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Original Research Article

Effects of different phases of menstrual cycle on lung functions in young girls of 18-24 years age

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ABSTRACT

Background: The dynamic cyclical changes in the levels of various hormones during different phases of menstrual cycle are known to affect functioning of different systems of the body, including the respiratory system. Objective of the study was to study the effects of different phases of menstrual cycle on lung functions in young girls of 18-24 years age.
Methods: 78 girls who were medical students of G.R. Medical College, Gwalior, India were chosen for the study. Their lung function parameters were recorded on Spiro Excel, a computerized spirometer. Four lung function parameters i.e. FVC, FEV1, FEV1/FVC% and PEFR were recorded in the different phases of menstrual cycle i.e. menstrual phase, proliferative phase and secretory phase.
Results: All lung function parameters except FEV1/FVC% were least in menstrual phase and highest in secretory phase with in between values in proliferative phase. The values were significantly different among the three phases. FEV1/FVC% values were maximum in menstrual phase, lowest in secretory phase with intermediate values in proliferative phase but the values were not significantly different among the three phases. Mean values of FVC, FEV1 and PEFR were higher in all the phases of menstrual cycle in normal BMI subjects as compared to the corresponding phases of underweight subjects.
Conclusions: Higher values of lung functions during proliferative and secretory phases can be attributed to the higher concentrations of sex hormones specially progesterone because in most of the studies progesterone is known to cause relaxation of bronchial smooth muscle.

Keywords: Lung function, Menstrual cycle, Young girls

INTRODUCTION

The normal reproductive years of the female are characterized by monthly rhythmical changes in the rates of secretion of the female hormones and corresponding physical changes in the ovaries and other sex organs. This rhythmical pattern is called the female monthly sexual cycle (or, less accurately, the menstrual cycle). The duration of the cycle averages 28 days and for 3-5 days actual bleeding occurs.[1] Menstrual cycle occurs in three phases: Menstrual, proliferative and secretory phase, which are regulated by sex hormones: estrogen, progesterone secreted from the ovary and also by gonadotropins: Luteinizing and follicle stimulating hormones secreted from anterior pituitary. Endogenous hormone levels vary around puberty and in menarche, menstrual phases, menstrual irregularity, lactation, during proximity to menopause etc. Furthermore many women use exogenous sex hormones: OCP's (Oral contraceptive pills), hormone replacement or infertility therapy which also leads to variations in the hormone levels.[2] The dynamic cyclical changes in the levels of various hormones during different phases of menstrual cycle are known to affect functioning of different systems of the body, including the respiratory system.[3]

Human lungs are able to adapt to the metabolic needs of the body and accordingly lung functions vary under different conditions. Since hormonal levels vary with metabolism, any variation in the female gonadal hormones during different phases of menstrual cycle may exert corresponding changes in the lung functioning also. Studies suggest that progesterone and estrogen levels strengthen the respiratory musculature and increase the relaxation of bronchial smooth muscles. This variation has been cited as the cause of change in lung functions during various phases of menstrual cycle.[4]

Some studies also showed association of lung function values with BMI.[5,6] and association of lung function values with obesity and menstrual cycle.[7] There are only few studies from India on pulmonary function tests in different phases of menstrual cycle.[8-11] But any study showing correlation of pulmonary function tests with different phases of menstrual has not been done in Madhya Pradesh region to the best of my knowledge.

So the present study is an attempt to evaluate the effects of different phases of menstrual cycle on pulmonary function tests and also to correlate pulmonary function tests with the body mass index (BMI) in apparently healthy young girls of 18-24 years from G.R. Medical College, Gwalior, Madhya Pradesh, India.

METHODS

The present study was conducted on 78 young girls of 18 to 24 years age group. The subjects were selected from students studying in Gajraj Raja Medical College, Gwalior, India. The subjects selected for the study were normal healthy young girls with no history of any disease, which could influence Pulmonary Function. The general and systemic examination of the subjects was done for all the systems with special emphasis on the respiratory system.

Inclusion criteria

- Females of 18-24 years age group
- Females having regular menstrual cycle of 26-30 days

Exclusion criteria

- Age below 18 years and above 24 years
- History of irregular menstrual cycle
- Subject on oral contraceptive pills, hormone replacement therapy
- History of known chronic obstructive pulmonary disease and restrictive lung disease.
- History of known cardiovascular illness, hypertension and psychiatric illness.
- History of smoking, alcohol addiction or medication.

Equipments used

Following equipments were used in the study

1. Spiro Excel Machine (Computerized spirometer) manufactured by Medicaid Systems, Chandigarh was used to measure the pulmonary Functions. The logic built into the Spiro Excel evaluates the patient/ subject as an adult or a child, male or female and selected the suitable set of equation for computation of predicted norms.

Table 1: Technical features of Spiro excel machine.

Flow meter	Bi-directional digital turbine
Range for flow measurement	0.03 -20 L/Sec.
Range for volume measurement	10 L
Accuracy of measurement	3% or 50 ml
Dynamic resistance @ 12 L/Sec	<0.7 cm H_2O/ L/Sec.
Mouthpieces	31 and 21 mm
Power Supply	No external supply required, works on 5V from CPU
Dimensions	160 x 50 x 25 mm
Weight	100 gm

Interpretation of results by Spiro Excel machine (Computerized Spirometer) were done by Indian (Kamat et al) method.

2. Weight was measured using weighing machine with subject standing without shoes. Every subject was wearing routine outfit while observing the weight. Extra items like apron and sweaters were removed whenever the subject came wearing them. Weight was recorded in kilograms and the zero error was minimized to maximum. Machine was checked repeatedly from time to time to avoid error.

3. Stadiometer was used for measurement of height while the subject was standing erect. Height was recorded in centimetres.

BMI was calculated by the formula

$$BMI = \frac{Weight\ in\ kg}{Hight\ in\ m^2}$$

Subjects were classified according to WHO criteria of BMI.[12]

Table 2: WHO classification of adults according to BMI.

Classification	BMI
Underweight	<18.50
Normal range	18.50-24.99
Overweight	25.00
a) Pre-obese	25.00-29.99
b) Obese class I	30.00-34.99
c) Obese class II	35.00-39.99
d) Obese class III	40.00

4. Sphygmomanometer and Stethoscope were used for the measurement of blood pressure.

Method of collection of data

After explaining the aims and objectives of study written consent was taken from all the subjects.

All the subjects were given Proforma containing name, age in completed years, gender and dietary habits (whether vegetarian or non-vegetarian), history of smoking, whether active or passive and its duration, history of recurrent respiratory infections or significant past history of any other disease, family history of COPD (asthma or emphysema) and history of allergy, to be filled up.

We recorded the menstrual history which specifically included date of last menstrual period (LMP), duration of menses, date of last three consecutive menstrual cycles. Data of all the subjects was acquired in the following three phases of menstrual cycle.

- Menstrual phase
- Proliferative phase
- Secretory phase

Subjects were asked to report three times on the 2nd or 3rd, 10th -12th and 20th-22nd days of menstrual cycle. These days were calculated from LMP dates that were filled in the proforma. Pulmonary function tests were carried out of the subjects in the sitting position before lunch and values of different parameters were recorded.

Statistical analysis

The results were expressed as Mean + Standard Deviation (Mean+SD). Statistical analysis was done through Graph pad prism.[4] Comparison of pulmonary function parameters in different phases of menstrual cycle was done by using one way ANOVA (Analysis of Variance) by bonferroni post-hoc test.

Procedure for test administration

PFT were performed in calm and comfortable environment in 2 Steps.

- Preparation
- Test administration

Preparation

- It was ensured that the subjects were not wearing items of apparel that were tight or restrictive (e.g. necktie, buttoned shirt collar, tight belt etc.).
- Clean, disinfected mouthpiece was provided to every subject for the procedure.

Test administration

- Clear and simple instructions were given to the subject followed by a demonstration.
- Nose was closed during the manoeuvre by nose clips.
- Mouthpiece was positioned in such a way that the subject's chin was slightly elevated and neck was extended.
- The subject was asked to exhale into the mouthpiece of Spiro Excel machine as forcefully as possible after deep inspiration. The test was repeated three times and the highest values were considered for analysis.
- In the manoeuvre each subject was motivated and encouraged to give her best performance.

RESULTS

Mean age of the whole group (78 females) was 19.67±1.35 years, mean height was 154.26±6.11 cm, mean weight was 49.72±8.83 Kg and mean body mass index (BMI) was 20.85±3.28 Kg/m^2.

Table 3: Lung function parameters in different phases of menstrual cycle.

Parameters (Mean ± SD)	Menstrual Phase	Proliferative Phase	Secretory phase
FVC (L)	2.59±0.32	2.68±0.31	2.82±0.34
FEV1 (L)	2.41±0.29	2.49±0.28	2.60±0.30
FEV1 /FVC (%)	93.09±3.83	92.97±3.97	92.42±3.99
PEFR (L/Sec.)	5.77±0.76	6.04±0.72	6.49±0.81

51 (65.39%) were normal, 19 (24.36%) were underweight while 7 (8.97%) were pre-obese and only 1 (1.28%) was obese. Mean values of FVC in menstrual, proliferative, secretory phases were 2.59±0.32, 2.68±0.31, 2.82±0.34 litres respectively. Mean values of FEV1 in menstrual, proliferative, secretory phases were 2.41±0.29, 2.49±0.28, 2.6±0.30 litres respectively. Mean values of FEV1 /FVC (%) in menstrual, proliferative, secretory phases were 93.09±3.83, 92.97±3.97, 92.42±3.99 respectively. Mean values of PEFR in menstrual, proliferative, secretory phases were 5.77±0.76, 6.04±0.72, 6.49±0.81 litres/sec respectively (Table 3).

Table 4: Comparison of lung function parameters in menstrual and proliferative phase.

Parameters (Mean ± SD)	Menstrual Phase	Proliferative Phase	p-Value	t-Value
FVC (L)	2.59±0.32	2.68±0.31	<0.001***	6.54
FEV1 (L)	2.41±0.29	2.49±0.28	<0.001***	6.63
FEV1 /FVC (%)	93.09±3.83	92.97±3.97	>0.05	0.30
PEFR (L/Sec.)	5.77±0.76	6.04±0.72	<0.001***	4.08

***Highly significant

The difference FVC values in menstrual and proliferative phase were significant (p<0.001). The difference of FEV1 values in menstrual and proliferative phase was significant (p<0.001). The difference of FEV1/FVC (%) values in menstrual and proliferative phase was not significant. (p>0.05). The difference of PEFR values in menstrual and proliferative phase was significant (p<0.001) (Table 4). The difference of FVC values in menstrual and secretory phase was significant (p<0.001). The difference of FEV1 values in menstrual and secretory phase was significant (p < 0.001). The difference of FEV1 /FVC (%) values in menstrual and secretory phase was not significant (p>0.05) was 5.77±0.76 and 6.49±0.81 litres/sec respectively. The difference of PEFR values in menstrual and secretory phase was significant (p <0.001) (Table 5).

Table 5: Lung function parameters in menstrual and secretory phase.

Parameters (Mean ± SD)	Menstrual Phase	Secretory Phase	p-Value	t-Value
FVC (L)	2.59±0.32	2.82±0.34	<0.001***	15.70
FEV1 (L)	2.41±0.29	2.60±0.30	<0.001***	15.29
FEV1 /FVC (%)	93.09±3.83	92.42±3.99	>0.05	1.65
PEFR (L/Sec.)	5.77±0.76	6.49±0.81	<0.001***	10.94

***Highly significant

Table 6: Lung function parameters in proliferative and secretory phase.

Parameters (Mean ± SD)	Proliferative Phase	Secretory Phase	p-Value	t-Value
FVC (L)	2.68±0.31	2.82±0.34	<0.001***	9.16
FEV1 (L)	2.49±0.28	2.60±0.30	<0.001***	8.67
FEV1 /FVC (%)	92.97±3.97	92.42±3.99	>0.05	1.35
PEFR (L/Sec.)	6.04±0.72	6.49±0.81	<0.001***	6.85

***Highly significant

Table 7: FVC as a percentage of predicted parameter in different phases of menstrual cycle

Parameters (Mean ± SD)	Menstrual Phase	Proliferative Phase	Secretory Phase
FVC (Absolute in L)	2.59±0.32	2.68±0.31	2.82±0.34
FVC (% of Pred.)	76.37±9.01	79.20±8.93	83.12±9.61

The difference of FVC values in proliferative and secretory phase was significant (p<0.001). The difference of FVC values in proliferative and secretory phase was significant (p<0.001). The difference of FEV1 /FVC (%) values in proliferative and secretory phase was not significant (p>0.05). The difference of PEFR values in proliferative and secretory phase was significant (p< 0.001) (Table 6).

Mean values of FVC (Absolute in litres) in the menstrual, proliferative and secretory phases were 2.59±0.32, 2.68±0.31, 2.82±0.34 respectively. Mean values of FVC (% of Pred.) in the menstrual, proliferative and secretory phases were 76.37±9.01, 79.20±8.93, and 83.12±9.61 respectively (Table 7).

Table 8: FEV_1 as a percentage of predicted parameter in different phases of menstrual cycle.

Parameters (Mean±SD)	Menstrual Phase	Proliferative Phase	Secretory phase
FEV1 (Absolute in L)	2.41±0.29	2.49±0.28	2.60±0.30
FEV1 (% of Pred.)	81.36±9.72	84.20±9.45	87.91±9.97

Mean values of FEV_1 (Absolute in litres) in the menstrual, proliferative and secretory phases were 2.41±0.29, 2.49±0.28, 2.60±0.30 respectively. Mean values of FEV_1 (% of Pred.) in the menstrual, proliferative and secretory phases were 81.36±9.72, 84.20±9.45, 87.91±9.97 respectively (Table 8).

Mean values of FEV_1/ FVC (Absolute in %) in the menstrual, proliferative and secretory phases were 93.09±3.83, 92.97±3.97, 92.42±3.99 respectively. Mean values of FEV1/ FVC (% of Pred.) in the menstrual, proliferative and secretory phases were 109.36±4.47, 109.22±4.62, 108.59±4.66 respectively (Table 9).

Table 9: FEV_1/FVC as a percentage of predicted parameter in different phases of menstrual cycle.

Parameters (Mean ± SD)	Menstrual Phase	Proliferative Phase	Secretory phase
FEV1/ FVC (Absolute in %)	93.09±3.83	92.97±3.97	92.42±3.99
FEV1/FVC (% of Pred.)	109.36±4.47	109.22±4.62	108.59±4.66

Table 10: PEFR as a percentage of predicted parameter in different phases of menstrual cycle.

Parameters (Mean ± SD)	Menstrual Phase	Proliferative Phase	Secretory phase
PEFR (Absolute in L/Sec)	5.77±0.76	6.04±0.72	6.49±0.81
PEFR (% of Pred.)	85.65±11.36	89.61±10.34	96.35±11.95

Table 11: Lung function parameters in different phases of menstrual cycle as per BMI.

Menstrual cycle	BMI (Kg/m2)	FVC (L)	FEV1	FEV1/ FVC (%)	PEFR (L/sec)
Menstrual phase	<18.5	2.42±0.21	2.27±0.19	94.10±3.45	5.59±0.53
	18.5–24.9	2.62±0.33	2.44±0.32	93.02±3.76	5.88±0.86
	25-29.99	2.80±0.32	2.52±0.23	90.14±4.22	5.47±0.38
	>30	2.64	2.59	98.00	5.56
Proliferative phase	<18.5	2.51±0.23	2.36±0.21	94.21±2.71	5.83±0.58
	18.5–24.9	2.73±0.31	2.52±0.30	92.81±4.26	6.13±0.79
	25-29.99	2.85±0.33		90.76±4.33	5.93±0.42
	>30	2.72	2.54	2.68	
Secretory phase	<18.5	2.65±0.31	2.47±0.22	93.21±3.39	6.17±0.52
	18.5–24.9	2.85±0.34	2.63±0.32	92.40±4.13	92.40±4.13
	25-29.99	3.00±0.37	2.70±0.25	90.36±4.64	6.26±0.47
	>30	2.88	2.68	93.00	7.27

Mean values of PEFR (Absolute in litres/sec) in the menstrual, proliferative and secretory phases were 5.77±0.76, 6.04±0.72, 6.49±0.81 respectively. Mean values of PEFR (% of Pred.) in the menstrual, proliferative and secretory phases were 85.65±11.36, 89.61±10.34, 96.35±11.95 respectively. Mean values of FVC among underweight in menstrual, proliferative, secretory phases were 2.62±0.33, 2.73±0.31, 2.85±0.34 litres respectively (Table 10).

Mean values of FEV1 among normal weight in menstrual, proliferative, secretory phases were 2.44±0.32, 2.52±0.30, 2.63±0.32 litres respectively. Mean values of FEV1 /FVC (%) among pre-obese in menstrual, proliferative, secretory phases were 90.14±4.22, 90.76±4.33, 90.36±4.64 respectively. Mean values of PEFR among obese in menstrual, proliferative, secretory phases were 5.56, 5.92, 7.27 litres/sec. respectively (Table 11).

DISCUSSION

There was increase in FVC values in successive phases from menstrual to secretory phase. The FVC values of proliferative phase was significantly higher compared to menstrual phase ($p < 0.001$) Likewise the values of FVC were significantly higher in secretory phase as compared to proliferative phase ($p<0.001$). The maximum difference in the values of FVC was found between menstrual and secretory phase ($p<0.001$). The values of FVC in different phases and the differences were found to be in accordance with various studies.[3,8-11] Present trends in FVC values partially matched with the results of Hebbar KR their values of FVC were also higher in secretory phase as compared to menstrual phase but values of FVC in follicular phase were less than in menstrual phase.[14] The trend of our FVC values in different phases were not in accordance with Da Silva SB et al and Das TK.[15,16]

The FEV_1 values of proliferative phase were significantly higher compared to menstrual phase ($p<0.001$) In the same fashion the values of FEV1 were significantly higher in secretory phase as compared to proliferative phase with ($p<0.001$). The maximum difference in the values of FEV1 was found between menstrual and secretory phase ($p<0.001$). The values of FEV1 in different phases and the differences were found to be in accordance with various studies.[3,9,10,13] Our FEV_1 values partially matched with the results of Hebbar KR and Kannan N et al in the way that their values of FEV_1 in follicular phase were less than in menstrual phase.[8,14] The trend of present FEV_1 values in different phases were not in accordance with Da Silva SB et al and Das TK.[15,16] They did not find significant difference of FEV_1 in different phases of menstrual cycle.

The FEFR values of proliferative phase were significantly higher compared to menstrual phase ($p<0.001$). Likewise the values of PEFR were significantly higher in secretory phase as compared to proliferative phase ($p<0.001$). The maximum difference in the values of PEFR was found between menstrual and secretory phase ($p<0.001$). These findings were found to be on par with various studies.[9,13,15] Our PEFR values partially matched with the results of Hebber KR and Kannan N in the way that their values of PEFR were in follicular phase were less than in menstrual phase.[8,14] While Chong E et al found minimal effect of menstrual cycle on PEFR in healthy non asthmatic Asian women.[17]

The values of FEV_1/FVC (%) in different phases and the differences were found to be in accordance with Hebbar KR et al and Dabhoiwla S et al.[4,14] The trend of our FEV1/FVC (%) values in different phases were not in accordance with other studies.[3,8,10,13] They found increase in FEV1/FVC (%) values in successive phases from menstrual to secretory phase.

The findings of FVC (% of pred.) were similar with the findings of Jeon YH et al their values of FVC (% of pred.) were 76.8±9.5 in menstrual period and 77.2±9.5 in non-menstrual period respectively.[7] The values of FVC, FEV1, and PEFR were higher in different phases of menstrual cycle in normal BMI group than the corresponding values in underweight BMI group. This is in accordance with the study done by Shah HD et al in which they compared FEV_1 & PEFR in 17-21 years males and found statically lower values in underweight as compared to normal weight boys.[5] On comparing normal BMI subjects the pre-obese subjects had lower PEFR values in corresponding phases of menstrual cycle. This is in conformation with study done by Ghobain MA.[6] In our study FVC & FEV_1 values in pre-obese group were higher than the corresponding values of normal BMI group. This is against the findings obtained by Satyanarayana P et al who found negative correlation of these parameters with increasing BMI.[18] The reasons of our finding may be that these subjects were not frank obese and the number in this group was less, only 7 subjects were there in this pre-obese group. One of other reasons may be that overweight girls generally have increased fat in their lower extremities rather than on abdomen and thorax which would have direct effect on diaphragmatic movement making lung function values diminished.[6]

After ignoring one subject which is present in obese group FEV1/FVC (%) decreased marginally from underweight to pre-obese group in corresponding phases of menstrual cycle. Although the differences in the values are not much but still it is in accordance with the study done by Satyanarayana P, et al.[18] Increased levels of progesterone in the secretory phase have a dual effect of overall smooth muscle relaxation and hyperventilation.[4] Bidikar MP et al also indicated bronchodilator effect of progesterone in their study.[9] Das TK also emphasized the role of progesterone in increasing the respiration by stimulating central controlling mechanisms of respiration.[16]

The pulmonary function values of proliferative phase were also significantly higher than those of menstrual phase. This is in accordance with other studies. Many studies including the present study showed lower lung function values in menstrual phase than other phases.[9,10,14]

Though statistically significant differences were demonstrated in our study, our results need to be interpreted in the background of certain limitations. An adequately powered study design which uses the objective measurements of the hormonal levels and the detailed pulmonary functions including diffusion studies, are expected to provide a better insight to the suggested relationship.

CONCLUSION

Higher values of lung functions during proliferative and secretory phases can be attributed to the higher concentrations of sex hormones specially progesterone because in most of the studies progesterone is known to cause relaxation of bronchial smooth muscle. Our study also suggests possible role of sex hormones especially progesterone in treating asthmatic females or at least reduction in the doses of bronchodilators can be done while concomitantly using progesterone.

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