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Study of Pulmonary Function Test in Normal Females in Different Phases of Menstrual Cycle

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Abstract
Introduction: *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: *30 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 (FEV1), FEV_1/FVC, Forced expiratory flow between 25% to 75% (FEF25%-75%), peak expiratory flow rate (PEFR).*
Results: *FVC, FEV1 were significantly higher during the luteal phase as compared to menstrual and Follicular phase; whereas FEF25%-75% and PEFR were non significantly higher during the luteal phase as compared to menstrual phase.*

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I. 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. 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 life style related habits like exercise, during menstrual bleeding phase [1].

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. A few previous studies have observed changes in chemical ventilatory responses [13], minute ventilation during menstrual cycle. Significant lower values of lung functions were reported in estrogenic phase [14] while other studies found non significant higher values in progestrogenic phase [15].

It has been reported that hyperventilation & increase in oxygen consumption occur during the luteal phase of menstrual cycle and if pregnancy occurs, the respiratory stimulation continues throughout gestation [16]

The present study was planned to evaluate more precisely the possible effects due to hormonal changes on ventilation in different phases of menstrual cycle, particularly during luteal phase when progesterone level is normally high.

II. Material and method

Initially 42 subjects (menstruating girls) of age 18-30 years were evaluated, out of which 7 were excluded from the study because of history of cough, irregular cycles. Remaining 35 girls were subjected to

pulmonary function tests on computerized spirometer- Pony graphic, 5 subjects could not perform spirometry inspite of best efforts to educate them, so they were excluded.

The study of finally selected 30 girls were carried out for pulmonary function tests in the department of Physiology, Sardar Patel Medical college, Bikaner. The permission from institutional ethical committee (IEC) was taken prior to the study. The informed written consent was taken from each participant.

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 timing of the lung functions study during the cycle were same every time in the morning as per schedule in the three phases of menstrual cycle. Their menstrual phases were estimated based on menstrual history questionnaires and last date of menstrual bleeding, namely, menstrual, follicular and luteal

1. During menstrual phase (1^{st} to 3^{rd} day)
2. Follicular phase (8^{th} to 10^{th} day)
3. Luteal phase (20^{th} to 22^{nd} day)

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.

Method of Spirometry

The following PFT indices were measured using computerized spirometer- Pony graphic. 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. Before each test the subjects were familiarized with the machine and a detailed instruction cum demonstration up to satisfaction of both subject and doctor would be done.

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.

Three readings were taken on three consecutive days of that particular phase of the cycle. Pulmonary function test recorded were as follows

- Forced Vital Capacity
- Forced Expiratory volume in 1 sec (FEV_1)
- FEV_1/FVC
- Forced expiratory flow between 25% & 75% of Vital capacity -FEF25%-75%
- Peak expiratory flow rate

In each subject the pulmonary function tests were performed during the three phases of cycle as follows

1. Between 1^{st} and 3^{rd} day of menstruation
2. Between 8^{th} to 10^{th} day of follicular phase
3. Between 20^{th} to 22^{nd} day of luteal phase

Statistical methods were applied for analysis of observation. The significance of the parameters was assessed by applying student' s 't 'test.

Table 1 Comparison of percentage predicted FVC between two age group in three phases of menstrual cycle

	Group	Age	Mean	SE	t
Menstrual phase	I II	18-21 22-25	77.985 78.068	±3.2889 ±3.162	0.018
Follicular phase	I II	18-21 22-25	75.214 74.875	±3.287 ±2.997	0,076
Luteal phase	I II	18-21 22-25	80.957 82.762	±3.094 ±3.595	0.380

Table 2 Comparison of percentage predicted FEV1 between two age group in three phases of menstrual cycle

	Group	Age	Mean	SE	t
Menstrual phase	I II	18-21 22-25	85.635 86.793	±2.810 ±3.769	0.246

Follicular phase	I II	18-21 22-25	82.414 83.268	±3.042 ±3.541	0.182
Luteal phase	I II	18-21 22-25	89.650 90.431	±2.468 ±3.985	0.166

Table 3 Comparison of percentage predicted FEV1/FVC between two age group in three phases of menstrual cycle

	Group	Age	Mean	SE	t
Menstrual phase	I II	18-21 22-25	112.907 116.175	±2.181 ±0.658	1.434
Follicular phase	I II	18-21 22-25	113.00 116.362	±1.185 ±0.619	2.600
Luteal phase	I II	18-21 22-25	113.207 113.812	±1.925 ±1.474	0.249

Table 4. Comparison of percentage predicted FEF25-75% between two age group in three phases of menstrual cycle

	Group	Age	Mean	SE	T
Menstrual phase	I II	18-21 22-25	105.771 112.349	±6.000 ±7.540	0.682
Follicular phase	I II	18-21 22-25	100.771 109.837	±6.256 ±7.220	0.1.211
Luteal phase	I II	18-21 22-25	106.171 105.125	±6.455 ±8.245	0.951

Table 5 Comparison of percentage predicted PEFR between two age group in three phases of menstrual cycle

	Group	Age	Mean	SE	T
Menstrual phase	I II	18-21 22-25	88.657 91.974	±6.827 ±6.827	0.454
Follicular phase	I II	18-21 22-25	82.085 88.625	±4.794 ±6.911	0.777
Luteal phase	I II	18-21 22-25	91.392 90.031	±3.693 ±5.931	0.194

Table 6 Calculated value of 't' for percentage predicted values of various pulmonary function parameters for different phases of menstrual cycle

S.no.	Phases	FVC	FEV1	FEV1/FVC	FEF25%--75%	PEFR
1.	Between menstrual & follicular phase	0.9611	1.02	0.11	0.53	0.83
2.	Between menstrual& luteal phase	1.19	1.14	0.70	0.50	0.04
3.	Between follicular & luteal phase	*2.15	*2.16	0.982	0.046	0.91

*$p<0.05$

III. Results & Discussion

The present study showed that various pulmonary function parameters show variation during different phases of menstrual cycle of women in reproductive age group. The observed FVC, FEV1 were higher during luteal phase as compared to follicular and menstrual phase, The values were significant when compared between follicular and luteal phase. The percentage predicted value of FVC and FEV1 is significantly increased in luteal phase. 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 (Johanesson M. [10], Mannan, et al. [11], Rajesh CS [12], Elena Saprova, et al. [16]) have also shown similar result.

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. [17] who studied the effects of intramuscular progesterone on patients with asthma. They found that the dosage of bronchodilators were less in patients. 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. [18] 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.

Fluctuating levels of circulating mediators could also be responsible for the changes in bronchial tone, PGF2α, a powerful bronchoconstrictor reaches its highest level in endometrium premenstrually & menstrually. [19]. There is evidence that these endometrial changes may be reflected in the systemic blood, other mediators are those held in the blood basophil reservoirs – leukotriene & histamine which are also powerful bronchoconstrictors.

It is suggested that the study be carried out in large population along with quantitative measurements of progesterone levels to correlate with pulmonary functions.

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