Correlation of pupil-to-limbus diameter ratio with physiological hemodynamic parameters in different phases of menstrual cycle

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ABSTRACT

Background: There are changes in ovarian hormones throughout the menstrual cycle which is associated with alterations in neurohumoral mechanisms that regulate cardiovascular homeostasis. The pupil-limbus diameter ratio will give an idea about the status of autonomic functions. Aims and Objectives: The aim of this study was to correlate pupil-to-limbus diameter ratio (PLD) with physiological hemodynamic parameters, such as blood pressure (BP) and pulse rate in different phases of the menstrual cycle. Materials and Methods: It was a cross-sectional study conducted among the 1st-year and 2nd-year female MBBS students with the age of 17–22 years. Physiological hemodynamic parameters, such as pulse and BP, were measured in all the participants. After recording the photographs of eyes during follicular and luteal phase of menstrual cycle, it was transferred to the power point slides and the diameter was measured manually by the two-box method. Results: The PLD of the left eye and right eye between follicular and luteal phase ($P < 0.05$) was statistically significant. Conclusion: It is useful for detection of variations in autonomic functions during different phases of menstrual cycle in medical students so that intervention measures can be started at the earliest which will help to prevent further complications.

KEY WORDS: Pupil-Limbus Ratio; Hemodynamic Parameters; Menstrual Cycle; Autonomic Functions

INTRODUCTION

Females show cyclical changes during the reproductive period which is called the menstrual cycle. It is associated with psychological, physical, and behavioral changes.[1] Vital part of women life is menstrual cycle. There are changes in ovarian hormones throughout the menstrual cycle which is associated with alterations in neurohumoral mechanisms that regulate cardiovascular homeostasis.[1] During menstruation, estrogen and progesterone levels are low. After that, during follicular phase, there occurs gradual increase in estrogen which reaches peak just before ovulation due to the coordinated activity of gonadotropin-releasing hormones and gonadotropins secreted by the anterior pituitary, whereas in postovulatory, that is, luteal phase, corpus luteum secretes progesterone and estrogen and reaches a peak around 7 days after ovulation. Later, these hormones start declining if there is no fertilization and implantation.[2]

Sex hormones such as estrogen and progesterone released from the ovary and also gonadotrophic hormones such as follicle-stimulating hormone and luteinizing hormone secreted from the anterior pituitary regulate the menstrual, follicular, and luteal phases of the menstrual cycle.[3] Changes
in the functional variables of different systems may be related to variations in the levels of hormones across the menstrual cycle,[4] which, in turn, may be associated with autonomic modulation.[5]

The number of environmental factors may have an impact on the menstrual cycle such as psychosocial stress, disturbed endocrine functions, strenuous physical exercise, decreased body fat, and lifestyle factors, such as smoking and high fat consumption. All these together disturb menstruation and will have an impact on reproductive functioning in a woman.[6] Amount of body fat plays a pivotal role in reproductive functions. Either decreased or increased weight of an individual has detrimental effect on menstrual cycle and infertility.[7] As underweight girls’ population in India is considerable, they are highly prone for menstrual irregularities and infertility problems.[8]

PLD ratio is one of the developing autonomic function tests.[9] Pupil is constricted and dilated depending on the autonomic functions. Pupil dilates with increased sympathetic activity, whereas pupil constricts with increased parasympathetic activity. However, the limbus diameter remains constant. Hence, taking pupil limbus diameter ratio will give an idea about the status of autonomic functions. Understanding the activities of autonomic functions can benefit individuals to begin with various treatment modalities if there are any alterations. However, studies are limited in this area.[7]

There are very few studies related to autonomic function modulation during different phases of menstrual cycle.[10] However, literatures on pupil to limbus diameter ratio (PLD) as an autonomic function test in different phases of menstrual cycle and its correlation with physiological hemodynamic parameters are not available. Hence, the present study is designed.

Objective

The objective of this study was to correlate the PLD with physiological hemodynamic parameters such as blood pressure (BP) and pulse rate in different phases of menstrual cycle.

MATERIALS AND METHODS

The study commenced after obtaining the approval from the Institutional Ethics Committee. It was a cross-sectional study conducted among the 1st-year and 2nd-year female MBBS students with the age of 17–22 years. Voluntary participants of medical students were included for the present study and written informed consent from each of them have been obtained. Information on individual’s identity and medical and family history was collected. Anthropometric parameters, such height and weight, were recorded. Body mass index (BMI) was calculated as weight (kg) divided by height (m²). Waist circumference measurement was taken at the end of normal expiration, between the lower rib margin and the iliac crest, with the help of non-elastic measuring tape. Physiological hemodynamic parameters like pulse rate were recorded for one entire minute and BP has been recorded in participants seated using a sphygmomanometer.[9]

PLD Ratio

It was recorded by capturing the photograph of eye using the mobile phone camera. Before capturing the image of the eye, the participants were exposed to the ambient light levels for at least 5 min. Luxmeter was used to measure the illumination and it will be kept constant for all the photographs. All the photographs were recorded between 9 am to 11 am in the morning to avoid diurnal variations. After recording the photographs, it was transferred to the power point slides and the diameter was measured manually by the two-box method.[10] The photographs were taken in all the participants during the two phases of menstrual cycle namely, follicular phase – 6th day to 13th day of menstrual cycle and luteal phase – 15th day to 28th day or before the next menstrual bleeding.[1]

Statistical Analysis

Statistical analyses were performed using SPSS version 21 software. Values were expressed as mean and standard error for the continuous variables. Correlations between the variables were investigated by Pearson’s correlation coefficient. Comparison between the groups was analyzed by t-test. Statistical significance was considered if $P < 0.05$.

RESULTS

Pearson’s correlation of pupil-limbus ratio of the right with pulse rate and BP in the follicular phase is given in Table 1. The correlation of the pupil-limbus ratio of the right eye in follicular phase with pulse was 0.018, it was found to be 0.069 with systolic and diastolic BP. Similarly, correlation of pupil-limbus ratio of the left eye in follicular phase with pulse was 0.019, with systolic BP 0.020, and with diastolic BP, it was found to be 0.070.

Pearson’s correlation of pupil-limbus ratio of the right with pulse rate and BP in the luteal phase is given in Table 2. The correlation of the pupil-limbus ratio of the right eye in luteal phase with pulse was 0.062, it was found to be 0.023 with systolic and 0.075 with diastolic BP. Similarly, the correlation of the pupil-limbus ratio of the left eye in luteal phase with pulse was 0.062, with systolic BP 0.023, and with diastolic BP, it was found to be 0.075.

Comparison of pupil-limbus diameter ratio in different phases was given in Table 3. The PLD ratio of the left eye
Table 1: Correlation of pupil-limbus ratio with pulse rate and blood pressure in the follicular phase (n=111)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pulse</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLD ratio of the right eye in the follicular phase</td>
<td>R: 0.018,  P: 0.851</td>
<td>0.069, 0.531</td>
<td>0.069, 0.531</td>
</tr>
<tr>
<td>PLD ratio of the left eye in the follicular phase</td>
<td>R: 0.019,  P: 0.845</td>
<td>0.020, 0.838</td>
<td>0.070, 0.467</td>
</tr>
</tbody>
</table>

PLD: Pupil-to-limbus diameter ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 2: Correlation of pupil-limbus ratio with pulse rate and blood pressure in the luteal phase (n=111)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pulse</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLD ratio of the right eye in the luteal phase</td>
<td>R: 0.062,  P: 0.516</td>
<td>0.075, 0.807</td>
<td>0.433</td>
</tr>
<tr>
<td>PLD ratio of the left eye in the luteal phase</td>
<td>R: 0.062,  P: 0.517</td>
<td>0.023, 0.811</td>
<td>0.075, 0.434</td>
</tr>
</tbody>
</table>

Table 3: Comparison of PLD ratio of study population (n=111)

<table>
<thead>
<tr>
<th>Component</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLD ratio of the left eye between follicular and luteal phases</td>
<td>2.271</td>
<td>0.024*</td>
</tr>
<tr>
<td>PLD ratio of the right eye between follicular and luteal phases</td>
<td>2.312</td>
<td>0.022*</td>
</tr>
</tbody>
</table>

PLD: Pupil-to-limbus diameter ratio

between the follicular and luteal phase (t = 2.271, P = 0.024) was statistically significant. Similarly, the comparison of the PLD ratio of the right eye between the follicular and luteal phase was found to be statistically significant with a t value of 2.312 and P value was found to be 0.022.

DISCUSSION

The correlation of pupil-limbus diameter ratio with pulse rate and BP in follicular and luteal phases is given in Tables 1 and 2, respectively. There was no significant correlation found between PLD ratio with these parameters in the present study. The result of the present study is in consistent with the results which said that there was difference in the values of systolic BP in various phases of menstrual cycle which was not statistically significant. Diastolic BP in different phases also showed no significant difference statistically.[5] These results were in parallel with findings of other studies who observed increased systolic BP in different phases of menstrual cycle which was higher in luteal phase might be due to increased progesterone levels,[5] whereas other researchers said that hormonal changes taking place in different phases of menstrual cycle might be due to increased norepinephrine during luteal phase may be the cause for higher systolic BP in this phase.[9] Hence, it is possible to conclude that changes in ovarian hormones in various phases of menstrual cycle may change the activities of autonomic nervous system with vagal dominance in follicular phase and sympathetic dominance in luteal phase.[5] There is increased estrogen and progesterone in proliferative and secretory phases. Estrogen causes release of nitric oxide, a vasodilator substance. There was increased plasma norepinephrine in secretory phase when there was increased estrogen and progesterone. Hence in secretory phase, opposing actions of norepinephrine and nitric oxide will not alter the blood vessel diameter when acted on it together. This may be the reason for no change in diastolic BP.[11] Literatures have shown significant positive correlation between pulse and BP with PLD ratio of both the eyes.[12] On contrary, studies have reported the significant positive correlation of BP with PLD ratio in healthy women. Further, literatures have shown the correlation of pupil-limbus ratio of both the eyes with BP and pulse. The diameter of the pupil and BP are influenced by sympathetic nervous system can be the reason for the observed correlation.[9] Changes in autonomic activity causes alteration in the diameter of pupil. Changes in BP also depend on the autonomic functions. Sympathetic activation causes increase in the BP and parasympathetic activation causes decrease in BP.[6]

The present study also compared the PLD ratio of the left eye between follicular and luteal phases and the PLD ratio of the right eye between follicular and luteal phases [Table 3] and the result showed a significant difference in PLD ratio of left and right eye between follicular and luteal phases. Menstrual cycle is one of the physiological changes in females indicating the endocrine functions and reproductive health.[13] Menstrual cycle characteristics like length of the cycle, duration of bleeding reflects woman’s hormonal homeostasis, and predicts non-invasive measure of reproductive health.[14] There are changes in autonomic functions in various phases of menstrual cycle. Hence, the factor which causes disturbance of menses shall also be present in autonomic activity of that individual.[15] BMI is the major factor which helps to maintain cardiac autonomic modulation and alteration in the same produces sympathovagal imbalance.[16,17] These results were in consistent with the findings of other researchers who showed increased sympathetic and decreased parasympathetic responses in luteal phases.[18] Researchers have shown that it could be due to diet, nutrition deficiencies, and hormonal imbalances.[19-21] High estrogen during the menstrual cycle indicates high vagal tone and reduced sympathetic activity.[22]
Since autonomic activities are related with many systemic functions, autonomic disruption can cause disturbance in systemic functions also. Autonomic disturbances are related to disorders of the cardiovascular system. Hence, it is necessary to include autonomic function testing as a part of routine test.\(^{[23]}\)

The strength of the study is the usage of non-invasive method to measure autonomic functions and the limitation of the study is sample size.

**CONCLUSION**

It is useful for the detection of variations in autonomic functions during different phases of the menstrual cycle in medical students so that intervention measures can be started at the earliest which will help to prevent further complications.

**REFERENCES**


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