Effect of menstrual cycle on pulmonary functions and respiratory efficiency

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Abstract

Background: The cyclic hormonal changes during different phases of menstrual cycle are responsible for various physiological changes including its diverse role on reproductive organs. Their effects on extra-reproductive systems like airway dynamics and respiratory efficiency are very few in literature.

Aim: To evaluate the effects of menstrual cycle on various parameters of lung functions and respiratory efficiency in young females.

Materials and methods: 75 young non-pregnant females of age group 18-30 years were selected randomly for this study. Their menstrual phases were estimated based on menstrual history questionnaires and last date of menstrual bleeding, namely, menstrual, follicular and luteal. Their pulmonary function tests and respiratory efficiency was measured using computerized spirometer thrice in each phases of menstrual cycle. The various parameters evaluated were: forced vital capacity (FVC), forced expiratory volume in 1st sec (FEV\(_1\)), Maximum mid expiratory flow rate (MMEFR), peak expiratory flow rate (PEFR), maximum voluntary ventilation (MVV), 40 mm respiratory endurance test (RET), breath holding time after full expiration and maximum inspiration (BHT ex and BHT ins) and maximum expiratory pressure (MEP).

Results: FVC, FEV\(_1\), and MMEFR were significantly higher during the luteal phase as compared to menstrual and Follicular phase; whereas PEFR and MVV were significantly higher during the luteal phase as compared to menstrual phase only. On respiratory efficiency tests the BHT ex, BHT ins and MEP were significantly higher during the luteal phase as compared to menstrual and Follicular phase; also it was observed that BHT ex were significantly higher during the follicular phase as compared to the menstrual phase.
**Conclusion:** Respiratory efficiency and pulmonary functions parameters were higher during the luteal phase of menstrual cycle. Main reason behind this could be the progesterone hormones’ effect on respiratory apparatus, whose levels remains on higher side during the luteal phase.

**Key words**
Menstrual cycle, Pulmonary function test, Respiratory efficiency, Luteal phase.

**Introduction**
Menstruation is a vital component of every female’s reproductive life span. It has cyclic characteristics due to hormones secreted by the hypothalamus-pituitary-ovarian axis. It lasts for an average of 28 days and is divided in three phases: menstrual, follicular and luteal. The follicular and luteal phase is separated by a brief period of ovulation. The course and timing of menstruation is steered through a multifaceted endocrine interplay. Estrogen level increases during follicular phase until ovulation. Follicle Stimulating Hormone (FSH) level rises, and then has a short dip before a new rise, around ovulation. Luteinizing Hormone (LH) that initiates ovulation has a large surge in its level around ovulation. The serum levels of progesterone are very low during the follicular phase, but high during the luteal phase. These hormonal variations are responsible for various physiological changes as well as psychological changes. A lot of restrictions also being imposed on young females, particularly in developing nations, influencing their daily activities and lifestyle related habits like exercise, during menstrual bleeding phase [1]. The effects of cyclical hormonal changes on reproductive organs are also well-known; their effects on other organ systems are not well established.

Multiple scientific efforts have described the effects of menstrual cycle on various issues related to respiratory health like exacerbations of bronchial asthma [2-4], hospital admissions [5, 6], bronchial hyper reactivity (BHR) [7]. A significant increase in ventilation in the luteal phase as compared to other phases of menstrual cycle was observed in earlier studies [8-12]. They suggest progesterone is a cause of increased ventilatory capacity during luteal phase, as progesterone has its effect on airway smooth muscle (ASM) relaxation. However, there are many studies which contradict the data highlighting the changes in respiratory parameters during different phases of menstruation. Also, there were none of the studies available till date about the effect of menstrual cycle on respiratory efficiency. Therefore the current study was done to evaluate the effects of menstrual cycle on various parameters of the lung functions and respiratory efficiency.

**Materials and methods**
This was a cross sectional (descriptive) study conducted during June 2015 to May 2016. The permission from institutional ethical committee (IEC) was taken prior to the study. The informed written consent was taken from each participant.

**Sampling description:** The samples of the study included 75 female undergraduate and postgraduate students selected at random from medical and paramedical courses of different constituent colleges of University. Sample size calculation was done with the help of openepi software. This software module calculated sample sizes for comparing two means. After using the confidence interval (95%), power (90%), ratio of sample size of group 2 to group 1, mean and standard deviation of values from a previous study [11], and with consideration of 10% attrition rate, the sample size taken in this study was 75.

**Inclusion and exclusion criteria:** Detailed history was obtained from each participant for any respiratory illness or any allergic symptoms in the recent times, and they were excluded accordingly. Females with irregular menstrual
cycles, on hormonal therapy, post-hysterectomy were excluded from the study. All the participants were unmarried and never used any contraceptive pills. Those not willing to participate in study were also excluded from the study.

The different phases of menstrual cycle were estimated according to the menstrual history related questionnaire and date of last menstrual period, as follows:

- During the first or second day of the menstrual bleeding (referred as menstrual phase).
- 3-4 day after complete stoppage of bleeding (referred as follicular phase).
- 2 weeks after the mid follicular phase (referred as luteal phase).

All the participants were asked to report thrice in the Respiratory research laboratory in the Department of Physiology for pulmonary function test and respiratory efficiency test, according to their phases of menstrual cycle (once in each phase). The Height and weight of each participant were recorded every time, but for reporting only the first time measurements were considered.

**Pulmonary functions test (PFT):** The following PFT indices were measured using MedSpiror (Spirowin) computerized spirometer: Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 Sec (FEV₁), Forced Expiratory Volume in 1 Sec as percentage of FVC (FEV₁%), Maximum Mid Expiratory Flow Rate (MMEFR), Peak Expiratory Flow Rate (PEFR) and Maximal voluntary ventilation (MVV). All the pulmonary function test maneuvers were carried out with the participant in seating posture and a nose clip applied and maintaining an airtight seal around the mouthpiece. They were asked to keep their neck in neutral position, neither flexed nor extended. The same spirometer was used throughout the study and the tests were performed by the same investigator. The equipment was calibrated fully as per manufacturer’s instruction. A new disposable mouth piece was used every time in a new participant. The principal investigator demonstrated the appropriate technique every time before the test.

**FVC maneuver:** The participants were asked to take a deep breath (maximal inspiration) and after minimal pause at full inspiration, they were prompted to ‘blast’ (not just ‘blow’) the air from their lungs into the mouth piece as rapid and forceful as possible, followed by continued complete exhalation to the end of test. Throughout the maneuver, enthusiastic coaching of the participant using appropriate body language and phrases, such as ‘keep going’ was used. This maneuver determines all the above mentioned PFT indices, except MVV. At least three maneuvers were obtained for each participants; the best of three values was accepted.

**MVV maneuver:** The participant was asked to breathe as rapidly as possible for 12 to 15 seconds using a depth of inhalation greater than his resting tidal volume. During this maneuver the participant were encouraged throughout, with occasional glances at the tracing to help them to obtain the best result.

**Respiratory efficiency test:** The following Respiratory efficiency tests were conducted: 40 mm Hg Respiratory endurance test (RET), Breath holding time after full expiration (BHT ex), Breath holding time after full inspiration (BHT ins), and Maximum Expiratory Pressure (MEP).

For RET the participant, seated and with nose clip applied and maintaining an airtight seal, were asked to blow in the mercury manometer tubing and maintain at the pressure for 40 mm of Hg for maximum possible duration. For MEP test, the participants were asked to blow the mercury manometer tube for maximum possible pressure, with nose clip applied and maintaining an airtight seal. This maneuver was done after
full inspiration. For breath holding times, the participants were asked for hold the breath as long as possible after full expiration and full inspiration, with some interval in between both events.

**Statistical analysis:**

The statistical analysis was done using Microsoft office Excel 2007 and OpenEpi, open source software for epidemiologic statistics. The mean and standard deviation (SD) of each parameter were calculated. The Analysis of Variance (ANOVA) was used to compare the means of various parameters in three phases of menstrual cycle. For comparing the means of various parameters in two phases of menstrual cycle unpaired T test was used. For statistical significant differences p value less than 0.05 were taken. The statistically significant differences on unpaired t test were expressed as alphabets a, b, c, as following:

- **a** = significant difference (p<0.05) between menstrual and follicular phase on unpaired t test.
- **b** = significant difference (p<0.05) between follicular and luteal phase on unpaired t test.
- **c** = significant difference (p<0.05) between menstrual and luteal phase on unpaired t test.

**Results**

The age of the participants was 23.68 ± 3.69 years. All belong to the normal weight according to the WHO criteria of obesity (based on BMI). On PFT, it was observed that FVC, FEV₁, and MMEFR were significantly higher during the luteal phase as compared to menstrual and Follicular phase; whereas PEFR and MVV were significantly higher during the luteal phase as compared to menstrual phase only. On respiratory efficiency tests the BHT ex, BHT ins and MEP were significantly higher during the luteal phase as compared to menstrual and Follicular phase; also it was observed that BHT ex were significantly higher during the follicular phase as compared to the menstrual phase (Table 1 to 3).

**Table 1:** Descriptive Anthropometric parameters of all the participants.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.68 ± 3.69</td>
<td>18 – 30</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.45 ± 10.45</td>
<td>148 - 171</td>
</tr>
<tr>
<td>Weight (in Kg)</td>
<td>58.75 ± 6.69</td>
<td>48.9 - 73.7</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td>21.97 ± 3.44</td>
<td>18.9 - 24.8</td>
</tr>
</tbody>
</table>

**Table 2:** PFT (spirometry) in different phases of menstrual cycle.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Menstrual</th>
<th>Follicular</th>
<th>Luteal</th>
<th>ANOVA (p value- two tailed)</th>
<th>Unpaired t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (in liters)</td>
<td>2.59 ± 0.43</td>
<td>2.54 ± 0.38</td>
<td>3.01 ± 0.70</td>
<td>0.0000000044</td>
<td>b, c</td>
</tr>
<tr>
<td>FEV₁ (in liters)</td>
<td>2.05 ± 0.32</td>
<td>2.22 ± 0.28</td>
<td>2.54 ± 0.42</td>
<td>0.00000000000003</td>
<td>b, c</td>
</tr>
<tr>
<td>FEV₁/FVC (FEV1%)</td>
<td>86.13 ± 8.88</td>
<td>87.83 ± 9.15</td>
<td>86.30 ± 8.0</td>
<td>0.420</td>
<td></td>
</tr>
<tr>
<td>PEFR (in liters per second)</td>
<td>5.01 ± 0.17</td>
<td>5.09 ± 0.82</td>
<td>5.30 ± 0.62</td>
<td>0.010</td>
<td>c</td>
</tr>
<tr>
<td>MMEFR (in liters per second)</td>
<td>3.48 ± 0.56</td>
<td>3.52 ± 0.58</td>
<td>4.08 ± 0.49</td>
<td>0.00000000000010</td>
<td>b, c</td>
</tr>
<tr>
<td>MVV (in liters)</td>
<td>85.22 ± 20.67</td>
<td>91.53 ± 25.04</td>
<td>99.91 ± 27.75</td>
<td>0.00149</td>
<td>c</td>
</tr>
</tbody>
</table>
Table - 3: Respiratory efficiency tests in different phases of menstrual cycle.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Menstrual</th>
<th>Follicular</th>
<th>Luteal</th>
<th>ANOVA (p value)</th>
<th>Unpaired t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>RET (in seconds)</td>
<td>12.59 ± 2.34</td>
<td>12.54 ± 3.83</td>
<td>13.01 ± 4.04</td>
<td>0.093</td>
<td>-</td>
</tr>
<tr>
<td>BHT ex (in seconds)</td>
<td>22.05 ± 4.23</td>
<td>26.22 ± 5.52</td>
<td>29.54 ± 5.42</td>
<td>0.000000000083</td>
<td>a, b, c</td>
</tr>
<tr>
<td>BHT ins (in seconds)</td>
<td>38.13 ± 8.88</td>
<td>39.83 ± 9.15</td>
<td>46.30 ± 8.01</td>
<td>0.000000000055</td>
<td>b, c</td>
</tr>
<tr>
<td>MEP (in mm of Hg)</td>
<td>69.01 ± 8.17</td>
<td>70.09 ± 9.82</td>
<td>76.30 ± 9.67</td>
<td>0.0000027</td>
<td>b, c</td>
</tr>
</tbody>
</table>

Discussion
The present study showed that various pulmonary function indices as well as respiratory efficiency parameters show significant variation during different phases of menstrual cycle of women in reproductive age group. Few significant observations in the present study matched with the results obtained in other studies. Dimple Arora, et al. [8] and Raksha Hebbar K, et al. [9] in their studies observed that mean value of FVC and FEV1 were significantly higher in secretory (luteal) phase, followed by follicular phase and least in menstrual phase. Many other studies (Johaneson M. [10], Mannan, et al. [11], Rajesh CS [12], Elena Saprova, et al. [13]) have also shown similar results. However, none of these studies mentions about MVV. MVV being an effort dependent maneuver, the performing it very accurately is equally important. The MVV were found to be statistically significant higher value during luteal phase. The respiratory efficiency tests were not performed in any of the previous studies. Although, this present study indicates consistently that respiratory efficiency were significantly higher during luteal phase as compared to other two phases of menstrual cycle. The explanation to these observations is taking cue from the hormonal variations during various phases of menstrual cycle. As it is also important to note that progesterone levels are highest during the luteal phase of menstrual cycle, and progesterone is known to be a smooth muscle relaxant and thus, it may cause bronchodilation too. This phenomenon could be correlated from the observations of Beynon, et al. [14] who studied the effects of intramuscular progesterone on patients with asthma. They found that the dosage of bronchodilators were less in patients receiving progesterone. Low levels of progesterone in premenstrual phase may cause relative decrease in the values of lung volumes and capacities. Another study by Gibbs CJ, et al. [15] reported exacerbation of asthma in premenstrual phase. They showed that females with asthma had reported symptom worsening just few days before menstrual bleeding and improvement in the symptoms with the abatement of menses every time. Thus the diagnosis of premenstrual asthma is made upon the demonstration of significant variation in airway function during the period just prior to the onset of menses. Another important observation were related to significant increase in pulmonary functions in females taking oral contraceptive pills and these drugs significantly prevented the exacerbation of asthma as suggested by R Hebbar in her study [9]. Pardeep, et al. [16] have also suggested that hormone pills containing progesterone decrease the resistance offered by small bronchioles. These aspects also need to be studied in further detail. But it seems here also that progesterone does contribute at a much larger scale.

Conclusion
It was seen that pulmonary functions as well as respiratory efficiency were significantly improved in the luteal of menstrual cycle. The reason could be the bronchodilator effect of progesterone, whose levels remain higher during this phase. Clinicians treating young female patients suffering from respiratory disorders may keep this in mind about the phases of menstrual cycle while prescribing bronchodilator drugs. Also conditions like, premenstrual asthma can be better tackled with the help of these observations. Further studies are recommended to study the...
effect of ovarian hormones like estrogen and progesterone on bronchial smooth muscle.

Acknowledgement

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References