Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Review Article

Clinical implementation of ocular health findings in different phases of the menstruation cycle - A systematic review

Animesh Mondal[1]*, **Nishtha Verma**[1], **Sourav Karmakar**[1], **Gaurav Kumar Bhardwaj**[1]

[1] *Dept. of Optometry and Vision Science, Amity University, Amity Education Valley Campus, Manesar, Gurugram, India*

ARTICLE INFO

Article history:
Received 25-06-2023
Accepted 21-07-2023
Available online 29-12-2023

Keywords:
Menstrual cycle
Ocular health
Tear film
Cornea
Accommodation
Choroid

ABSTRACT

Menstrual cycles are essential to women's health and play a significant role in their daily lives. While the hormonal changes during the menstrual cycle are recognized, research has focused on investigating their specific effects on ocular and visual characteristics. This review aims to comprehensively explore the potential alterations in ocular parameters and alterations to visual performance throughout the cycle of menstruation. Following a search in various research repositories, including PubMed, Google Scholar, Ovid, and EMBASE, both original and review publications were reviewed, and information was utilized in this study. Studies with changes in Ocular parameters during all three menstrual cycle phases were noted. The reported studies documented only normally menstruating women. This study provided valuable knowledge and awareness of the risk factors for menstrual cycle-related ocular symptoms and changes and the impact of these conditions on women's life. This information can be used to develop evidence-based guidelines for managing menstrual cycle-related ocular problems and their significance in clinical practice.

1. Introduction

Ocular health is an essential aspect of overall well-being, and its relationship with hormonal changes has garnered significant attention in recent years. The average menstrual cycle, a complex interplay of hormonal fluctuations in women, has been associated with various physiological and psychological changes.[1] Interestingly, emerging evidence suggests that these hormonal changes can also impact ocular health, leading to alterations in visual function and ocular symptoms throughout different phases of the menstrual cycle.[2] During the menstrual cycle, hormonal fluctuations, primarily involving estrogen and progesterone, regulate various physiological processes in the body.[3] These hormonal changes influence multiple organ systems, including the visual system. The ocular surface, tear film, cornea, and other ocular structures have been reported to exhibit changes in response to these hormonal variations.[4] Several studies have investigated the ocular health findings during various menstrual cycle phases, shedding light on potential mechanisms and clinical implications.[5] It is essential to understand these findings, as they can aid in diagnosing and managing ocular conditions and enhance overall eye care for women. A significant amount of a woman's life is devoted to the menstrual cycle, affecting most women. Some women may notice particular shifts in their eyesight and ocular complaints during their menstrual cycles. These alterations may be clinically relevant, especially in diagnostic, treatment, and prescribing medical aid. Awareness of any volatility affiliated with menstruation would be crucial for the eye care professional and the general population when deciding whether any change witnessed is within acceptable bounds. This review

* *Corresponding author.*
E-mail address: 1997ani1optm7@gmail.com (A. Mondal).

https://doi.org/10.18231/j.ijceo.2023.091

aims to provide an overview of the ocular health findings observed during different phases in normal menstruating women. We will explore the impact of hormonal changes on various ocular parameters.

2. Objectives

1. Evaluate the work done in the respective field.
2. Summarize the clinical relevance of the existing knowledge.
3. Previous reviews for pregnant as well as diseased women have been done, but not for normal menstruating women.

3. Materials and Methods

In this part, we will cover the approach used to conduct a literature review to investigate the menstrual cycle's influence on ocular health.

3.1. Eligibility criteria

For the objectives mentioned above, Literature associated with any ocular surface parameter changes in normally menstruating women around the globe was given a significant amount of focus in this study. In addition to reviewing journal articles, the process entailed reviewing papers presented at conferences, and the original studies that documented changes in typically menstruating women were included. In contrast, studies on pregnancy, contraceptive pills, and diseased women were excluded. Articles in English-language were tallied; none of the other languages were included.

3.2. Search strategy

After searching for several research repositories, such as PubMed, Google Scholar, Ovid, and EMBASE, were located and used to inform this study. The effects of the menstrual cycle on ocular structures have been the subject of extensive study and publication; however, a study has yet to present an all-encompassing perspective.

"Menstrual cycle and ocular health, Retinal vascular changes, corneal thickness, choroid thickness, Tear film stability, Anterior chamber depth, Accommodation, Crystalline lens, Conjunctival changes, Refractive changes, Intra Ocular Pressure, Colour vision" were some keywords that were included throughout the search. The title and abstract were used for the initial review, and chosen articles were thoroughly evaluated for inclusion.

3.3. Data extraction

The combined search results were narrowed using a set of inclusion and exclusion criteria, and the titles and abstracts were assessed for relevancy. Each manuscript that met the criteria for inclusion underwent a thorough evaluation by the reviewers. The authorized study was uploaded utilizing the data extraction form that had been generated. The researchers collected data from the investigations: first, the author, age, gender, menstrual status, sample size, and ocular health findings of all three phases of a normally menstruating woman.

3.4. Data synthesis

To provide a qualitative analysis of the findings and components of the included study, summarized in the form of tables the information gathered from the pertinent research. After extracting the data, the best approach for using the data was picked. Studies that met the criteria for full-text inclusion, but studies relating women's usage of birth control pills, hormonal research to treat illnesses, disease, and the menstrual cycle were disregarded.

3.5. The risk of bias assessment

The quality was evaluated using the ROBIS, which evaluates the possibility of bias in systematic reviews.[6]

After judging the risk of bias in all 4 Domains concerning the criteria for research eligibility, the techniques used to find or choose research, the procedures used to gather data and evaluate studies, and the synthesis and conclusions. The risk of bias in this review was found to be low.

4. The Findings and Discussion

4.1. Study selection and study characteristics

The initial search strategy identified two hundred sixty-two articles for all keywords. Seventy-one duplicates were removed, and one hundred ninety-one articles were screened. The abstract of 191 articles was inspected, out of which 147 were excluded, and the intention for exclusion is mentioned in (Figure 1). Twenty articles were focused on and included. Study designs of the research included are illustrated in (Table 1).

4.2. Ocular health findings during the menstrual cycle

4.2.1. Tear film changes

The ocular surface of the human eye, including tears, possesses estrogen and progesterone receptors, affecting tear formation and blink rate.[4] Females using oral contraceptives showed reduced tear secretion and increased blink rate compared to a control group.[5] For the eye blink rate (EBR), no significant differences were observed across the menstrual cycle.[2–6] However, subjective dry eye symptoms measured by OSDI worsened. The tear function index (TFI) remained unchanged across different menstrual phases.[7,9] Study[8] showed that Tear production increased in the first two days of menstruation and slightly decreased in the last two days. Found no significance between the right and left eyes. Tear production associated

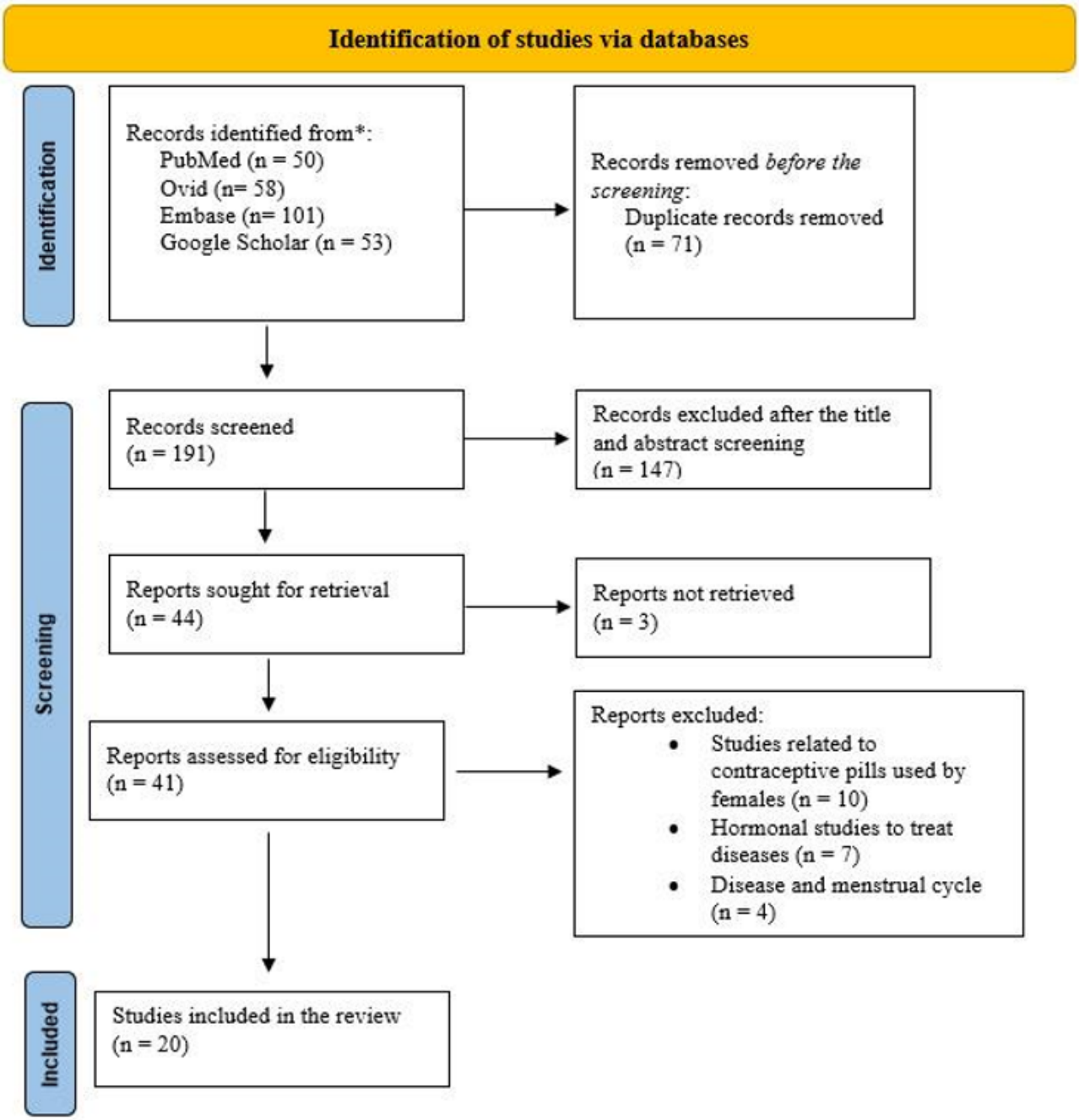

Figure 1: The illustrated flow chart of the study selection process

Table 1: Design of the Studies

Author	Year	Age (years)	Study Sample	Study Design	ROBIN-I
Colorado, Luisa H. et al.,[4]	2020	22.3 ± 3.7	26	Prospective observational study	Moderate
Versura P et al.,[7]	2007	29.2 ± 6.5	29	Prospective case-control study	Moderate
Oboh, Roland A et al.,[8]	2021	20.82 ± 3.2	103	Descriptive survey	Moderate
Cavdar E et al.,[9]	2014	32.1 ± 7.2	17	Prospective study	Moderate
Goldich Y et al.,[10]	2011	19.5 ± 1.5	22	Prospective - Case series	Moderate
Rana, Poonam et al[11]	2018	13-55	100	Random cohort study	High
Ghahfarokhi, Negar Amiri[12]	2015	21-43	50	Prospective study	Moderate
Kardam Vyas, A et al.,[13]	2020	13-55	100	Retrospective study	Moderate
Fortepiani L et al.,[14]	2021	25.8 ± 5.0	28	Cohort study	Moderate
Mishra Deepak et al.,[15]	2020	26.6 ± 2.6	126	prospective, observational study	Moderate
Kiely, Patricia M. et al[16]	1983	19	6	Prospective study	High
Giuffrè, Giuseppe et al,[17]	2007	25 ± 6.4	16	Cohort study	Moderate
Millodot, M. et al[18]	1974	21-31	9	Experimental study	Moderate
Gong, Juan Fen et al[19]	2015	15-16	120	Cohort study	Moderate
Adhikari, Ambika et al[20]	2021	18-25	100	Prospective study	Moderate
Mondal A et al.,[21]	2021	18-24	60	Cohort study	Moderate
Fatih Ulaş et al.,[22]	2013	20-30	23	Prospective study	High
Chapman AB et al.,[23]	1997	21-40	16	Cohort study	Moderate
Haneda, Mayumi et al[24]	2022	21.3 ±4.0	26	Prospective study	Moderate
Guo L et al.,[25]	2021	27.0 ± 1.73	62	Prospective study	Moderate

with menstruation showed significant variations among age groups.[26] Reduction of tear stability in the follicular phase with tear break-up time (TBUT); no cyclic fluctuations were found with the ferning test.[7,26,27] Natural menstrual cycle changes can contribute to non-modifiable dry eye issues.[9] The following (Table 2) represents the tear film changes throughout the menstrual cycle.

4.2.2. Conjunctival changes

The conjunctiva can appear more congested and bloodshot during the menstrual cycle due to hormonal fluctuations that cause blood vessels in the conjunctiva to dilate. Specialists[9,28] demonstrated a strong correlation between hormonal oscillations, subjective complaints, tear generation, tear stability, surface dryness, and inflammation.[29] The Maturation Index (MI), which measures the maturity of conjunctival smears, varies with hormonal fluctuations during menstruation, with different types of conjunctival cells prevailing in each phase.[7] The relative number of conjunctival cells destroyed during exfoliation determines the MI. Parabasal cells are prevalent in atrophic settings (post-menopause or childhood). Intermediate cells dominate in the postovulatory phase due to progesterone. Superficial cells predominate in the follicular stage due to estrogen stimulation.

Hence, cyclic variations were observed in all three phases (menstrual phase: 68.5±4.5, follicular phase: 81.5±5.5, luteal phase: 64.5±2.5), and similar results were seen in dry eye conditions.[7,30] The brush cytology score for inflammation follows a pattern of (3.8±1.1) in the menstruation phase, (5.2±1.5) in the follicular phase, and (3.3±1.6) in the luteal phase, with a higher score indicating a shift towards a pathological value.

4.3. Corneal changes

According to the authors, early in the cycle is when the central cornea is thinnest. Ovulation and the cycle's conclusion were linked to increased corneal thickness[10] In another study, A pachymeter corneal thickness test showed no variations in thickness between the left and right eyes. However, it revealed significant thickening of the cornea during the luteal phase compared to ovulation and the menstrual phase.[12,13] Studies[5,31] a progressive decrease in corneal thickness from the menstrual phase to the ovulatory phase, followed by an increase until the luteal phase. Estrogen and progesterone, discovered in human corneal receptors, are believed to play a role in corneal physiology as these hormones are entrenched in the corneal nucleus.[32–35]

Menstruating women exhibited thicker corneas but thinner foveae. Central corneal thickness was higher during ovulation compared to the start and end of the menstrual cycle.[14,15,36] Assessing menstrual history is recommended for female patients undergoing refractive surgery due to potential impacts on surgical outcomes.

Table 2: Tear film changes observed in the menstrual cycle

Studies	Parameters	Follicular phase (Mean and Standard Deviation)		Ovulation (Mean	Luteal phase	Outcome/ p-value
	The Ocular Surface Disease Index (OSDI) questionnaire (score)	4.5 (±1.5)		5.8 (±2.1)	7.8 (±2.8)	Increased score in Luteal Phase – Worsening of symptoms in the Luteal Phase in comparison to the other two p-value: 1 vs. 2 = 0.0001; 1 vs. 3 =0.001; 2 vs. 3 = 0.0001
Versura P et al.,[7]	Tear production (mm)	Schirmer I	15.8 (±10.2)	17.3 (±6.3)	14.7 (±9.4)	It was not significant in cyclic variation but showed variation concerning age p-value: 1 vs. 2 =0.5; 1 vs. 3 = 0.7; 2 vs. 3 =0.3 1 vs. 2 =0.5; 1 vs. 3 =0.2; 2 vs. 3 = 0.4
		Schirmer II (Jones test)	7.2 (±2.1)	7.6 (±1.9)	8.1 (±2.4)	
	Tear stability (sec)	Break-up Time	11.1 (±1.9)	12.1 (±2.4)	13.4 (±1.8)	Reduced tear stability found in the Follicular phase p-value: 1 vs. 2 = 0.15; 1 vs. 3 = 0.03; 2 vs. 3 = 0.001
		Ferning test	2.2 (±0.6)	2.1 (±0.3)	1.9 (±0.5)	No significant cyclic variation observed p-value: 1 vs. 2 = 0.5; 1 vs. 3 = 0.09; 2 vs. 3 = 0.1
	Tear Function Index	184.5 (±36.8)		165.7 (±39.7)	154.6 (±28.9)	It correlates Production and Drainage and found no cyclic fluctuations p-value: 1 vs. 2 = 0.2; 1 vs. 3 = 0.06; 2 vs. 3 = 0.5
	Serum albumin in tears (mg/ml)	0.196 (±0.03)		0.364 (±0.10)	0.180 (±0.02)	Increased concentration of exudated serum of tears in follicular phase as compared to the other two phases p-values: 1 vs. 2 = 0.0001; 1 vs. 3 = 0.08; 2 vs. 3 =] 0.0001
Oboh, Roland A et al.,[8]	Tear production	26.73		28.34	24.23	A significant increase in production was observed in the follicular phase (0.0008) and decreases in the luteal phase of the cycle (0.002)
Colorado LH et al.,[4]	OOC (0–100) Overall Ocular Comfort	21 (± 20)		26 (± 23)	33 (±23)	A high score was found in the luteal phase (p = 0.047)
	Tear Break-up Time (sec)	5.8 (± 2.9)		5.4 (± 2.8)	4.8 (±2.3)	Tear break-up time found to be less in the luteal phase (p = 0.020)
	The Ocular Surface Disease Index score	43.4 (± 21.6)		59.8 (± 23.7)	54.8 (±23.9)	The score found in the follicular phase was lower than the other two phases (p = 0.004)
Cavdar E et al.,[9]	Tear Break-up Time (TBUT) (sec)	Right Eye	11.0 (± 4.6)	11.1 (± 7.0)	9.6 (± 5.8)	No significant difference observed (p > 0.05)
		Left Eye	10.0 (± 4.3)	10.1 (± 5.7)	9.1 (± 5.2)	
	Schirmer (mm)	Right Eye	14.0 (± 7.1)	12.8 (± 5.3)	13.4 (± 5.5)	
		Left Eye	13.7 (± 7.2)	14.0 (± 6.5)	12.7 (± 5.6)	

Table 3: Corneal changes observed in the menstrual cycle

Studies	Follicular Phase Micron (SD)		Ovulation Micron (SD)		Luteal Phase Micron (SD)		Outcome/ p-value
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye	
Ghahfarokhi, Negar Amiri et al.[12]	540.82 (±11.70)	541.40 (±11.36)	555.98 (±7.26)	556.50 (±7.11)	535.48 (±13.8)	536.38 (±12.83)	The variation in corneal thickness between menstrual cycle phases was statistically significant (P < 0.001).
Kiely, Patricia M. et al.,[16]	Increased corneal thickness observed towards the ovulatory phase of the cycle		Thickening of cornea observed		Moderate thinning was observed at the end of the cycle		_____
Goldich Y et al.,[10]	535 (±40)		542 (±41)		543 (±42)		The central cornea was least thick at the start of the menstrual cycle and statistically substantially thicker at ovulation and at the end (P<.001).
Mishra Deepak et al.,[15]	541.68 (±4.15)	541.84 (±4.27)	559.08 (±4.50)	559.35 (±4.50)	544.44 (±8.06)	544.65 (±8.06)	When compared to the beginning and end of the menstrual cycle, the CCT value was considerably (P<0.001) greater during ovulation.
Kardam Vyas, A et al.[13]	533.24 (±29.4)	534.49 (±30.08)	547.51 (±31.8)	548.25 (±29.9)	537.22 (±29.6)	538.28 (±29.97)	Thickest observedin ovulation and its thinnest in the follicular phase(p <0>).
Giuffrè, Giuseppe et al,[17]	536 (±42)		549 (±46)		559 (±44)		At ovulation and the conclusion of the cycle, the difference in corneal thickness was statistically significant (P = 0.003 and P = 0.001, respectively).
Fortepiani L et al.,[14]	569 (± 47.5)		_____		577 (± 39.8)		Increase in CCT towards the end of the cycle (p = 0.080)

Study[16] discovered both the horizontal and vertical meridians' steepens centrally at the start of the cycle, contradicting findings agreed with those reported by experts[17,37] flattening of meridians after ovulation. Blood estrogen shows significance with horizontal keratometry values during the follicular phase.[18] It was hypothesized that a decrease in estrogen levels during the menstrual cycle would result in a steepening of horizontal corneal curvature.[9] Corneal sensitivity was low before the menses, as the sensitivity threshold increased in a few studies[12,18,38] Another study reported that the drop in corneal sensitivity was linked to the preovulatory estrogen peak.[39] (Table 3) shows corneal changes during the menstrual cycle.

4.3.1. Refractive changes

Multiple studies[31,40] support the link between cyclical variations in blood estrogen levels and changes in ocular surface stability during the menstrual cycle. In the follicular stage, visual discomfort was reported for six minutes, leading decreased visual acuity beyond the usual baseline of 0.02 logarithm.[12] Significant differences were observed in cylinder lens, meridian, and interpupillary distance in nearsighted healthy females during the menstrual cycle.[19] The spherical lens revealed a measurably stark contrast between all of them.[41] Estrogen levels significantly affected corneal curvature, emphasizing their impact on refractive surgery outcomes. Refractive parameters remained unchanged throughout the cycle.[9]

4.3.2. Intraocular pressure

A correlation between intraocular pressure (IOP) and the menstrual cycle was found in the study,[31] with variations observed at different cycle stages. Administration of progesterones and estrogens, either alone or together, resulted in a slight decrease in IOP. These findings support previous research indicating that natural hormonal changes during the menstrual cycle do not significantly affect IOP or aqueous flow.[36,40] Study[20] emphasized the importance of considering significant IOP fluctuations in both eyes throughout the menstrual cycle, with the highest level during the menstrual phase and the lowest during the secretory phase. Intraocular pressure peaks in the middle of the cycle was seen in a study on days 13-15, compared to days 1-3 and 26-28[41] (Table 4) for a visual representation of intraocular changes during the menstrual cycle.

4.3.3. Anterior chamber

Researchers[14] can not infer the route of action of progesterone or estrogen at experimental medication dosages. However, the absence of impact on aqueous input suggests that the steroid effect mainly focused on the outflow channels. A decrease in the rate of aqueous production was observed on days 14 and 25 compared to days 1 or 7, indicating a consistent reduction. Statistical analysis revealed a significant variation in the rate of aqueous production, which correlated with the values of the outflow facility, suggesting that both were influenced by hormonal changes.[42] In contrast, other studies found no association between menstruation, aqueous flow rate, or intraocular pressure. Additionally, no significant difference was observed in Anterior Chamber Depth across the follicular, ovulation, and luteal phases.[21,40,43]

4.4. Crystalline lens changes

Research suggests indirect effects of the menstrual cycle on the lens, including a higher risk of developing cataracts in the late luteal phase compared to the early follicular phase. This shift can be attributed to menstrual-related symptoms such as headaches, drowsiness, irritability, trouble reading, and blurred vision. The study did not experience accommodation issues before menstruation, but the overall amplitude of accommodation was low and decreased during menstruation. Over time, the crystalline lens developed a more spherical shape with increased thickness due to accommodation and ageing. The accommodation also led to changes in the curvature radius on the lens's posterior lens.[31]

4.4.1. Accommodative responses

During menstruation, women may experience accommodative problems such as the limited magnitude of accommodation, accommodative insufficiency, and accommodative infacility.[9] Menstrual-related symptoms have been observed, including headache, poor focus, irritation, trouble reading, obstructive vision after prolonged close work, and blurred vision. A study reported that during the follicular phase, the amplitude of accommodation needed was higher than what was available, accommodative insufficiency was present, and there was difficulty with -2D accommodative flippers. Many cases showed a significant amount of accommodation lag. However, these issues disappeared in the ovulatory phase, indicating a shift in adaptation.[21] Visual discomfort during the follicular stage decreased resistance to contact lens wear, and changes in visual performance have also been noted.[44] The following table (Table 5) represents the accommodative changes in the menstrual cycle.

4.4.2. Colour vision discrimination

Authors[4,45] During ovulation, colour discrimination was highest compared to other menstrual cycle phases, according to studies. The Farnsworth-100-color Munsell's arrangement test was used to evaluate colour perception, and it showed that colour prejudice was highest during ovulation. However, the impact on visual acuity or contrast sensitivity was not noticeable. The values for colour discrimination were lower at the beginning and end of the phase than at ovulation. It is unclear whether the improved

Table 4: Intraocular pressure changes observed in the menstrual cycle

Studies	Menstrual Phase (Mean and Standard Deviation) (mmHg)		Proliferative Phase (Mean and Standard Deviation) (mmHg)		Secretory Phase (Mean and Standard Deviation) (mmHg)		Outcome/ p-value
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye	
Adhikari Ambika et al.,[20]	13.85	14.74	15.54	15.69	15.96	16.06	IOP significantly variesacross different menstrual phases (p <0.001)
Rana Pooja et al.,[11]	12.65 (±2.48)	12.86 (±2.16)	13.15 (±2.29)	13.25 (±2.08)	13.03 (±2.48)	12.91 (±2.17)	P= 0.000
Fatih Ulaş et al.,[22]	15.10 (±3.58)		14.55 (±2.78)		14.84 (±3.65)		Not significant (P=0.259)
Guo L et al.,[25]	15.16 (±1.74)		14.9 (±1.47)		15.3 (±1.19)		Not significant (P =0.15)
Fortepiani L et al.,[14]	15.9 (± 4.19)		—		16.4 (± 2.76)		Not significant

Table 5: Accommodative changes observed in the menstrual cycle

Studies	Parameter	Before Menstruation	During Menstruation	Outcome/ p-value
Mondal A et al.,[21]	The amplitudeof Accommodation (D)	10.3 (±2.8)	7.1 (±2.0)	During Ovulation, the Amplitude of Accommodation was receded (p-value<0.001)
	Lag of Accommodation (D)	+0.50 (±0.25)	+1 (±0.25)	Lag of accommodation was observed in females during their menstruation (p =0.000)
	Difficulty with Monocular Accommodative Facility with -2.00DS (Cycle per minute)	60	14	During menstruation difficulty with -2D was faced in the monocular estimated method MEM (p=0.000)
	Accommodative Insufficiency	9.5 (±4.6)	5.2 (±2.5)	Insufficient Accommodation observed during menstruation (p<0.001)
	Accommodative Infacility	60	56	Not significant
	Accommodative Excess	60	60	Not significant

colour vision during ovulation is solely due to hormone shifts or if other factors related to women's mental health play a role. Hormonal factors, such as estradiol, may affect the cortical circuitry involved in colour perception along the visual pathway.

4.4.3. Choroidal changes

Choroidal thickness in young, healthy women undergoes significant changes throughout the menstrual cycle. During the mid-luteal phase, choroidal thickness decreases dramatically compared to the other two phases. On the other hand, choroidal thickness typically increases from the follicular to the ovulatory stages until the mid-luteal stage when it drops significantly.[22,40] The most substantial increases in choroidal thickness were observed in the central, temporal, and nasal choroidal segments during the early follicular and mid-luteal phases. These thicker segments exhibited a greater amplitude of choroidal change.[4,22] It is essential to standardise the timing of choroidal layer thickness measurements in fertile women to improve the interpretation of OCT data. The manual calculation is currently used for choroidal segmentation since no computerised technique is available. The mid-luteal phase was associated with lower serum osmolality compared to the mid-follicular phase, while arterial pressure and pulse rate did not significantly change throughout the follicular, ovulatory, and mid-luteal phases.[22,23] Choroidal blood flow velocity decreases in the late follicular phase and increases in the mid-luteal phase, as measured by laser speckle flowgraph (LSFG) using mean blur rate (MBR)

as a quantitative index of relative blood flow velocity. The LSFG index was 7.7% higher in the mid-luteal phase than in the late follicular phase. Therefore, considering the menstrual cycle is crucial for interpreting LSFG reports in the future.[24] The choroidal vascularity index (CVI) varies in the menstrual cycle's mid-luteal phase. It is essential to consider while assessing choroidal structures in healthy women. The mean sub-foveal, nasal, and temporal choroidal thickness, and even choroidal vascularity index, significantly changed in the mid-luteal phase concerning the early follicular and ovulatory phase.[46] The following table (Table 6) illustrates the choroidal changes during the menstrual cycle.

4.4.4. Retinal changes

Studies[22,28] have indicated that axial length (AL) and refractive defects may influence retinal microvascular alterations. However, there was no statistically significant difference in mean arterial pressure (MAP), spherical equivalent (SE), intraocular pressure (IOP), foveal avascular zone (FAZ) area, or superficial retinal capillary plexus-perfusion density (SCP-PD) parameters. Negative correlations were found between macular flow densities and AL. Increased MAP has been associated with the narrowing of the major retinal artery and enlargement of the central retinal vein. Hypertension-induced changes in the retinal microcirculatory system may impact retinal thickness. Others[25] have hypothesized that changes in the structure and function of the retinal microcirculatory system brought on by hypertension might impact retinal thickness. Contrasting reports exist regarding the association between serum osmolality changes and blood pressure during the menstrual cycle. Some studies have reported a mean arterial and serum osmotic pressure drop during the mid-luteal phase, suggesting vasodilation.[43,46,47] Other studies have reported a drop in serum osmolality from the follicular to the luteal stage without changes in blood pressure. In the ovulatory phase, lower deep retinal capillary plexus-perfusion density (DCP-PD) parameters were observed in specific retinal subfields. When interpreting DCP-PD parameters using OCTA in healthy women, the menstrual phase should be considered. The following table (Table 7) represents the retinal changes during the menstrual cycle.

Further research is needed to understand vascular changes in the retina throughout the menstrual cycle.[25] On the other hand, there needs to be more information on the vascular changes in the retina throughout a woman's monthly menstrual cycle.

4.4.5. Visual field changes

In scientific investigations, healthy females have shown significant shifts in short-wavelength automated perimetry (SWAP) mean sensitivity during menstruation, as evidenced by studies[14,30,48,49] These shifts in visual field sensitivity coincide with the oscillations of sex hormones over the menstrual cycle. However, standard achromatic automated perimetry (SAP) tests did not reveal such distinctions. The variations observed in SWAP test results suggest that it may be more sensitive to detecting minor alterations in visual field analysis influenced by sex hormones in healthy women.[48]

5. Implications

Parameters affecting ocular physiology or not should be known by the practitioners. Before making any diagnosis or including or excluding female subjects from research studies, consider the impact of hormonal fluctuations on female ocular indices.

Eye blink rate (EBR)- No significant differences were observed across the menstrual cycle. Sometimes females are excluded from the study due to a lack of knowledge during their menstrual cycle.

Tear film- Suitability for contact lenses as the females show dry eye symptoms during the follicular stage of the menstrual cycle.

Cornea- Fluctuations in corneal thickness, i.e., thinnest in the beginning and thickest at the end of the cycle, should be considered before assessing the females during their cycle. It might give false readings in a menstruating woman who comes for an eye examination, especially in some diseases like keratoconus, glaucoma, and many more. Such corneal alterations may be significant to consider when assessing candidates for laser refractive surgery, and thickness matters even before planning any corneal or refractive surgeries.

Corneal sensitivity- Due to decreased sensitivity during the luteal phase compared to the menstrual phase, foreign body invasion and adaptation to contact lens usage may be negatively impacted. Tolerance, however, may decrease when sensitivity levels revert to the baseline.

Accommodative- Knowing a patient's menstrual cycle status is crucial for determining whether their condition requires accommodative treatment because the cycle phases alter accommodative reactions.

Intraocular pressure- The intraocular pressure varies significantly throughout the menstrual cycle, which is vital for many diseases like glaucoma diagnosis and treatment. It is also essential to comprehend these variations before deciding on any medication or surgical procedures.

Color vision- Improvement of colour vision observed in the ovulatory period should be accounted for while recording colour vision and even if female subjects are involved in any research studies.

Choroid- Choroidal thickness increases between the follicular and ovulatory stages, so there is a need for standardized scheduling of choroidal layer thickness in women of fertile age to improve the applicability of the analysis of OCT. Furthermore, The MBR was also 7.7% greater in the mid-luteal phase compared to the late

Table 6: Choroidal changes observed in the menstrual cycle

Studies	Parameter	Follicular Phase	Ovulatory Phase	Luteal Phase	Outcome/ p-value
Fatih Ulaş et al.,[22]	Subfoveal CT (mm)	383.87 (± 84.4)	373.74 (±82.4)	359.09 (± 79.7)	Choroidal thickness was observed to be decreased in the mid-luteal phase (p= <0.001) A significant difference between follicular and luteal phase (p= <0.001)
	Range	232–472	232–488	225–465	
	Temporal CT (mm)	350.61 (±76.1)	343.70 (±75.5)	329.65 (±72.2)	
	Range	210–465	210–480	196–442	
Chapman AB et al.,[23]	Arterial pressure (mmHg)	70.22 (±3.69)	69.33 (±4.63)	69.84 (±4.18)	No significant difference found
	Pulses (beats per minute)	66.39 (±3.33)	67.39 (±2.73)	66.30 (±2.31)	
	Osmolarity, mol/kgH2O	287.4 (± 0.9)	—	282.3 (± 0.9)	Concentration and osmolarity were reduced in the luteal phase (p <0.01)
	Serum Na, meq/l	139.5 (± 0.3)	—	138.2 (± 0.4)	
	mean arterial pressure (MAP)	81.7 (± 2.0)	—	75.4 (± 2.3)	It reduces in the luteal phase in comparison with the follicular phase (p< 0.005)

Table 7: Retinal changes observed in the menstrual cycle

Studies	Parameter		Follicular Phase	Ovulatory Phase	Mid-Luteal Phase	Outcome/ p-value
Chapman AB et al.,[23]	Serum osmolarity		287.4 (± 0.9)	_	282.3 (± 0.9)	Serum osmolarity was observed to decrease in the mid-luteal phase in comparison to the follicular phase (p <0.01)
Guo L et al.,[25]	DCP-PD	Nasal	56.39 (±3.0)	54.11 (±2.9)	55.70 (±3.3)	Deep retinal capillary plexus were significantly low in Nasal and Inferior ETDRS subfields during the Ovulatory phase (p < 0.001)
	Deep retinal capillary plexus	Inferior	54.86 (±2.5)	52.90 (±3.3)	55.21 (±2.6)	

follicular phase, suggesting that the menstrual cycle may need to be considered in interpreting LSFG data in the future.

Retina- Menstrual phase should be considered if any significant changes are observed in the partial subfield of DCP-PD while assessing healthy menstruating women, especially in the nasal and inferior macular subfield**.**

6. Limitations of the Studies

Limitations of the evidence included in this study were the small sample size.[4,13,15,22,24,25] A hormonal blood test was not performed to assess the variation in hormone levels, and hormone levels were not quantified biochemically to acquire a better understanding.[4,13,15,20,25] Lack of assessment of the choroidal changes, the relationship between choroidal function and morphology in healthy subjects in all menstrual cycle phases.[22,24] CCT and LH levels were not correlated because LH levels were not assessed throughout the menstrual cycle, which could be included in further studies.[15]

Further research can be conducted to understand better how IOP fluctuates during menstruation in different age groups and glaucoma patients. Furthermore, no hormonal profile was measured in this investigation to directly correlate IOP alterations and ocular parameters to hormonal changes such as estrogen, progesterone, or LH. In the future, this may be regarded as a field of study for researchers.[20] The effects of hormone concentrations, other vasoactive drugs, and menstrual cycle anomalies must also be investigated.[25]

7. Conclusions

The eye reacts to sexual hormones, and many researchers have investigated the intricate alterations in a woman's eyes during menstruation. These modifications may affect everything from the anterior segment's properties to the choroids' changes. Because of this, concerns have arisen over the effect of female hormone levels on the circulation of the eye. As part of this assessment, we concluded that there is significant data on the ocular alterations that occur throughout a woman's menstrual cycle and sometimes

conflict.

8. Source of Funding

None.

9. Conflict of Interest

None.

References

1. Nillni YI, Toufexis DJ, Rohan KJ. Anxiety Sensitivity, the Menstrual Cycle, and Panic Disorder: A Putative Neuroendocrine and Psychological Interaction. *Clin Psychol Rev*. 2011;31(7):1183–91.
2. Thimm M, Weis S, Hausmann M, Sturm W. Menstrual Cycle Effects on Selective Attention and Its Underlying Cortical Networks. *Neuroscience*. 2014;258:307–17.
3. Fehring RJ, Schneider M, Raviele K. Variability in the Phases of the Menstrual Cycle. *J Obstet Gynecol Neonatal Nurs*. 2006;35(3):376–84.
4. Colorado LH, Edwards K, Dinh L, Ha S, Liu D, Luu A, et al. Associations between the menstrual cycle, lifestyle factors and clinical assessment of the ocular surface: a prospective observational study. *BMC Womens Health*. 2020;20(1):23.
5. Feldman F, Bain J, Matuk AR. Daily Assessment of Ocular and Hormonal Variables Throughout the Menstrual Cycle. *Arch Ophthalmol*. 1978;96(10):1835–8.
6. Whiting P, Savović J, Higgins JPT, Caldwell DM, Reeves BC, Shea B, et al. ROBIS: A new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol*. 2016;69:225–34.
7. Versura P, Fresina M, Campos EC. Ocular Surface Changes over the Menstrual Cycle in Women with and without Dry Eye. *Gynecol Endocrinol*. 2007;23(7):385–90.
8. Oboh RA, Onwukwe NA, Mube WA, Uzoechi NC. Effect of Menstruation on Tear Production Among Undergraduate Students of Madonna University. 2021;3(4):42–51.
9. Cavdar E, Ozkaya A, Alkin Z, Ozkaya HM, Babayigit MA. Changes in Tear Film, Corneal Topography, and Refractive Status in Premenopausal Women during Menstrual Cycle. *Cont Lens Anterior Eye*. 2014;37(3):209–12.
10. Goldich Y, Barkana Y, Pras E, Fish A, Mandel Y, Hirsh A, et al. Variations in Corneal Biomechanical Parameters and Central Corneal Thickness during the Menstrual Cycle. *J Cataract Refract Surg*. 2011;37(8):1507–11.
11. Rana P. Study of Corneal Thickness Changes during Different Phases of Menstrual Cycle (Doctoral dissertation, Sumandeep Vidyapeeth); 2018.
12. Ghahfarokhi NA, Vaseghi A, Ghahfarokhi NA, Ghoreishi M, Peyman A, Dehghani A, et al. Evaluation of Corneal Thickness Alterations during Menstrual Cycle in Productive Age Women. *Indian J Ophthalmol*. 2015;63(1):30–2.
13. Vyas AK, Rana P, Kothari RN, Patel Z, Soni A. A Retrospective Study: Impact of Various Phases of Menstrual Cycle on Corneal Pachymetry. *Indian J Clin Exp Ophthalmol*. 2020;6(1):114–6.
14. Fortepiani L, Foutch BK, Wilson MR. The Effects of Sex, Oral Contraception, and Menstrual Cycle Phase on Intraocular Pressure, Central Corneal Thickness, and Foveal Thickness: A Descriptive Analysis. *Vision (Basel)*. 2021;5(4):48.
15. Mishra D, Bhushan P, Sachan S, Singh MK, Jayadev C, Kusumgar P. Variations in the Central Corneal Thickness during the Menstrual Cycle in Indian Women. *Indian J Ophthalmol*. 2020;68(12):2918–20.
16. Kiely PM, Carney LG, Smith G. Menstrual Cycle Variations of Corneal Topography and Thickness. *Am J Optom Physiol Opt*. 1983;60(10):822–9.
17. Giuffrè G, DiRosa L, Fiorino F, Bubella DM, Lodato G. Variations in central corneal thickness during the menstrual cycle in women. *Cornea*. 2007;26(2):144–6.
18. Millodot M, Lamont A. Influence of Menstruation on Corneal Sensitivity. *Br J Ophthalmol*. 1974;58(8):752–6.
19. Gong JF, Xie HL, Mao XJ, Zhu XB, Xie ZK, Yang HH, et al. Relevant Factors of Estrogen Changes of Myopia in Adolescent Females. *Chin Med J (Engl)*. 2015;128(5):659–63.
20. Adhikari A, Shet R, Mandal R, Vaghela Y. Variations in Intraocular Pressure During Different Phases of Menstrual Cycle. *J Ophthalmol Res*. 2021;4(2):183–91.
21. Mondal A, Babu A. Accommodative Inertia in Menstruation. *RGUHS J Allied Health Sci*. 2021;1(2):6–10.
22. Ulaş F, Doğan Ü, Duran B, Keleş A, Ağca S, Çelebi S, et al. Choroidal thickness changes during the menstrual cycle. *Curr Eye Res*. 2013;38(11):1172–81.
23. Chapman AB, Zamudio S, Woodmansee W, Merouani A, Osorio F, Johnson A, et al. Systemic and renal hemodynamic changes in the luteal phase of the menstrual cycle mimic early pregnancy. *Am J Physiol*. 1997;273(5):777–82.
24. Haneda M, Hashimoto Y, Mishima A, Saito D, Yoshitomi T, PLoS One. Changes in Choroidal Circulation Hemodynamics during the Menstrual Cycle in Young, Healthy Women. *PLoS One*. 2022;17(6):e0270501–10.
25. Guo L, Zhu C, Wang Z, Gao Z, Zhang Z, Pan Q, et al. Retinal Vascular Changes during the Menstrual Cycle Detected with Optical Coherence Tomography Angiography. *J Ophthalmol*. 2021;2021:5514575.
26. Tatlipinar S, Gedik Ş, Irkeç M, Orhan M, Erdener U. Ocular ferning during the menstrual cycle in healthy women. *Eur J Ophthalmol*. 2001;11(1):15–8.
27. Masmali AM, Purslow C, Murphy PJ. The tear ferning test: a simple clinical technique to evaluate the ocular tear film. *Clin Exp Optom*. 2014;97(5):399–406.
28. Johnson ME, Murphy PJ. Changes in the Tear Film and Ocular Surface from Dry Eye Syndrome. *Prog Retin Eye Res*. 2004;23(4):449–74.
29. Srivatsa LP. Daily assessment of ocular variables throughout the menstrual cycle. *Metab Pediatr Syst Ophthalmol (1985)*. 1988;11(3):113–4.
30. Kramer P, Lubkin V, Potter W, Jacobs M, Labay G, Silverman P. Cyclic changes in conjunctival smears from menstruating females. *Ophthalmology*. 1990;97(3):303–7.
31. Soni PS. Effects of Oral Contraceptive Steroids on the Thickness of Human Cornea. *Am J Optom Physiol Opt*. 1980;57(11):825–34.
32. Wickham LA, Gao J, Toda I, Rocha EM, Ono M, Sullivan DA. Identification of Androgen, Estrogen and Progesterone Receptor MRNAs in the Eye. *Acta Ophthalmol Scand*. 2000;78(2):146–53.
33. Hadeyama T, Nakayasu K, Ha NT, Nakamura S. Expression of estrogen receptors alpha and beta, androgen receptors and progesterone receptors in human cornea. *Nippon Ganka Gakkai Zasshi*. 2002;106(9):557–64.
34. Suzuki T, Kinoshita Y, Tachibana M, Matsushima Y, Kobayashi Y, Adachi W, et al. Expression of Sex Steroid Hormone Receptors in Human Cornea. *Curr Eye Res*. 2001;22(1):28–33.
35. Gupta PD, Johar K, Nagpal K, Vasavada AR. Sex Hormone Receptors in the Human Eye. *Surv Ophthalmol*. 2005;50(3):274–84.
36. Oliver KM, Walsh G, Tomlinson A, Mcfadyen A, Hemenger RP. Effect of the Menstrual Cycle on Corneal Curvature. *Ophthalmic Physiol Opt*. 1996;16(6):467–73.
37. Manchester PT. Hydration of the Cornea. *Trans Am Ophthalmol Soc*. 1970;68:425–61.
38. Guttridge NM. Changes in Ocular and Visual Variables during the Menstrual Cycle. *Ophthalmic Physiol Opt*. 1994;14(1):38–48.
39. Riss B, Binder S, Riss P, Kemeter P. Corneal Sensitivity during the Menstrual Cycle. *Br J Ophthalmol*. 1982;66(2):123–6.
40. Dadaci Z, Alptekin H, Acir NO, Borazan M. Changes in choroidal thickness during pregnancy detected by enhanced depth imaging optical coherence tomography. *Br J Ophthalmol*. 2015;99(9):1255–9.
41. Schmalenberger KM, Tauseef HA, Barone JC, Owens SA, Lieberman L, Jarczok MN, et al. How to Study the Menstrual Cycle: Practical Tools and Recommendations. *Psychoneuroendocrinology*. 2021;123:104895.

42. Vaid RL, Buchh H, Ahuja L, Wali V. Rate of Aqueous Formation during Normal Menstrual Cycle. *Indian J Ophthalmol*. 1975;23(2):1–6.
43. Hashemi H, Mehravaran S, Rezvan F. Changes in corneal thickness, curvature, and anterior chamber depth during the menstrual cycle. *Can J Ophthalmol*. 2010;45(1):67–70.
44. Brule J, Lavoie MP, Casanova C, Lachapelle P, Hébert M. Evidence of a Possible Impact of the Menstrual Cycle on the Reproducibility of Scotopic ERGs in Women. *Doc Ophthalmol*. 2007;114(3):125–34.
45. Giuffrè G, Rosa LD, Fiorino F. Changes in Colour Discrimination during the Menstrual Cycle. *Ophthalmologica*. 2006;221(1):47–50.
46. Aşikgarip N, Temel E, Örnek K. Assessment of Choroidal Vascularity Index during the Menstrual Cycle. *Eur J Ophthalmol*. 2022;32(5):2740–6.
47. Deschênes MC, Descovich D, Moreau M, Granger L, Kuchel GA, Mikkola TS, et al. Postmenopausal Hormone Therapy Increases Retinal Blood Flow and Protects the Retinal Nerve Fiber Layer. *Invest Ophthalmol Vis Sci*. 2010;51(5):2587–600.
48. Akar Y, Yucela I, Akarb ME, Taskinb O, Özera HO. Menstrual cycle-dependent changes in visual field analysis of healthy women. *Ophthalmologica*. 2005;219(1):30–5.
49. Seymenoğlu G, Baser EF, Zerdeci N, Gülhan C. Corneal Biomechanical Properties during the Menstrual Cycle. *Curr Eye Res*. 2011;36(5):399–403.

Author biography

Animesh Mondal, Assistant Professor https://orcid.org/0000-0002-6372-4220

Nishtha Verma, Optometrist https://orcid.org/0000-0002-9428-4467

Sourav Karmakar, Assistant Professor https://orcid.org/0000-0002-7754-0289

Gaurav Kumar Bhardwaj, Associate Professor https://orcid.org/0000-0002-3542-8977

Cite this article: Mondal A, Verma N, Karmakar S, Bhardwaj GK. Clinical implementation of ocular health findings in different phases of the menstruation cycle - A systematic review. *Indian J Clin Exp Ophthalmol* 2023;9(4):468-479.