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A STUDY OF FORCED VITAL CAPACITY IN DIFFERENT PHASES OF MENSTRUAL CYCLE AND ITS CORRELATION WITH SERUM PROGESTERONE AND BODY MASS INDEX IN LUTEAL PHASE AMONG HEALTHY FEMALES

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ABSTRACT: Progesterone is known to cause hyperventilation. Considering this fact, the present study was conducted on fifty healthy young volunteers with the age range of 18-25 years during their early follicular, ovulatory and luteal phases of menstrual cycle. Forced Vital Capacity (FVC) and serum progesterone levels were measured by portable spirometer (RMS HELIOS 401) and progesterone kit in IMMULITE®1000 analyzer respectively in each phase of the cycle. The anthropometric measurements such as height, weight and Body Mass Index (BMI) were measured. Serum progesterone was higher during the luteal phase which was statistically significant. FVC correlated positively with serum progesterone but failed to show any statistical significance. FVC also showed a positive correlation with BMI (18.5-24.9kg/m^{2}) which was statistically significant. This concludes a directly proportional relationship between BMI and FVC. FVC reflected a better value in luteal phase which is statistically significant as compared to the other two phases of the menstrual cycle. These observations suggest a potential role of raised progesterone levels leading to the improvement of pulmonary function during the luteal phase of the menstrual cycle.
KEYWORDS: Progesterone, FVC, BMI, Pulmonary function test, Menstrual cycle.

INTRODUCTION: In women, sex hormones play an important role in their health and literature provides some intriguing pieces of information. Menstruation is a physiological phenomenon which occurs in women during her reproductive years. Menstrual cycle occurs in three phases which are regulated by sex hormones: estrogen and progesterone.[1] Estrogen and progesterone levels affect many systems of body; not just the reproductive tract.[2]Progesterone levels fluctuate during the menstrual cycle with a difference of twenty fold between different phases of cycle.[3]

Progesterone is a known respiratory stimulant.[4]It causes increase in lung function parameters during the luteal phase due to hyperventilation. [5]Moreover, progesterone leads to bronchial relaxation in the luteal phase of menstrual cycle.[6]

FVC is one of the parameter that is usually assessed in pulmonary function. Studies show significant increase in FVC in luteal phase as compared to the early follicular and ovulatory phase of the cycle.[7]Furthermore, progesterone was positively correlated with FVC. [8]Other studies have shown that administration of synthetic progesterone did not affect the lung function parameters.[9]These evidences exhibit the presence of a relationship of progesterone with lung function parameters in luteal phase of menstrual cycle.

Researchers have linked BMI to changes in lung function.[10]Previously it has been reported that BMI has been negatively associated with values of FVC. [11]Also, BMI showed a significant positive correlation with FVC.[12]

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Although several studies have shown that BMI may affect pulmonary function, these data are still in question. So the present study was undertaken to compare FVC in different phases of menstrual cycle and its correlation with serum progesterone and BMI in healthy young females.

METHODS: The present study was carried out in Department of Physiology, A.J.Institute of Medical Sciences & Research Centre, Mangalore between January 2011 and August 2011.

Fifty healthy females with the age range of 18-25 years with the regular menstrual cycle of 28 days were included in this study. To confirm the regularity of the cycle, it was charted for 3 months.

Subjects with a history of any respiratory and cardiovascular diseases, irregular menstruation, pregnancy, hypertension, diabetes mellitus, use of contraceptive pills or any medication were excluded from the study.

Ethical clearance was obtained from the Institutes Ethical Committee. To ensure their voluntary participation, subjects were briefed about objectives of the study and an informed written consent was taken prior to the study. Brief history of the subjects was taken and all the subjects were subjected to physical examination to rule out any illness that would interfere with the outcome of the study.

The physical characters such as weight in kilograms, height in centimeters of all subjects were recorded in light clothing. BMI was calculated using Quetelet's index, BMI= weight (kg)/height^2 (m).Subjects were categorized as underweight (<18.5 kg/m^2); normal (18.5-24.9kg/m^2); overweight (25-29.9kg/m^2) and obese (30-34.9 kg/m^2). There were 40 volunteers in normal category with very few numbers of students in the rest.

From the date of onset of menstrual cycle, probable date of ovulation was calculated, based upon which, different phases of menstrual cycle was determined. Early follicular phase was calculated as the 4th day of the present cycle; ovulatory phase was calculated 14 days prior to the onset of next cycle, luteal phase as the period after ovulation to the next menstruation. If the calculated day fell on a holiday, then the subsequent cycle was taken. Subjects were asked to come on the 3rd, 13th and 21st days of menstrual cycle.

Fasting blood samples were taken on these days. The blood was then centrifuged. Collected serum samples were then taken to the lab and serum progesterone levels were estimated using IMMULITE PROGESTERONE kit in IMMULITE$_®$ 1000 analyzers (Revision A, Version 5.XX, year 2000, manufactured by The Quality System of Siemens Healthcare Diagnostics Products Ltd. Baroda).

Based on the hormone assay, subjects were confirmed to be in a particular phase of menstrual cycle. The very next day volunteers were asked to come and FVC was assessed using computerized spirometer RMS HELIOS 401.

The test was performed over 3 maneuvers according to the American Thoracic Society recommendations [13]and we accepted the best maneuver. Results were then compared with different phases of menstrual cycle and statistically analyzed.

The results were expressed as Mean ± Standard Deviation. Statistical analysis was done through SPSS for windows version 17. Comparison of serum progesterone levels were done using Wilcoxon rank test in different phases of menstrual cycle. Comparison of FVC in different phases of menstrual cycle was done using ANOVA. Correlation between progesterone and FVC was done by

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Spearman's rank correlation coefficient. Correlation between BMI with FVC was done by Pearson's correlation coefficient.

RESULTS: On analysis of fifty female subjects, the average age (years) was 18.48±1.41 (mean±SD). On analysis of anthropometric characteristics of the fifty female subjects, the average weight (kg) was 53.82±7.80 (mean±SD); average height (m) was 1.57±0.043; the average BMI (kg/m^2) was 21.34±3.17. (Table-1)

Table-1: Physical characteristics of the subjects

Physical characteristics	Mean ± SD
Age(years)	18.48 ±1.41
Weight (kg)	53.82 ±7.80
Height(m)	1.57±0.04
BMI(kg/m^2)	21.34±3.17

The average (mean ±SD) progesterone levels (ng/mL) in early follicular, ovulatory and luteal phases were 0.946± 0.96; 2.72±2.94 and 7.84±7.34 respectively which was statistically significant ($p<0.001$) (Table-2, Graph-1)

Table-2: Comparison of progesterone in different phases of menstrual cycle

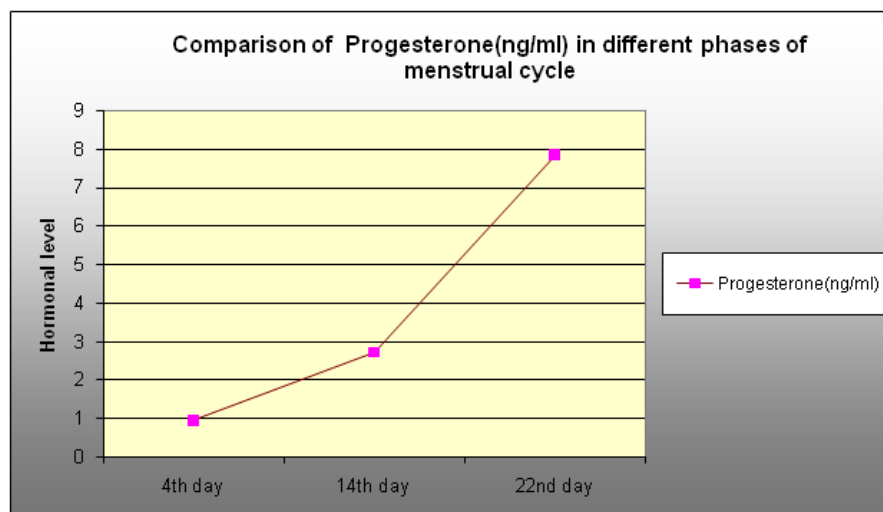| HORMONE LEVEL (Mean ±SD)	Early follicular phase	Ovulatory Phase	Luteal phase	H	p
Progesterone(ng/mL)	0.94±0.96	2.72±2.94	7.84±7.34	43.724	< .001***

Ns-not significant   *significant- < 0.05
** Highly significant-<0.01   *** very highly significant-<0.001

Graph-1: Comparison of Progesterone in different phases of menstrual cycle

The actual value (mean ±SD) of FVC (L) in early follicular, ovulatory and luteal phases were 2.40±0.36 (64.48±9.04 %predicted), 2.49±0.43 (66.1±8.38 %predicted) and 2.68±0.46 (69.7±7.05

%predicted) respectively. The FVC was statistically highly significant (p0.004) in luteal phase when compared to early follicular and ovulatory phase. (Table-3, Graph-2)

Table-3: Comparison of FVC (L) in different phases of menstrual cycle

Parameters (Mean±sd)	Early follicular phase	Ovulatory phase	Luteal phase	F value	p value
FVC(Absolute value)	2.40±0.36	2.49±0.43	2.68±0.46	5.73	0.004 **
FVC(% PREDICTED)	64.48±9.04	66.1±8.38	69.7±7.05	5.34	0.006 **

*significant- < 0.05   ns-not significant   ** highly significant-<0.01
*** Very highly significant-<0.001

Graph-2: Comparison of mean of FVC in different phases of menstrual cycle
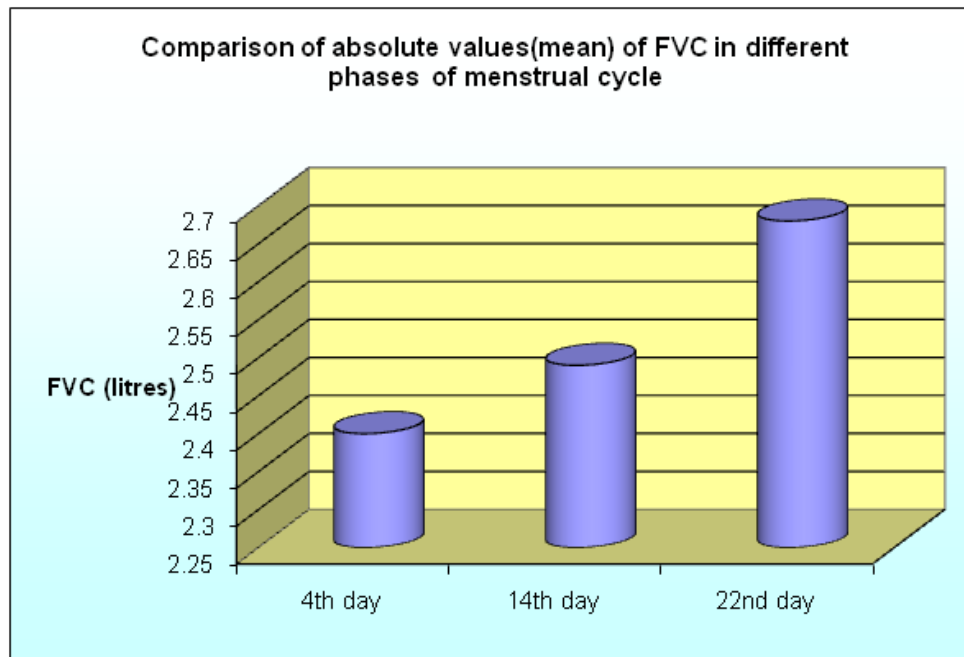
Spearman's rank correlation between progesterone levels and FVC was done in luteal phase of menstrual cycle and it was found that there was a positive correlation between progesterone and FVC (p 0.159,r =0.20), which was not statistically significant. Pearson's correlation between BMI (normal) and FVC was done and it was found that that there was a positive correlation between BMI and FVC, which was statistically significant with FVC (p= 0.01, r=0.35). (Table-4, Graph-3)

Table-4: Correlation of FVC between serum progesterone and BMI

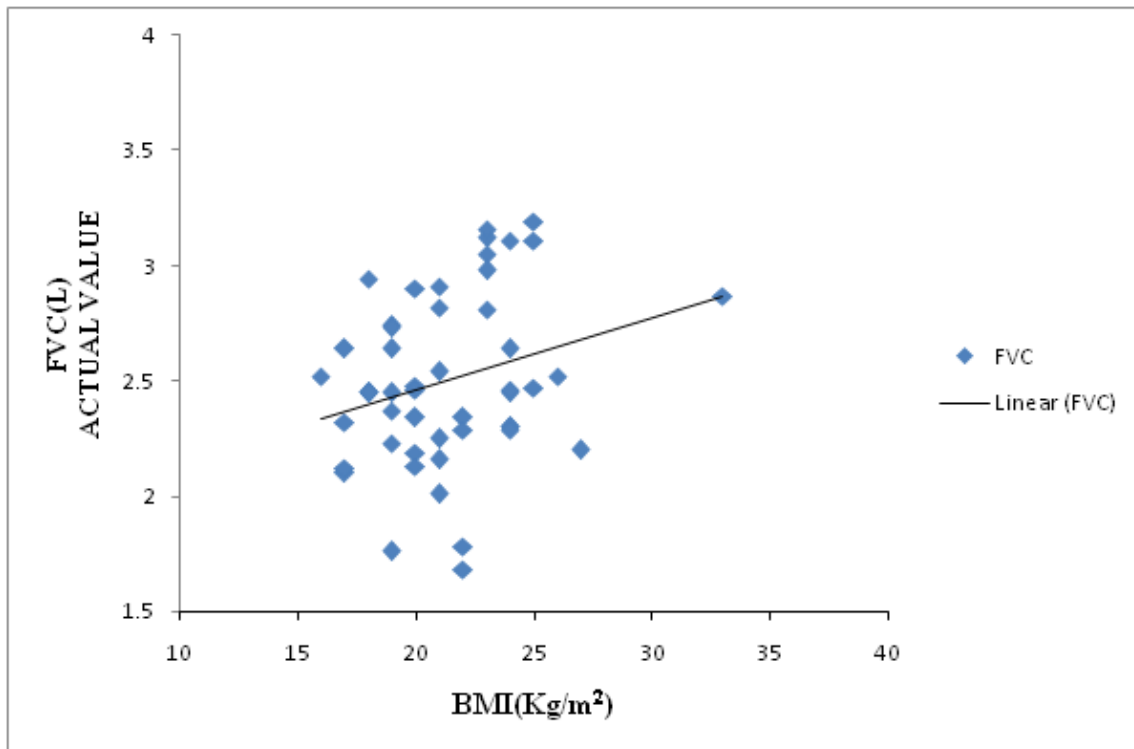| Correlation between FVC and	r	p
Serum progesterone	0.202	0.159 ns
BMI(normal)	0.350	0.01*

ns- Not significant   *significant- < 0.05
** Highly significant-<0.01   *** very highly significant-<0.001

Graph-3: Scatter diagram showing positive correlation between FVC and BMI

DISCUSSION: For most women, menstrual cycle is an integral part of a major portion of their lives. The cyclical variation in ovarian hormonal levels during each menstrual cycle is associated with characteristic changes in physiological functions.

Menstrual cycle was classified as early follicular phase, ovulatory phase and luteal phase in some of the studies. Progesterone levels were done to confirm the phases of the menstrual cycle. FVC were assessed during the three phases of the menstrual cycle which was then correlated with serum progesterone and BMI in healthy females.

The serum levels of progesterone were studied during all the phases of menstrual cycle. Serum progesterone levels were significantly higher in luteal phase in comparison to those of early follicular and ovulatory phase. These observations are consistent with those reported by other studies. [2, 5, 7]

In the present study, FVC was found to be increased significantly and gradually from early follicular through ovulatory to luteal phases of menstrual cycle. The result is in consensus with other studies. [2, 5,7,14]

Available literature has unfurled several suggestions foregrounding the effect of higher progesterone level in changing FVC in healthy females.

In the present study, serum progesterone levels were positively correlated with the values of FVC which was not statistically significant. This was comparable with some of the studies. [8,14] In the present study, improved pulmonary function in luteal phase might be related to high progesterone level which induces hyperventilation by : 1.Direct stimulation of respiratory center.[15] Respiratory response to progesterone is mediated at a hypothalamic site through an estrogen (E2) dependent progesterone receptor (PR) mediated mechanism requiring RNA and protein synthesis (gene

expression).[16]2.Increased oxygen consumption due to increased basal metabolic rate.[9]Increase in basal oxygen consumption may be due to hyperventilation.[17] The exogenous progesterone preparations are also found to show an increase in resting minute volume.[7]

Moreover, progesterone may potentiate prostaglandin induced relaxation of bronchial smooth muscles. For this reason bronchial relaxation is well marked during luteal phase through a β- adreno-receptor mediated mechanism. [18]

In the present study since most of the volunteers were within normal BMI ($18.5-24.9 kg/m^2$), only the BMI within the normal range was correlated with FVC in luteal phase. There was a positive correlation between BMI and FVC in luteal phase of menstrual cycle which was statistically significant. This finding was consistent with some of the studies.[12, 19] This is due to the related increase in muscle strength; the pulmonary function initially increases in parallel with weight gain.[20]

Body mass index has been intended to study the effects of increased weight on pulmonary function tests, but its use is only well-grounded for lung function indices where the contribution of fat and muscles are synergistic. [21] It has been recognised that many women are prone for asthmatic attacks just a few days before the menstrual period. This display of asthma in females is called 'premenstrual asthma'.[22] Thus this study provides the importance of role of progesterone in respiratory drive/respiratory effects in women .The respiratory stimulant action of progesterone is being put to use clinically in the treatment of hypoventilation syndrome and emphysema. Studies have shown that exogenous progesterone preparations increase resting minute volume. This data adds up to the recent concept on premenstrual asthma, due to exaggeration of normal cyclical variation in lung functions in patients suffering from asthma.

CONCLUSION: In the present study, improvement in FVC is probably due to increased serum progesterone level in the luteal phase of menstrual cycle. In addition, FVC was positively correlated with serum progesterone and BMI; but was statistically significant with BMI.

LIMITATIONS: The study was carried out on a small group in single institution. The study included small number of students in overweight and obese groups so a larger sample size will emphatically be of great value in predicting the relationship between FVC and BMI.

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