

An Observational Study of Variation in the Pulmonary Functions with the Phases of Menstrual Cycle in Females of Different Age Groups

Sheeba Shaheen¹, Vibha Gangwar^{2,*}, Nitin Ashok John², Shweta Gupta²

ABSTRACT

Background and Aim: Many evidences are available showing influence of estrogen and progesterone on respiratory function. Still, there is no clear picture of this. Therefore, we aimed this study to evaluate the pulmonary functions in various phases of menstrual cycle in females of different age groups. **Methods:** Sixty healthy females with normal menstrual cycle participated in study. They were divided into 3 groups of 20 females each. The age ranged between 15-25, 26-35 and 36-45 years in group I, II and III respectively. Their pulmonary functions were measured in menstrual, follicular and secretory phase of a single cycle after taking detailed history and preliminary examination. **Results:** There was no significant difference in pulmonary functions in all the three phases of menstrual cycle between the groups. In menstrual phase, ratio of forced expiratory volume in first sec and forced vital capacity (FEV1/FVC) FEV1/FVC ratio while in follicular phase, forced expiratory volume in first sec (FEV1), FEV1/FVC ratio and forced expiratory flow during 25% to 75% of expiration (FEF_{25-75%}) were significantly higher in group I than other groups. No significant difference was found in parameters in secretory phase between three groups. **Conclusion:** Pulmonary functions didn't change with the phases of menstrual cycle contradicting the results of previous studies. Pulmonary functions in terms of FEV1 and FEV1/FVC ratio and FEF_{25-75%} were significantly better in menstrual phase and follicular phase in age groups of 15-25 years than older age groups.

Key words: Follicular phase, Menstrual phase, Secretory phase, Pulmonary functions, Age group.

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INTRODUCTION

Menstrual cycle includes the duration from the first day of menstrual bleeding of one cycle to the first day of menstrual bleeding of next cycle with an average duration of 28 days.^[1] It is divided into menstrual, proliferative and secretory phase.^[2] The proliferative phase lasts for 1-14 days which also includes menstrual phase (1-5 days) and secretory phase starts from fifteenth day and lasts at the onset of next menstrual phase.^[3] Rhythm of menstrual cycle is controlled by Gonadotropin Releasing Hormone (GnRH), Luteinizing Hormone (LH) and Follicular Stimulating Hormone (FSH) secreted from hypothalamo-pituitary axis and oestrogen and progesterone secreted from ovary.^[4] Fluctuation in the level of these hormones in menstrual cycle affects not only reproductive system but also the functional parameters of other systems including brain, musculoskeletal system, cardiovascular system and respiratory system.^[5] Progesterone which is secreted in secretory phase after ovulation, relaxes smooth muscles in gut, genitourinary tract, vascular tree and bronchial smooth muscles. It is known to strengthen the smooth bronchial muscles. It stimulates respiration

by stimulating the respiratory centres.^[6] The alveolar PO₂ in males is more than the females during the luteal phase.^[1] It may also have some effect on the physical performance and VO₂ max.^[7]

Respiratory diseases are the third leading cause of death (9.2% of total deaths) in India as reported in 2017.^[8] Although there are various pathophysiological factors affecting chronic respiratory diseases, women are increasingly affected from these disorders for unknown reasons. The frequency of asthma and allergic diseases is greater in girls than boys around puberty and thereafter.^[9] The hormonal changes and other factors during adolescence may contribute to it. Symptoms of asthma aggravate during the premenstrual or menstrual phase of menstrual cycle in some female patients.^[10] These data suggest that female gender is an important risk factor for respiratory diseases and there is a possibility of role of female hormones in mediating these diseases but the exact physiology behind this is still not known.

Differences in pulmonary functions between males and females are present throughout life and have

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been associated with sex specific responses to environmental and lifestyle insults and sex hormones.^[11,12] The Isparta Menopause and Health study found that lower FEV1 and FVC was associated with menopause and this was explained by age.^[13]

Many studies have been done to evaluate the effect of various phases of menstrual cycle on pulmonary functions but the clear picture is not available. Also, changes in pulmonary functions in different phase of menstrual cycle with age are not studied till now.

Therefore, we planned this study with the hypothesis that hormonal changes in various phases of menstrual cycle cause change in respiratory functions too and increasing age may have a negative effect on these changes, based on the previous researches.

MATERIALS AND METHODS

This observational prospective study was done as a project of short-term studentship under Indian Council of Medical Research, in the department of physiology, Dr. Ram Manohar Lohia Institute of medical sciences, Lucknow, India from May 2019 to September 2019. Sixty apparently healthy females with normal regular menstrual cycle of twenty-eight days were selected to participate in the study by simple random sampling technique. Subjects having history of any pelvic pathology, menstrual irregularity, long term medication, use of oral contraceptives, smoking, current pregnancy, pulmonary and endocrine disorder were excluded from the study. As this work involved human subjects, it had been done in accordance with the code of ethics of the world medical association (Declaration of Helsinki) and was approved by ethics committee of institute. A written consent was obtained from all the subjects after explaining the procedure and their privacy rights were considered properly. All the participants were divided into three groups of 20 subjects each according to their age. The age ranged between 15 to 45 years, 26 to 35 years and 36 to 45 years in group I, II and III respectively. The participants were asked to fill a detailed questionnaire to assess their medical history. Their height, weight, pulse and blood pressure was recorded. BMI was calculated with the help of Quetlet's index. Their menstrual history was recorded specially containing date of last menstrual cycle, dates of last three consecutive menstrual cycles and duration of menses. The probable date of ovulation was calculated by the date of onset of menstruation, based upon which different phases of menstrual cycle were determined. Follicular phase was calculated as the 4th day of the present cycle, ovulatory phase 14 day prior to the onset of next cycle and luteal phase as the period after ovulation to the onset of next menstrual cycle. The subjects were asked to report three times: between 2nd and 4th day (menstrual phase), 10th and 12th day (follicular phase) and 22nd and 24th day (secretary phase) of a single menstrual cycle in the morning hours between 11.00 am to 1.00 pm.

Pulmonary functions were assessed with the help of "Easy On PC" spirometer [nidd Medical Technologies, Inc. MA] with software named "Easy Connect" in all the three phases. The subjects were explained the whole procedure in detail. They were made to sit on a stool and were asked to inhale to their maximum ability. Then mouthpiece was placed between the lips creating air tight seal. The nose clip was attached and the subjects were to do a maximum forced and rapid expiration followed by rapid forced inspiration. The procedure was performed for three times and the machine gave best manoeuvre result.

Statistical Analysis of Data

Data were expressed as mean \pm standard deviation. Comparison of pulmonary function tests in various phases of menstrual cycle in various groups were done by ANOVA (Analysis of variance) test with the help of Excel's statistics tool. *P* value less than 0.05 was considered as significant.

RESULTS

This study included sixty female subjects from the staff of Dr. Ram Manohar Lohia Institute of Medical sciences, Lucknow. They were divided into three groups according to their age. The mean age of the participants was 19.55 ± 2.74 years, 30.56 ± 2.71 years and 38.79 ± 2.78 years. Their mean BMI was 20.76 ± 4.09 , 21.98 ± 3.40 and 21.95 ± 3.44 kg/m² in group 1, 2 and 3 respectively (Table 1).

The parameters of pulmonary function tests in menstrual, proliferative and secretary phase were similar in all the groups and there was no significant difference (Table 2).

Pulmonary functions were also compared between all the groups in menstrual, proliferative and secretary phases separately. In menstrual phase, there was no significant difference in all parameters except FEV1/FVC ratio which significantly females of group 1 than group 2 and 3 ($P=0.004$). In proliferative phase, the mean FEV1, FEV1/FVC and FEF_{25-75%} were significantly higher in group 1 than group 2 and 3 ($P=0.034$, $P=0.001$ and $P=0.007$ respectively). No significant difference was found in other parameters. There was no significant difference in pulmonary functions in luteal phase between all the groups ($P>0.05$) (Table 3).

DISCUSSION

Many studies have been done to evaluate the effect of menstrual cycle on lung functions which involved the young girls^[14-18] but we included subjects of three age groups viz 15-25 years, 26-35 years and 36-45 years in our study and evaluated the changes of pulmonary functions in all these age groups.

We determined the phases of menstrual cycle on the basis of duration of the menstrual cycle as done in other studies^[16,19] but some studies confirmed these phases by serum progesterone and estrogen levels.^[20]

We found no significant change in lung functions in various phases of menstrual cycle in our study and contradicted the results of previous studies in which the lung functions were better in secretary phase than that of menstrual and follicular phase.^[15-18,21] However, some studies also found results similar to our study.^[22] Pauli BD *et al.* found premenstrual worsening of asthma symptoms and Peak Expiratory Flow Rate (PEFR) but they did not relate these changes to the deterioration in spirometry and airway reactivity or to the absolute levels of circulating progesterone and estradiol.^[23]

Mannan *et al.* found significantly increased FEV1, FVC and FEV1/FVC in luteal phase than follicular and menstrual phase in their study. The *P* value was <0.001 . They attributed this change to higher concentration of plasma progesterone level in secretary phase which relaxes the bronchial smooth muscle.^[24] In our study, there was no change in FEV1, FVC and FEV1/FVC ratio with the phases of menstrual cycle. Timon R *et al.* and Da Silva SB also reported no changes in FVC and FEV1 during the different phases of menstrual cycle.^[22,25] These results can be explained on the basis of study done by Hayes *et al.* who reported that estrogen could affect central nervous activity but not peripheral reflexes which are involved in respiratory mechanism.^[26]

Table 1: Anthropometric parameters of the subjects.

Parameters	Group 1 (Mean \pm SD)	Group 2 (Mean \pm SD)	Group 3 (Mean \pm SD)	1P-Value
Weight (Kg)	50.41 \pm 13.12	52.25 \pm 10.56	51.11 \pm 8.81	0.881
Height (meters)	154.95 \pm 7.14	153.67 \pm 4.95	152.42 \pm 4.49	0.383
Body mass index (kg/m ²)	20.76 \pm 4.09	21.98 \pm 3.40	21.95 \pm 3.44	0.493

Table 2: Pulmonary functions in different phases of menstrual cycle in group 1, 2 and 3.

Parameter		Menstrual phase	Follicular phase	Secretary phase	'P value
		Mean \pm SD	Mean \pm SD	Mean \pm SD	
FEV1 (L)	Group 1	2.13 \pm 0.56	2.15 \pm 0.53	2.01 \pm 0.56	0.676
	Group 2	1.93 \pm 0.37	1.98 \pm 0.28	2.02 \pm 0.34	0.776
	Group 3	1.82 \pm 0.41	1.78 \pm 0.40	1.90 \pm 0.40	0.695
FVC (L)	Group 1	2.47 \pm 0.63	2.47 \pm 0.63	2.34 \pm 0.68	0.759
	Group 2	2.38 \pm 0.38	2.39 \pm 0.38	2.48 \pm 0.40	0.733
	Group 3	2.32 \pm 0.43	2.26 \pm 0.45	2.38 \pm 0.42	0.715
FEV1/FVC	Group 1	86.32 \pm 6.4	87.00 \pm 6.63	85.85 \pm 8.69	0.875
	Group 2	81.02 \pm 6.93	83.41 \pm 5.70	83.01 \pm 5.44	0.534
	Group 3	78.12 \pm 8.40	78.69 \pm 7.35	79.39 \pm 7.95	0.904
FEF _{25-75%} (L/S)	Group 1	2.49 \pm 0.88	2.57 \pm 0.78	2.40 \pm 0.89	0.815
	Group 2	2.17 \pm 0.82	2.24 \pm 0.55	2.27 \pm 0.62	0.931
	Group 3	1.83 \pm 0.70	1.83 \pm 0.72	1.97 \pm 0.82	0.831
PEF (L/S)	Group 1	4.40 \pm 1.47	5.91 \pm 7.07	4.08 \pm 1.31	0.345
	Group 2	3.93 \pm 1.47	4.40 \pm 1.16	4.35 \pm 1.26	0.570
	Group 3	4.01 \pm 1.10	4.05 \pm 1.23	4.43 \pm 1.29	0.575
FIVC (L)	Group 1	2.47 \pm 0.77	2.44 \pm 0.61	2.54 \pm 0.65	0.897
	Group 2	2.48 \pm 0.44	2.39 \pm 0.52	2.49 \pm 0.42	0.832
	Group 3	2.37 \pm 0.40	2.34 \pm 0.57	2.40 \pm 0.44	0.957
PIF (L/S)	Group 1	3.21 \pm 1.12	3.17 \pm 1.11	3.26 \pm 1.12	0.970
	Group 2	3.17 \pm 1.08	2.94 \pm 0.87	3.10 \pm 0.67	0.771
	Group 3	2.96 \pm 0.87	2.89 \pm 1.06	3.18 \pm 1.26	0.729
VC (L)	Group 1	2.49 \pm 0.69	2.51 \pm 0.64	2.43 \pm 0.7	0.932
	Group 2	2.37 \pm 0.42	2.45 \pm 0.42	2.38 \pm 0.46	0.858
	Group 3	2.17 \pm 0.44	2.13 \pm 0.50	2.23 \pm 0.49	0.851
RV (L)	Group 1	1.14 \pm 0.39	1.04 \pm 0.41	1.10 \pm 0.4	0.708
	Group 2	1.10 \pm 0.38	1.15 \pm 0.26	1.14 \pm 0.32	0.929
	Group 3	1.03 \pm 0.39	0.99 \pm 0.49	0.85 \pm 0.40	0.474
Tidal volume (L)	Group 1	0.53 \pm 0.21	0.62 \pm 0.22	0.56 \pm 0.2	0.345
	Group 2	0.55 \pm 0.21	0.52 \pm 0.23	0.69 \pm 0.52	0.399
	Group 3	0.60 \pm 0.25	0.57 \pm 0.19	0.61 \pm 0.19	0.793

Dabhoiwala S *et al.* reported no significant difference in FEF_{25-75%} in various phases of menstrual cycle which was similar to the result of our study.^[19] Gokhle *et al.* and Nandhini R *et al.* found a significantly increased FEF_{25-75%} in secretary phase due to relaxation of bronchial smooth muscles in luteal phase.^[5,27]

PEF measures the airflow through the bronchi and thus degree of obstruction in airways. Rajesh CS,^[7] Handergulle SM *et al.*^[15] Kaur H^[17] Gavali MY^[28] and Arora D^[29] reported increased PEFR in luteal phase than the menstrual and follicular phase while our study didn't find any significant difference in PEFR in various phases of menstrual cycle.

We also measured vital capacity, residual volume and tidal volume in our study but found no significant change in these parameters with the phases of menstrual cycle. Other studies didn't measure these parameters.

We also studied the changes in pulmonary functions during menstrual cycle in various groups. No other study has done to compare pulmonary functions in different age groups. We found significantly better FEV1/FVC ratio in age group of 15-25 years in menstrual and proliferative phase but no difference in secretary phase. In proliferative phase, FEV1 and FEF_{25-75%} were also better in age group of 15-25 years than other age groups. These changes can be explained on the basis of structural changes in airway as well as in muscles and lung functions associated with ageing^[30] Aging also causes alterations in carotid chemoreceptors, respiratory neuronal circuits and cellular and molecular events that accompany the aging process.^[31,32] Young neurons respond to sex hormones differently from aged neurons.

Table 3: Comparison of pulmonary function tests between all the groups in Menstrual, proliferative and secretory phase.

Parameter		Group 1	Group 2	Group 3	¹ P value
		Mean±SD (n=20)	Mean±SD (n=20)	Mean±SD (n=20)	
FEV1 (L)	Menstrual phase	2.13±0.56	1.93±0.37	1.82±0.41	0.137
	Proliferative phase	2.15±0.53	1.98±0.28	1.78±0.40	0.034 [*]
	Secretary phase	2.01±0.56	2.02±0.34	1.90±0.40	0.726
FVC (L)	Menstrual phase	2.47±0.63	2.38±0.38	2.32±0.43	0.683
	Proliferative phase	2.47±0.63	2.39±0.38	2.26±0.45	0.425
	Secretary phase	2.34±0.68	2.48±0.40	2.38±0.42	0.753
FEV1/FVC	Menstrual phase	86.32±6.40	81.02±6.93	78.12±8.40	0.004 [*]
	Proliferative phase	87.00±6.63	83.41±5.70	78.69±7.35	0.001 [*]
	Secretary phase	85.85±8.69	83.01±5.44	79.39±7.95	0.058
FEF _{25-75%} (L/S)	Menstrual phase	2.49±0.88	2.17±0.82	1.83±0.70	0.058
	Proliferative phase	2.57±0.78	2.24±0.55	1.83±0.72	0.007 [*]
	Secretary phase	2.35±0.90	2.27±0.62	1.97±0.82	0.365
PEF (L/S)	Menstrual phase	4.40±1.47	3.93±1.47	4.01±1.10	0.549
	Proliferative phase	5.91±7.07	4.40±1.16	4.05±1.23	0.402
	Secretary phase	4.08±1.31	4.35±1.26	4.43±1.29	0.712
FIVC (L)	Menstrual phase	2.47±0.77	2.48±0.44	2.37±0.40	0.839
	Proliferative phase	2.44±0.61	2.39±0.52	2.34±0.57	0.877
	Secretary phase	2.54±0.65	2.49±0.42	2.39±0.44	0.740
PIF (L/S)	Menstrual phase	3.21±1.12	3.17±1.08	2.96±0.87	0.757
	Proliferative phase	3.17±1.11	2.94±0.87	2.89±1.06	0.650
	Secretary phase	3.25±1.12	3.10±0.67	3.18±1.26	0.912
VC (L)	Menstrual phase	2.49±0.69	2.37±0.42	2.17±0.44	0.241
	Proliferative phase	2.51±0.64	2.45±0.42	2.13±0.50	0.082
	Secretary phase	2.43±0.67	2.38±0.46	2.23±0.49	0.550
RV (L)	Menstrual phase	1.14±0.39	1.10±0.38	1.03±0.39	0.712
	Proliferative phase	1.04±0.41	1.15±0.26	0.99±0.49	0.551
	Secretary phase	1.10±0.40	1.14±0.32	0.85±0.40	0.080
Tidal volume (L)	Menstrual phase	0.53±0.21	0.55±0.21	0.60±0.25	0.615
	Proliferative phase	0.62±0.22	0.52±0.23	0.57±0.19	0.369
	Secretary phase	0.56±0.20	0.69±0.52	0.61±0.19	0.506

CONCLUSION

Our study concluded that

- There is no significant correlation of pulmonary functions with the phases of menstrual cycle thus it contradicts results of previous studies.
- FEV1 and FEV1/FVC ratio and FEF_{25-75%} are better in menstrual and follicular phase in age groups of 15-25 years than that in older age groups.

Continued research is needed to address the complex mechanisms on respiratory functions during different phases of menstrual cycle as the results of various studies are conflicting. Also, further studies should be done to understand the impact of sex hormones at different ages in menstrual cycle. We can customize and target hormone therapies for various

respiratory disorders that affect females at various ages by understanding of how sex hormones affect respiratory control system.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

FEV1: Forced expiratory volume in first second; **FVC:** Forced vital capacity; **FEF_{25-75%}:** Forced expiratory flow during 25% to 75% of expiration; **GnRH:** Gonadotropin releasing hormone; **LH:** Luteinizing hormone; **FSH:** Follicular stimulating hormone; **PEFR:** Peak expiratory flow rate.

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