

## Variations in Intraocular pressure (IOP) during different phases of Menstrual cycle among healthy young population.

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### Abstract:

**Aim:** To study the Variations in Intraocular pressure (IOP) during different phases of menstrual cycle among healthy young population.

**Methods:** A cross-sectional study. Healthy young female volunteers (n-46) with regular menstrual cycle and without any other ocular and systemic issues were included in the study. Menstrual, ocular and relevant data were collected using questionnaires. IOP was measured using computerized non-contact Tonometer individually for both the eyes during each phase of the cycle. The data were analysed using SPSS software version 17.0

**Results:** Data were analysed by ANOVA and with post hoc studies using Tukey HSD. Mean IOP of proliferative phase of right eye ( $14.41 \pm 2.67$ ) was mildly increased when compared to other two phases of the same eye and the mean IOP of luteal phase of the left eye is mildly increased ( $14.67 \pm 2.19$ ) when compared to other two phases in the same eye. Altogether there was a mild increase in the mean IOP in luteal phase of both the eyes when compared to menstrual and proliferative phase though the value of is  $P > 0.05$  which is statistically insignificant.

**Conclusion:** The current study concludes that there is no definite relationship of hormones of the menstrual cycle and IOP as the variation occurred in the values was statistically insignificant

**Keywords:** Intraocular pressure (IOP), Menstrual cycle, Oestrogen, Progesterone.

### I. Introduction

Intraocular Pressure (IOP) is the fluid pressure exerted by the intraocular fluid of the anterior cavity - Aqueous humour (Normal IOP-10-20mmHg). IOP is determined mainly by the balance between the production and drainage of aqueous humour [1,2]. Disparity in the production/drainage system of aqueous humour leads to increase in IOP than normal, which in turn causes optic nerve head damage and visual field defects [3,4]. Increased IOP is said to be a major risk for Glaucoma [5,6] a slow progressive neuro-degenerative disorder associated with death of retinal ganglion cells and degeneration of their connected optic nerve fibres which is second leading cause of irreversible blindness [1,2]. Women were found to be more prone for developing Glaucoma than men [7,8,9,10].

Menstrual cycle or the uterine cycle is the series of cyclic changes exhibited by female reproductive system for an average duration of 28 days, which commonly varies among individuals [11]. It is influenced by steroid sex hormones - Oestrogen, Progesterone, Follicular stimulating hormone (FSH) and Luteinising hormone (LH). These hormones were also reported to have protective role in ocular diseases in women [12]. The Menstrual cycle comprises of three phases (in normal 28 days cycle) [11]

- Proliferative phase → 4-14 days – Increased production of oestrogen
- Luteal phase → 15-28 days – Increased production of Progesterone
- Bleeding phase → 1-3 days – fall in level of oestrogen & progesterone

#### 1.1 Female sex hormones and IOP:-

Female sex hormones were reported to have influence on IOP. Oestrogen and progesterone receptors were found in human retina [13] and human ciliary epithelial cells were found to metabolise oestrogen, progesterone and androgens [14]. Subjects with primary open-angle glaucoma (POAG) were found with decreased levels of oestradiol [15,16]. Hormone replacement therapy with oestrogen and progesterone in post-menopausal women was found to be associated with reduced risk of glaucoma [17,18,19]. Also, it was reported that oestrogen and adrenocortical hormones share chemical similarity [20]. Interestingly, glucocorticoids receptors were found in human eye along with other sex hormone receptors [21]. Topical or systemic application

of glucocorticoids were found to decrease aqueous humour outflow and increase IOP [22,12,23]. Subjects with glaucoma were found to have increased cortisol level than normal individuals [24]. Thus, supporting the fact that female sex hormones influence IOP.

### 1.2 Menstrual cycle and IOP:-

Various opinions were reported regarding IOP changes during menstrual cycle. A study conducted on 75 healthy volunteers showed significant increase in IOP during different phases of menstrual cycle [25]. Fluctuation in IOP during all three phases [26] and marked increase in IOP during luteal phase was also reported [27]. During menstruation glaucoma and healthy individuals were reported to have increased IOP [28,29,30].

During pregnancy increase in IOP was reported which could be possibly due to the female sex hormone – Progesterone [31,32]. There are even studies reporting that female sex hormones doesn't influence IOP [33,34,35,36,37]. Thus the current study aimed at studying the variations in intraocular pressure during different phases of menstrual cycle among healthy young population.

## II. Methodology

The study was initiated after obtaining clearance from the Institutional ethical committee. A written informed consent was obtained from the participants following a brief explanation of the study procedure and its benefits. No stipend was given to the participants. Participants were healthy young females with regular endometrial cycle between the age group 18-28 yrs (n=46) excluding those with Glaucoma and other ocular pathologies, Diabetes Mellitus (DM), Hypertension (HT), and individuals in post-menopausal phase, pregnancy and undergoing Hormone-replacement therapy (HRT). Menstrual history, ocular history other required details of the participants were obtained using validated questionnaires. IOP was measured using Computerised Non-contact Tonometer.

### 2.1 Non-contact Tonometer:-

Computerised non-contact Tonometer is a non-invasive device used to measure IOP and the technique is called as Tonometry. The prototype was introduced by Grolman in 1972 [2,10]. The participants were comfortably seated on a stool facing the instrument and face resting on a chinrest. The instrument has a pneumatic system that generates a puff of air which is directed against the cornea. The central cornea is flattened, and at the point of corneal flattening the air column is shut off and the force is recorded and converted as IOP.

IOP was measured for both the eyes individually during each phase of the menstrual cycle. Three readings were taken and average of three is taken as mean IOP as IOP varies during phases of respiration [38].

## III. Results

Total number of participants enrolled for the study was 85 healthy female volunteers with regular menstrual cycle, but 39 of them dropped out due to their certain practical inconvenience. IOP was obtained from 46 participants and analysed statistically using SPSS software version 17.0 (n=46). The values were obtained for both the right and left eye separately during each phase.

Phases of menstrual cycle (right eye)	Mean (mmHg)	SD (mmHg)
Menstrual phase	14.1957	2.36286
Proliferative phase	14.2174	2.46678
Luteal phase	14.1087	2.34026

Table 1- Variations in IOP in right eye during all three phases of menstrual cycle

Phases of menstrual cycle (left eye)	Mean	SD (mmHg)
Menstrual phase	14.4130	2.67977
Proliferative phase	14.5870	2.85639
Luteal phase	14.6739	2.19144

Table 2- Variations in IOP in left eye during all three phases of menstrual cycle

The measurements were analysed by ANOVA and with post hoc studies using Tukey HSD. The mean values of IOP were varying within the phases and also between both right and left eye. The mean IOP of proliferative phase of right eye ( $14.41 \pm 2.67$ ) is mildly increased when compared to other two phases of the same eye and the mean IOP of luteal phase of the left eye is mildly increased ( $14.67 \pm 2.19$ ) when compared to other two phases in the same eye. Altogether there was a mild increase in the mean IOP in luteal phase of both

the eyes when compared to menstrual and proliferative phase though the value of is  $P \leq 0.05$  which is statistically insignificant.

Fig 1- Variations in IOP in right eye during all three phases of menstrual cycle

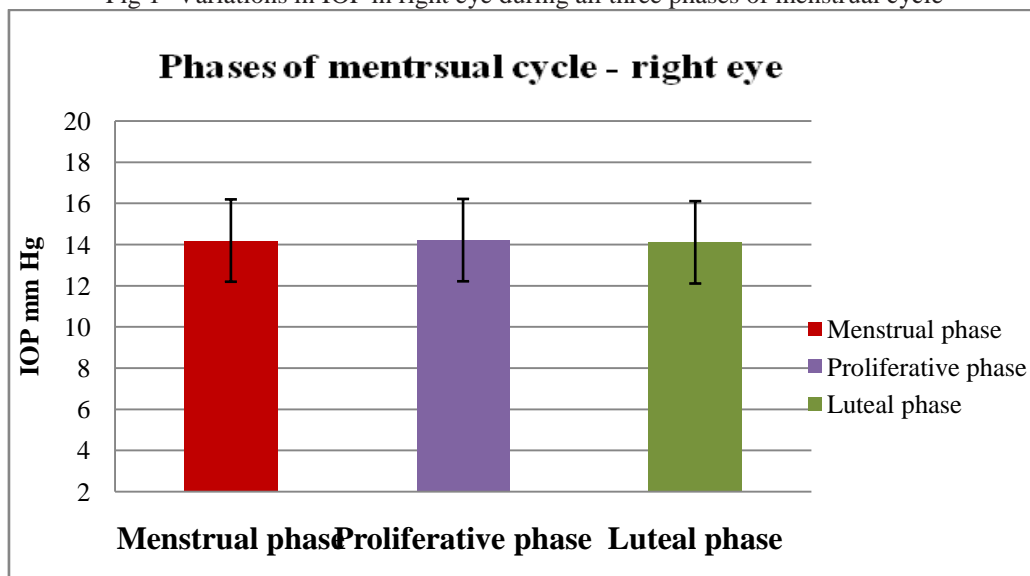
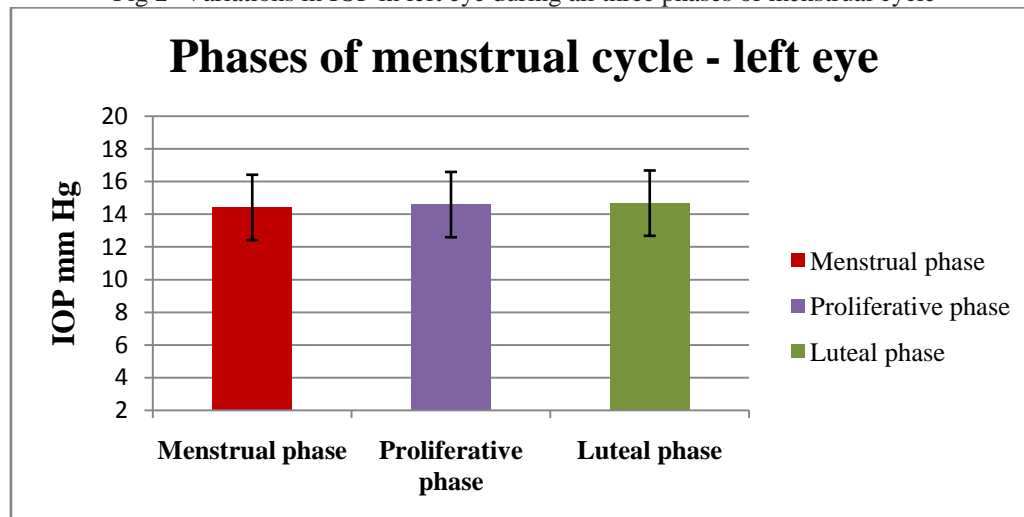


Fig 2- Variations in IOP in left eye during all three phases of menstrual cycle



#### IV. Discussion

The relationship between IOP and various hormones like corticosteroids, FSH, LH, Oestrogen, progesterone and androgens has been studied since years. The relationship of the gonadal functions on IOP was first done in 1920, after which the influence of sex hormones on IOP have been evaluated extensively by various studies [39,40].

In the current study, there is a mild borderline increase in IOP during luteal phase of both the eyes when compared to other phases. This shows that the increase may be due to progesterone. There is a very mild increase in IOP in the proliferative phase when compared to menstrual phase which may be due to peak of oestrogen.

There are studies that highlight about the protective role of sex hormones in different aspects during the lifetime of women. Oestrogen is found to be a neuroprotector and neuromodulator and in diseases associated with retinal ganglion cell death like glaucoma the neuroprotective effect of oestrogen has been proved to be beneficial [41,42].

Steroids are considered to play a most important role in the pathogenesis of ocular diseases. The role of effects of endogenous sex steroid produced in the ovary on retinal samples prepared from female rats was examined and concluded that neuroprotective effect of oestrogen may have therapeutic effects in retinal diseases associated with retinal ganglion cell death such as glaucoma [42]. The gene that codes for the enzymes that

metabolises sex steroid hormones have been discovered to be at higher levels in the ciliary epithelium of the human eye. The estrogen type 2 gene polymorphism and its relationship with elevation of IOP in glaucoma patients were confirmed which indicates the possible role of oestrogen in the regulation of IOP [43]. With these studies it is clear that oestrogen has a protective role in the regulation of IOP and hence the increase cannot be contributed by oestrogen.

Presence of sex steroid hormone receptors has been identified recently in lens, retina, choroid, cornea and ciliary body [13]. Sex and age related differences in oestrogen receptor expression were also detected in young female eyes but not in males and post-menopausal women<sup>(44)</sup>. But some of the studies say that there are separate receptors for female and male sex hormones in human eye [45,46]. This gives the idea that the exposure to endogenous sex hormones like oestrogen and progesterone during reproductive life of a woman plays an important role in various visual functions like prevention of retinal ganglion cell death, prevention of damage to optic nerve head, including the regulation of IOP [47]. The protective role of endogenous exposure of these hormones paved the way for the treatment of glaucoma in reducing the increased IOP. The postmenopausal women seem to be at higher risk to ocular hypertension and supplement with oestrogen and progesterone together or alone reduced the elevated IOP. Effect of HRT on tear function, lens opacity, ocular blood flow and intraocular pressure has been studied [48,49]. The effect of HRT in postmenopausal women has proven to reduce the elevated IOP [50,51,52] which shows the protective role of these hormones in the regulation and pathogenesis of glaucoma [16,45,46,47]. The risk of postmenopausal women for ocular hypertension may be due to lack of hormones. Hence it is clear that there is definite relationship between the female sex hormones and IOP that it regulates and plays a protective role.

In the current study, there is a mild increase in the level of IOP during luteal phase compared to proliferative and menstrual phase though statistically found to be insignificant. The association of IOP with menstrual cycle, in early and late reproductive women, pregnancy and menopause have also been studied [27,31,32,35]. Even these studies concluded that there is no significant increase in IOP during various phases of menstrual cycle though there were fluctuations in the values. Our result goes in hand with study of Sheila P who did mention about increase of 1 mm Hg of IOP in the luteal phase approximately. The increase may be contributed by both the hormones as in the luteal phase progesterone is the hormone in peak and oestrogen which is moderately increased.

But apart from the hormones contributing for the elevation of IOP the corneal thickness also plays a role in regulation of IOP. Thinner corneas have a higher risk of developing POAG than eyes with thicker cornea [53]. Women generally have thinner cornea than men, which may have contributed for the mild increase in IOP. Along with this fact, blinking and eyes rubbing also increases IOP significantly [1]. Lens wearing women seemed to have increased progesterone level and progesterone has the capacity to change the surface properties of cornea [54]. As corneal thickness has a role in varying the values of IOP and with more young women using lens the study could be extended with people wearing lens and software professionals who are exposed to increased stress on eyes.

## **V. Conclusion**

This current study concludes that there is no definite relationship of hormones of the menstrual cycle and IOP as the variation occurred in the values was statistically insignificant. In current study hormonal assay was not done. Also the value of IOP was not measured during pre-menstrual period. Considering the conflicting reports by various studies and the above two deficiencies in the present study, it would be prudent to do this study on a larger scale with more subjects. A continuous measurement of IOP across all phases of menstrual cycle coupled with hormonal assay would add to the credibility of this study in drawing a definite relationship of IOP with various hormones associated with menstrual cycle.

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