

**Research Article**

## **INFLUENCE OF MENSTRUAL CYCLE ON LUNG FUNCTIONS IN ASTHMATIC FEMALES**

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### **ABSTRACT**

The correlation between phases of menstrual cycle and aggravation of asthma is studied. Menstrual cycle is an integral part of life of women. There is widespread agreement that changes in the levels of estrogen and progesterone associated with menstrual cycle also affect different systems of the body. Levels of estrogen and progesterone are maximum in the secretory phase and minimum just before the menstruation. Bronchial asthma is one of the commonest chronic respiratory diseases. Premenstrual worsening of asthma symptoms has been reported to affect 33%-40% of asthmatic women. This exacerbation of asthma symptoms has been correlated with the estrogen and progesterone levels. The purpose of our study was to confirm the probable effects of female hormones on lung functions in asthmatic women in different phases of menstrual cycle. The study included 40 asthmatic females in the age group of 15-45 years. Pulmonary function tests (PFTs) were done in three phases of menstrual cycle i.e. follicular, secretory and menstrual phase in all the subjects. The mean value of lung functions i.e. FVC, FEV<sub>1</sub>, PEFR, FEV<sub>25-75</sub>, PEF<sub>200-1200</sub> in secretory phase were significantly higher than in menstrual phase ( $p < 0.005$ ). The PFTs in menstrual phase were even lower than the follicular phase ( $p < 0.04$ ). We concluded that the smooth muscle relaxant effect of progesterone and probably estrogen might have contributed to the above result.

**Key Words:** Menstrual Cycle, Pulmonary Functions, Asthma, Progesterone, Estrogen

### **INTRODUCTION**

Bronchial asthma is one of the commonest chronic diseases. Weinberger and Drazen (2001) reported asthma is one of the leading causes of emergency admissions in hospitals. It is a clinical syndrome characterized by recurrent episodes of airway obstruction. American Thoracic Society defined asthma as a "disease characterized by an increased responsiveness of trachea and bronchi to various stimuli, and manifested by widespread narrowing of the airways that changes in severity either spontaneously or as a result of treatment". Gender differences have been recognized in asthma (Becklake and Kauffmann, 1999) (Cotes, 1993). By the age of 14 years, risk of asthma is 4 times greater for boys but female predominance is seen in 15-50 years of age group (Ynhiia and Aracia, 2003). Women comprise 75% of adult admissions to the hospitals due to asthma (Skobeloff *et al.*, 1996) of which almost 50% of emergency visits occur during the peri-menstrual phase (Zimmermann *et al.*, 2000). This exacerbation of asthma occurring few days prior to menstruation has been termed as "Premenstrual Asthma" (Chhabra, 2005) (Chandler *et al.*, 1997). However, as some patients with cyclic variation in symptoms may have exacerbation at other times during the menstrual cycle, other terms have been used to describe this phenomenon. These include "Menstrual Associated Asthma" or Menstruation Linked Asthma (MLA) (Agarwal and Shah, 1997) (Nabuko *et al.*, 1999) or Peri-menstrual Asthma. (Shames *et al.*, 1998).

The premenstrual worsening of asthma symptoms has been reported to affect 33% to 40% of asthmatic women. This exacerbation of asthma symptoms during premenstrual phase has been correlated with the estrogen and progesterone levels. (Hanley, 1981) (Beynon *et al.*, 1988) (Rumball, 2001). Changes in progesterone and estrogen blood levels have effect on pulmonary functions and airway musculature.

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During premenstrual and menstrual phases, as these hormone levels are lower, asthmatics have been found to experience an increase in asthma attacks.

On contrary, some studies have reported lack of definitive changes in asthma severity over different phases of menstrual cycle (Zimmermann *et al.*, 2000; Weinmann *et al.*, 1987).

The purpose of our study was to confirm the probable effects of the female hormones on the bronchial musculature. This may explain changes in severity of symptoms of asthma during different phases of menstrual cycle. The results of our study may in some way help to modify the treatment of asthmatic women especially in the menstruating age groups, for example the dose of bronchodilatory medication may be appropriately changed during various phases of menstrual cycle on a routine basis.

Hence it was worthwhile to do the pulmonary function tests in asthmatic females in menstruating age group during various phases of menstrual cycle and to observe and compare the variations.

The limitation of the present study was the small sample size of the patients. Secondly, serum levels of estrogen and progesterone could not be estimated in the patients due to financial constraints.

### **MATERIALS AND METHODS**

In the present study, 40 known female patients of bronchial asthma attending General Medicine OPD, Chest and TB Clinic or Health institutes in or around were included in the study. The diagnosis of asthma was confirmed from history, clinical examination, investigations and old treatment records. Menstrual history was taken in detail and only females in menstruating age group were included. The patients were explained in detail about the purpose of the study.

The following criteria were considered while selecting a case for the study:

1. Only asthmatic women in menstruating age group i.e. 15 to 45 years were included in the study.
2. The patients who had suffered an asthmatic attack in last 2 months were not included in the study.
3. The females with respiratory illness other than asthma or any medical disease affecting lungs were excluded from the study.
4. Pregnant women were not included in the study.
5. Women on oral contraceptives i.e. having anovulatory cycles were not included.
6. Women with post-hysterectomy status were excluded from the study.

Only the patients fulfilling all the above criteria were included in the study. The Pulmonary functions of these were done in various phases of menstrual cycle. The variations in Pulmonary functions were then studied in asthmatics.

The Pulmonary Functions were done using a Vitalograph COMPACT II. It is an electronic spirometer. It fulfills the accuracy and precision criteria as per American Thoracic Society recommendations. It detected instantaneous expired and inspired respiratory air with a Fleisch Pneumotachograph type of flowhead. Inside the flowhead, there was a resistance in form of a series of parallel tubes which maintain laminar flow in the air passing through it. This created differential pressure which is measured by the transducer inside the instrument. Before performing the test, each female was asked to give an informed consent. The first time the subjects attempted the maneuvers they were given specific detailed instructions and demonstration on how to perform the tests.

The subjects were made to sit in an upright position without any back rest. They were instructed to take maximal inspiration and blow into the instrument rapidly and forcefully. Second time they were asked to take maximal inspiration and make a prolonged forceful expiration, followed by, re-inspiration from the mouthpiece. A close watch was kept to ensure that a tight seal was maintained between lips and mouthpiece of the device. The pulmonary functions were then recorded.

The spirometry done was standardized as per American Thoracic Society criteria. Three readings were taken at a sitting and the highest reading at any testing session was used in trend analysis. The subjects not performing properly and not meeting the standardization criteria were excluded from the study.

The readings from the instrument were recorded in each female three times during the menstrual cycle:

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1. One during the first or second day of the menstrual period henceforth referred to as the menstrual phase.
  2. The second reading was taken in the middle of the proliferative or follicular phase.
  3. The third reading was taken in the middle of the secretory or luteal phase.
- The indices which were measured in the study include:
1. Vital Capacity (VC).
  2. Forced Vital Capacity (FVC).
  3. Forced Expiratory Volume in one second (FEV<sub>1</sub>).
  4. FEV<sub>1</sub>/FVC
  5. Peak Expiratory Flow Rate (PEFR).
  6. Maximal Expiratory Flow Rate (MEFR or FEF<sub>200-1200</sub>).
  7. Maximal Mid-Expiratory Flow Rate (MMEFR or FEF<sub>25-75%</sub>).

After recording these indices they were subjected to statistical analysis.

## RESULTS AND DISCUSSION

The present study of comparison of Pulmonary functions in three phases of menstrual cycle was carried out in 40 asthmatic female patients with regular menstrual cycle in range of  $28 \pm 2$  days.

To minimize the error in the study the cases were divided into two groups each.

**Group I** – included 20 asthmatic patients in the 15-30 years age group.

**Group II** – included 20 asthmatic patients in the 31-45 years age group.

The mean values of all the parameters of lung function tests in all the phases were higher in Group I than Group II. The mean values of VC and FVC in both Group I and Group II were highest in secretory phase followed by follicular phase and lowest in menstrual phase. The mean values of all the lung functions i.e. FEV<sub>1</sub>, PEFR, FEF 25- 75%, PEF 200-1200, in both the groups were significantly higher in secretory phase followed by follicular phase and lowest in menstrual phase. No significant variation was found in values of FEV<sub>1</sub>/FVC in both the groups. (TABLE – 1&2)

**Table – 1 Pulmonary function tests in asthmatics in age group 15-30 years**

S.no	Pulmonary function test	Follicular phase	Secretory phase	Menstrual phase
1	VC	$2.43 \pm 0.35$	$2.53 \pm 0.38$	$2.33 \pm 0.34$
2	FVC	$2.44 \pm 0.38$	$2.52 \pm 0.37$	$2.33 \pm 0.39$
3	FEV 1	$1.82 \pm 0.20$	$2.00 \pm 0.22$	$1.71 \pm 0.25$
4	FEV 1/FVC	$76.5 \pm 11.69$	$80.85 \pm 8.9$	$74.05 \pm 11.65$
5	PEFR	$254.9 \pm 73.18$	$269.7 \pm 63.09$	$237 \pm 77.68$
6	FEF 25-75	$2.13 \pm 0.24$	$2.37 \pm 0.28$	$2.03 \pm 0.29$
7	PEF 200-1200	$2.83 \pm 0.58$	$2.99 \pm 0.58$	$2.69 \pm 0.61$

**Table – 2 Pulmonary function tests in asthmatics in age group 31-45 years**

S.no	Pulmonary function test	Follicular phase	Secretory phase	Menstrual phase
1	VC	$2.41 \pm 0.38$	$2.47 \pm 0.41$	$2.29 \pm 0.38$
2	FVC	$2.41 \pm 0.36$	$2.44 \pm 0.45$	$2.26 \pm 0.32$
3	FEV 1	$1.87 \pm 0.30$	$1.93 \pm 0.27$	$1.76 \pm 0.29$
4	FEV 1/FVC	$79.95 \pm 10.44$	$80.85 \pm 9.28$	$80.70 \pm 11.86$
5	PEFR	$275.35 \pm 68.54$	$281.05 \pm 50.63$	$255.0 \pm 73.63$
6	FEF 25-75	$2.13 \pm 0.54$	$2.24 \pm 0.37$	$2.04 \pm 0.51$
7	PEF 200-1200	$3.18 \pm 0.69$	$3.24 \pm 0.71$	$2.99 \pm 0.68$

Mean values of all the parameters in the 3 phases of menstrual cycle of each group were compared and subjected to statistical analysis.

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Three Pairs were made for the analysis.

Pair 1 -- Follicular and menstrual

Pair 2 – Secretory and menstrual

Pair 3 – Follicular and secretory

A statistically significant result was found when we compared the adjacent phase recordings with each other by the paired student's 't' test for majority of the parameters studied in majority of the cases.

The values of secretory phase compared with the menstrual phase were most significant within each test (p value <0.005).

The comparison is shown in table 3

**Table 3: Statistical analysis of pulmonary function tests in three phases of menstrual cycle**

Sr. No.	PFT's	Group Comparison	t test		p value		Significance	
			I	II	I	II	I	II
1.	VC (Lt)	Pair 1	-3.424	-4.884	0.003	0.000	S	S
		Pair 2	-3.552	-2.589	0.002	0.018	S	S
		Pair 3	-3.093	-0.997	0.006	0.331	S	NS
2.	FVC (Lt)	Pair 1	-5.432	-4.698	0.000	0.000	S	S
		Pair 2	-3.542	-2.415	0.002	0.026	S	S
		Pair 3	-2.153	-0.446	0.044	0.661	S	NS
3	FEV <sub>1</sub> (Lt)	Pair 1	-4.617	-4.514	0.000	0.000	S	S
		Pair 2	-5.434	-3.199	0.000	0.005	S	S
		Pair 3	-4.474	-1.288	0.000	0.213	S	NS
4	FEV <sub>1</sub> /FVC (%)	Pair 1	-1.722	-0.691	0.101	0.498	NS	NS
		Pair 2	-3.348	-0.082	0.003	0.936	S	NS
		Pair 3	-2.547	-0.609	0.020	0.550	S	NS
5	PEFR (Lt/Min)	Pair 1	-5.969	-6.984	0.000	0.000	S	S
		Pair 2	-5.723	-3.192	0.000	0.005	S	S
		Pair 3	-3.759	-0.831	0.001	0.416	S	NS
6	FEF 25-75% (Lt/Sec)	Pair 1	-2.759	-2.045	0.012	0.050	S	S
		Pair 2	-4.250	-2.872	0.000	0.010	S	S
		Pair 3	-3.521	-1.215	0.002	0.239	S	NS
7	PEF 200-1200 (Lt/Sec)	Pair 1	-4.022	-6.547	0.001	0.000	S	S
		Pair 2	-4.537	-3.316	0.000	0.004	S	S
		Pair 3	-3.329	-0.831	0.004	0.416	S	NS

The above results of our study were consistent to the result obtained in previous studies done by Pai and Prajna (2001) and Rao et al (1994). The most possible cause for this increase in the lung function parameters during the secretory phase of menstruation is the hyperventilation associated with increased levels of progesterone secretion in this phase. Rajesh et al reported that periodic hyperventilation improves respiratory muscle strength and lung capacities (Dempsey et al, 1986).

Progesterone induces hyperventilation through both central medullary and peripheral receptors and by increasing the sensitivity of respiratory receptor during the secretory phase (Rajesh, 2000). The fact that progesterone could cause relaxation of smooth muscles was studied by intramuscular injections of progesterone in patients with severe asthma (Beynon et al, 1988). It was also seen that the dose of bronchodilator drugs required reduction in patients that received progesterone by I.M. route.

In the present study it was observed that with increase or decrease of level of progesterone during various phases of menstrual cycle, the Pulmonary functions also increase and decrease correspondingly in asthmatics females in reproductive age group.

Hence this is to be borne in mind during management and planning of therapeutic regimens in patients with asthma.

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The present study also shows statistically significant increase in pulmonary functions in the follicular phase as compared to menstrual phase ( $p$  value  $< 0.04$ ). As only estrogens are found circulating in fair amount during this stage and levels of progesterone are negligible the present result may be explained by the possible smooth muscle relaxing effect of estrogens on the bronchial muscles. Previous study by Lindheim observed the relaxant effect of estrogen on vascular smooth muscles. He observed increase in blood pressure responses in postmenopausal women as compared to women in reproductive age group. Chandler associated estradiol with improvement of asthma symptoms (Chandler et al 1997). Hence, the present study shows that respiratory parameters of asthmatic women in reproductive age group show significant variation during different phases of menstrual cycle.

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