneal thickness in these phases. The table shows that there is a significant difference in central corneal thickness between the ovulation phase and the luteal phase with a p value of 0.02.

The results of the correlation test performed to assess more specifically between central corneal thickness in the 3 phases with the patient's BMI and refractive status are shown in the table below.

Table 5. Correlation test results for central corneal thickness with BMI and refractive status

	Body mass index	Refraction Status
	p value	p value
Central Corneal Thickness		
Follicular Phase	[a]0.233	[b]0.067
Ovulation Phase	[a]0.144	[b]0.102
Luteal phase	[a]0.134	[b]0.573

a = Kruskal-Wallis test; b = Pearson's test
Source : SPSS data processing, 2023

In table 5 above, the results of the correlation test for BMI with central corneal thickness obtained p = 0.233, p = 0.144, and p = 0.134 respectively in the follicular phase, ovulation phase, and luteal phase. While the correlation test for refractive status with central corneal thickness obtained p = 0.067, p = 0.102, and p = 0.573 in the follicular phase, ovulation phase, and luteal phase, respectively. This shows that there is no significant relationship between central corneal thickness at 3 phases with BMI or refractive status.

Corneal Topography

Corneal topography based on the test results of the average curvature of the corneal cylinders in both the right and left eyes, is shown in the following table.

Table 6. Image of the curvature of the corneal cylinders

Menstrual phase	Mean ± SD of Cylinder Curvature Right eye (D)			Left eye (D)		
	central (Ø3mm)	parasentral (Ø5mm)	peripheral (Ø7mm)	central (Ø3mm)	parasentral (Ø5mm)	peripheral (Ø7mm)
Follicular Phase	-0.91 ± 0.52	-0.99 ± 0.49	-1.17 ± 0.57	-1.00 ± 0.53	-1.09 ± 0.54	-1.19 ± 0.63
Ovulation Phase	-1.92 ± 6.51	-0.94 ± 0.49	-1.05 ± 0.51	-1.01 ± 0.53	-1.04 ± 0.48	-1.13 ± 0.58
Luteal phase	-0.91 ± 0.50	-0.99 ± 0.54	-1.11 ± 0.55	-0.99 ± 0.55	-1.11 ± 0.59	-1.16 ± 0.68

Source : SPSS data processing, 2023

Table 6 shows the average curvature of the right eye cylinder at 7 mm (peripheral) diameter of -1.17 D each; -1.05 D; and -1.11 D in the follicular, ovulatory, and luteal phases. Meanwhile, the average topography of the left eye's cornea at a diameter of 7 mm (peripheral) was -1.19 D each; -1.13 D; and -1.16 D in the follicular, ovulatory, and luteal phases. Other data shows the average cylindrical curvature of the right eye and left eye in the central and paracentral zones in the follicular, ovulation and luteal phases. The components of the curvature of the corneal cylinders in both eyes in the central, paracentral, and peripheral zones for each phase of the menstrual cycle are shown in the following table.

Table 7. Differences in the curvature of the corneas of the two eyes in the three menstrual phases

Zone	Mean ± SD	Median (diopters)	Minimum (diopters)	Maximum (diopters)	p value
Central (3mm)					
Follicular Phase	-0.96± 0.53	-0.93	-2.98	0.00	
Ovulation Phase	-0.97±0.52	-0.94	-2.67	0.00	[a]0.79
Luteal phase	-0.95± 0.53	-0.88	-3.19	0.00	
Paracentral (5 mm)					
Follicular Phase	-1.04±0.52	-0.99	-2.99	0.00	
Ovulation Phase	-1.00± 0.49	-0.96	-2.86	0.00	[a]0.26
Luteal phase	-1.05± 0.57	-1.00	-3.51	-0.23	
Peripheral (7mm)					
Follicular Phase	-1.19± 0.60	-1.14	-3.36	0.42	
Ovulation Phase	-1.09±0.55	-1.04	-3.35	0.00	[a]0.31
Luteal phase	-1.14± 0.62	-1.05	-4.21	0.00	

a = Friedman test

Source : SPSS data processing, 2023

From the table it can be seen that the average difference is -0.96 D each; -1.04D; and -1.19 D in the central, paracentral, and peripheral groups during the follicular phase. It can also be seen that the average difference is -0.97 D each; -1.00 D; and -1.09 D in the central, paracentral, and peripheral groups during the ovulation phase. In addition, in the luteal phase, there is an average difference of -0.95 D each; -1.05 D; and -1.14 D in the central, paracentral, and peripheral groups. However, based on statistical tests, the average difference in each of these phases was not significant ($p > 0.05$). Figures 5, 6 and 7 below show box plot diagrams showing the mean, median, standard deviation of the corneal curvature in the central, paracentral, and peripheral zones in each phase of the menstrual cycle.

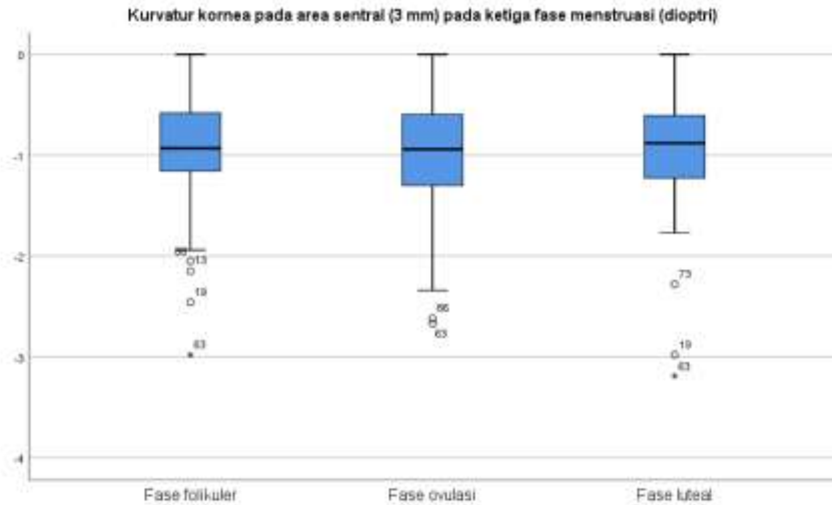

Figure 5. Box-plot diagram showing the quartile and median distribution of central corneal curvature values (3 mm zone) at each phase of the menstrual cycle

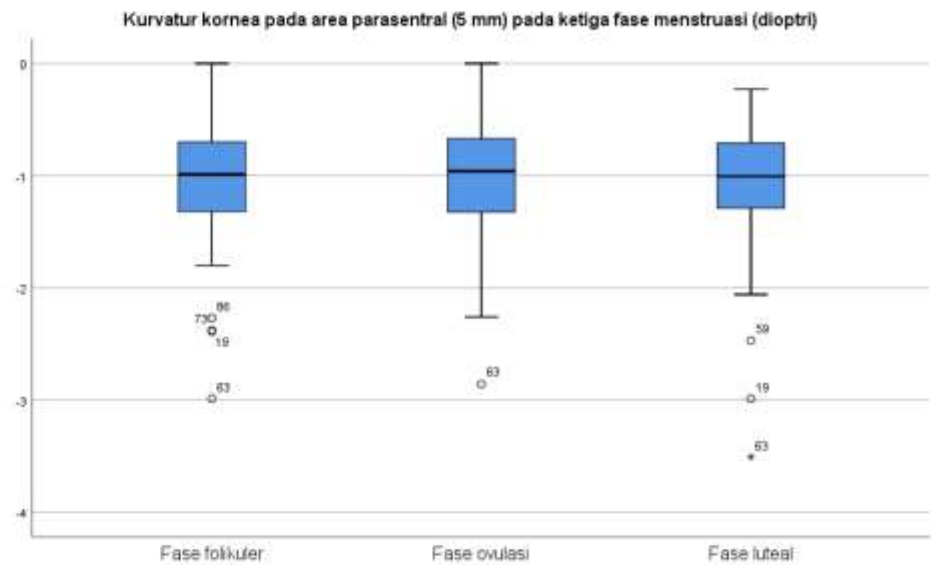

Figure 6. Box-plot diagram showing the quartile and median distribution of paracentral corneal curvature values (5 mm zone) at each phase of the menstrual cycle

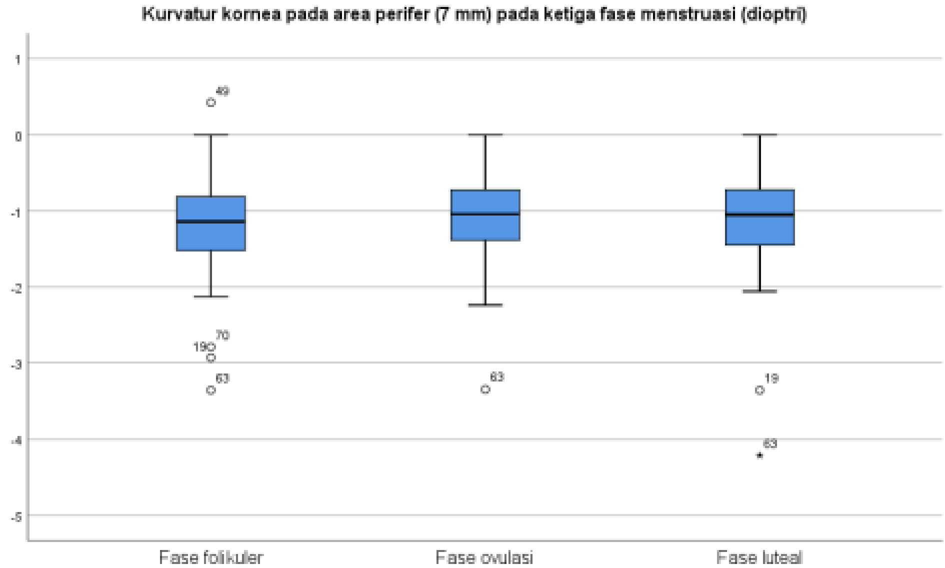

Figure 7. Box-plot diagram showing the quartile and median distribution of peripheral corneal curvature values (7 mm zone) at each phase of the menstrual cycle

DISCUSSION

Study Characteristics

This study showed that the majority of respondents were students of the Medical Education Program (MPPD), namely 31 people (70.5%) followed by students of the Specialist Doctor Education Program (MPPDS) of 9 people (6.8%) and 4 nurses. (3.0%). The results of this study also showed that as many as 24 respondents (54.5%) were not married with an average age of 29.6 years as a whole. In previous studies, the average age of the respondents was 25 ± 4 years, with the youngest being 21 years old and the oldest being 34 years old [11]. Another similar study was conducted involving 22 women with a mean age of 19.5 ± 1.5 years [12]. Subjects in other studies were employees who worked in hospitals with an age range between 21-43 years [9].

The average BMI score of the respondents in this study was within the normal range with an average of 23.4 kg/m2. Most of the respondents also had normal nutritional status (65.9%), were overweight (29.6%) and were underweight (4.6%). Previous research reported that research subjects had a median BMI of 25.1 kg/m2 in men and 22.2 kg/m2 in women who were still in the normal weight range and this is in accordance with this study [13]. The results of another study, which showed that the average BMI score of the study subjects was 24.4 ± 5.8 kg/m2 in group 1 and 24.6 ± 3.5 kg/m2 in group 2, each of which was also classified as normal weight category [14].

The condition of BMI is noteworthy because being overweight can be associated with more estrogen levels synthesized by adipose tissue, and vice versa [15]. In addition, the condition of being underweight or overweight can also affect the menstrual cycle and in many cases can lead to anovulatory cycle conditions, namely the absence of ovulation. In our study sample, there were several participants who were overweight or underweight, but their menstrual cycle history and menstrual duration were normal, so they were still included as our research sample.

The average menstrual cycle duration of all respondents in this study was within the normal range, namely 28.9 ± 2.2 days, with an average menstrual duration of 6.3 days. These results are similar to the reported duration of the menstrual cycle in the range of 26-32 days with a menstrual duration of 3-6 days [11]. Other related research shows that the average menstrual cycle length is 28 ± 1.7 days (26-31 days) [12]. In addition, other research subjects also had regular menstrual cycles, which ranged from 24-32 days [9]. Previous studies on menstruation also reported that the average menstrual cycle of research subjects was 28 ± 1 day [10]. The average menstrual cycle duration in another similar study was 28.1 ± 2.9 with a range of 24–34 days [16].

In this study, the highest average central corneal thickness in the right eye was during the ovulation phase with an average thickness of 538.1 ± 35.4 µm. In the left eye, the highest value was in the ovulation phase with an average thickness of 537.6 ± 37.2 µm with a similar thickness in the left eye during the ovulation and luteal phases. These results are in accordance with previous studies conducted by Mishra where central corneal thickness was found to be the thinnest at the beginning of the cycle and increased at ovulation and at the end of the cycle with an average central corneal thickness at the ovulation phase and the end of the cycle were 549 ± 46 and 559 respectively. ± 44 µm [11].

The central corneal thickness increased significantly between the start of the menstrual cycle and ovulation, with the increase being maintained until the end of the cycle. The highest average central corneal thickness in this study was found during the ovulation phase and the end of the cycle, namely 542 ± 41 and 543 ± 42 µm respectively [12]. Another study found that the highest average central corneal thickness, both in the left and right eyes, was at the time of ovulation. On days 1-3, the mean central corneal thickness was 541.40 ± 11.36 and 540.82 ± 11.70 µm for the left and right eyes, respectively. At ovulation, the thicknesses of the corneas were 556.50 ± 7.11 and 555.98 ± 7.26 µm for the left and right eyes, respectively. The mean values on days 27-32 were 536.38 ± 12.83 and 535.48 ± 13.08 µm for the left and right eyes [9].

In this study, a follow-up correlation test was carried out to assess the condition of the central corneal thickness in the three menstrual cycles associated with the body mass index of the refractive status of the respondents. Both showed insignificant results ($p > 0.05$). The same results were also obtained in a previous study which assessed anthropometric correlation with ocular parameters in 155 healthy young women where there was no significant relationship between BMI and the ocular parameters examined such as central corneal thickness, axial length of the eyeball, and anterior chamber depth, as well as refractive status [17].

This study showed that the average curvature of the right eye's cornea in the peripheral zone, namely at 7 mm in diameter, was -1.17 D each; -1.05 D; and -1.11 D in the follicular, ovulatory, and luteal phases. Meanwhile, the average curvature of the left eye's cornea in the peripheral zone, namely at 7 mm in diameter, was -1.19 D each; -1.13 D; and -1.16 D in the follicular, ovulatory, and luteal phases. As far as we have investigated, there have not been many studies regarding changes in corneal curvature associated with the menstrual cycle. In previous studies it was stated that an increase in horizontal and vertical curvature occurred at the beginning of the cycle and was more evenly distributed after ovulation [8]. Women have a slightly higher average corneal curvature than men.

Other studies also showed that the average horizontal curvature and vertical curvature of the central corneal strength in premenopausal women were 43.5 ± 1.25 D and 44.1 ± 1.53 D. Meanwhile, the average horizontal curvature and vertical curvature central corneal strength in postmenopausal women was 43.9 ± 1.4 D and 44.6 ± 1.3 D. These results suggest that changes in estrogen levels in postmenopausal women are associated with slight changes in the horizontal curvature of the cornea [19]. The presentation of supporting data in the form of refractive status in this study is complementary, but is not the aim of this study. Examination of refractive status in this study using an autorefractorometer was carried out by several different people and was only carried out once in each phase. Patient factors, equipment,

Menstrual Phase Against Central Corneal Thickness and Corneal Topography

The results of this study are in line with previous studies which stated that differences in corneal thickness were statistically significant with respect to different stages of the menstrual cycle [9]. The cornea is thickest during the menstrual cycle is reached at the time of ovulation and is thinnest at the end of the cycle and this must be taken into account when planning corneal refractive surgery. Changes in corneal thickness during the menstrual cycle have been reported in previous studies. However, there is no agreement on the exact time when the cornea becomes thickest. These changes could be secondary hormonal influences such as estrogen receptors that can be found on the human cornea and suggest that estrogen may have a role in corneal physiology. Significant changes can occur in the hydration of the cornea during a normal menstrual cycle. The changes are related more to the effects of estrogen than to progesterone. These hormones may be accessed via the aqueous humor or tear film because of their high lipid solubility. Another possibility would be the indirect action of the hormone on the cornea through its effect on tear film osmolarity [9].

The results of this study are not in line with previous studies which stated that ocular biometric parameters consisting of anterior chamber depth, axial length, central corneal thickness, lens thickness, steep keratometric readings, and flat keratometric readings did not vary significantly during the menstrual cycle according to optical low biometry. -coherence reflectometry (OLCR). Corneal biomechanical parameters such as corneal resistance factor and corneal hysteresis were determined by ocular response analysis instruments. This may have contributed to the insignificant results [20]. The same result was also shown by previous studies which stated that there was no difference in corneal thickness or foveal thickness between the follicular and luteal phases. The study suggests better isolating the hormonal differences between the follicular and luteal phases and collecting menstrual cycle data carefully [13]. Narrative study ofFigueiredo (2021)which discussed 32 articles stated that the menstrual phase causes significant changes in visual function, including in relation to spatial orientation and attention, visual campimetry and visual sensitivity. This relates specifically to the follicular and luteal phases [21]. The hormonal changes that occur during the menstrual cycle affect the homeostasis of the body [22].

The results of this study state that the central cornea is thickest in the ovulation phase. This is in line with similar previous studies [11]. The thickest cornea occurs in the middle of the cycle followed by the end and the beginning of the cycle. The effects of the menstrual cycle and fluctuations in hormone levels on the eye are manifold. This can affect the hydration of the cornea and the tear film, including the thickness of the cornea, and is related to variations in corneal biomechanics. In addition, the pituitary gland becomes hyperactive during ovulation which causes a higher secretion of antidiuretic hormone. This increases the intraocular pressure and causes hydration of the cornea thereby increasing the central corneal thickness [11].

This study stated that there was no significant relationship between corneal topography and the menstrual cycle. This is in line with previous studies which did not detect significant changes in keratometry values and apparent refraction during the study in women [23]. The role of the effect of estrogen on corneal topography varies between studies. Another study showed that no significant changes in corneal curvature occur in normal premenstrual women during the menstrual cycle [24]. Corneal topography to evaluate the effect of hormonal changes on keratometry and found that estrogen levels have a significant impact on the curvature of the cornea [25]. Elevation of the horizontal and vertical meridians was found to be associated with high levels of estrogen at the start of the menstrual cycle.

The thickness of the central cornea changes during the menstrual cycle, with the cornea being thinnest at the beginning of the cycle and thickest at the end. These changes may be secondary to hormonal influences; Estrogen receptors can be found in the human cornea, indicating that estrogen may have a role in corneal physiology [22]. Central corneal thickness changes under the influence of fluctuations in hormone levels during the menstrual cycle as hypothesized in the literature. Corneal thickness is highest during ovulation and thinnest in the early days of the menstrual cycle, by pachymetry. Sex steroid hormones, especially estrogen appear to affect the endothelial pump. Central corneal thickness increases at the peak of estrogen activity corresponding to the ovulatory phase of the menstrual cycle [26].

Estrogen has a rigidity-reducing effect on the cornea which can be explained at the molecular level although so far there has been no definite explanation of the mechanism. The effect of estrogen on ocular tissue, especially the cornea, is assumed to be a non-genomic pathway through the aqueous humor and tear film, leading to sex steroid hormone receptors in epithelial cells, stromal cells, and endothelial cells [27]. This further releases prostaglandins and activates collagenase which acts like a chain breaker. For corneal biomechanics, this means increased dispensability and reduced stiffness. The viscoelastic behavior of the cornea is also determined by proteoglycans, which act as interfibrillar or interlamellar adhesives. It can be assumed that the cohesion between the collagen fibrils and the noncollagen matrix can be reduced by estrogen,

The condition of central corneal thickening which fluctuates with the phase of the menstrual cycle is not followed by the refractive status which also changes significantly. It can be said that the condition of central corneal thickening that occurs is micro and does not affect the patient's refractive condition. This is supported by previous studies which showed that there were no significant differences in the values of keratometry and refractive status in their research subjects [23]. Another study that was conducted also presented insignificant results on the refractive status parameter assessed at the three phases of the menstrual cycle (p=0.44) [23]. In this study, the refractive status became complementary data because the measurement bias was sufficient to be an obstacle in the assessment.

Studies on variations in central corneal thickness and corneal topography during the menstrual cycle have mixed results among previous studies. This could be due to the number of participants, use of different types of pachymetry, and subjective methods of determining menstrual cycles. As far as we have investigated, there have not been many studies regarding changes in corneal curvature associated with the menstrual cycle. This is one of the strengths of our research. In addition, these studies did not originate from our country, which has its own epidemiological characteristics, such as race, nutritional status and different lifestyles.

There are several limitations in this research. First, this study did not assess conditions between one menstrual cycle and the next menstrual cycle. Second, the determination of the ovulation period is based on the results of a urine test, not based on a transvaginal ultrasound examination which is a more accurate standard for ovulation examination. In addition, this study did not directly assess related hormone levels and their effect on the condition of the cornea, but calculated the days according to the phase of the menstrual cycle.

CONCLUSION

From the results of the research conducted, the conclusions of this study are as follows. The mean value of central corneal thickness is highest during the ovulation phase, namely537.9 ± 36.1 μm.The difference in thickness of the central cornea hasstatistically significant values between the ovulatory and luteal phases ($p < 0.05$), compared with the other phases.The average value of the corneal topography in each phase of the menstrual cycle is respectively-1.19±0.60D,-1.09± 0.55 D, and-1.14± 0.62 D in the follicular, ovulatory, and luteal phases respectively.Differences in corneal topography in each phase of the menstrual cycle, nostatistically significant ($p > 0.05$).

The future is expectedThe phase of the menstrual cycle should be taken into consideration when making decisions about corneal refractive surgery. In addition, a more accurate determination of the ovulation period is needed to get maximum results. Then further research is needed to compare the conditions of central corneal thickness and corneal topography in one cycle with the next cycle. Finally, further research is needed to assess central corneal thickness and corneal topography based on examination of related hormone levels.

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