

## ORIGINAL ARTICLE

## RESPIRATORY FUNCTIONS IN ASTHMATIC AND NORMAL WOMEN DURING DIFFERENT PHASES OF MENSTRUAL CYCLE

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**Background:** Menstrual cycle is an integral part of life of women. There is widespread agreement that changes in the levels of oestrogen and progesterone associated with menstrual cycle also affect different systems of the body besides reproductive system. Levels of oestrogen 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 oestrogen and progesterone levels. The association between menstrual cycle and lung functions in normal females has also been recognised. The pathophysiology of this process is still not proved. The purpose of our study was to confirm the probable effects of the female hormones on lung functions in normal and asthmatic women in different phases of menstrual cycle and to compare them. **Methods:** The study was done on 40 normal and 40 asthmatic females in the age group of 15–45 years. Pulmonary function tests were done in three phases of menstrual cycle i.e. follicular, secretory and menstrual in all the subjects. **Results:** The mean value of lung functions, i.e., FVC, FEV, PEF, FEF<sub>25–75%</sub>, FEF<sub>200–1200</sub> were significantly lower in asthmatic females than normal ones ( $p < 0.01$ ) in all three phases. The lung functions of both asthmatic and non-asthmatic females 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 ( $p < 0.04$ ). **Conclusion:** Respiratory parameters of both asthmatic and non-asthmatic women in reproductive age group show significant variation in different phases of menstrual cycle. The smooth muscle relaxant effect of progesterone and probably oestrogen might have contributed to it. The lung function parameters in asthmatics were of lower value compared to normal women.

**Keywords:** Menstrual cycle, Pulmonary functions, Asthma, Progesterone, Oestrogen

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## INTRODUCTION

The correlation between phases of menstrual cycle and aggravation of asthma has extensively been studied.<sup>1–3</sup> Bronchial asthma is one of the commonest chronic obstructive lung diseases. It has been reported to be one of the leading causes of emergency admissions in hospitals.<sup>4</sup> It is a clinical syndrome characterised by recurrent episodes of airway obstruction. American Thoracic Society defined asthma as ‘a disease characterised 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’.<sup>4,5</sup>

Women comprise 75% of adult admissions to the hospitals due to asthma<sup>5</sup> of which 50% of emergency visits occur during perimenstrual phase<sup>4</sup>. Hormonal fluctuations during the menstrual cycle are hypothesised to influence the course of asthma among women. Both progesterone and oestrogen have been involved in improving pulmonary

functions and asthma. During premenstrual and menstrual phases as these hormones levels are lower, asthmatics have been found to experience an increase in asthma attacks. Moreover, progesterone has been shown to suppress the immune system. It may reduce the inflammation that’s occurring as a result of hyper-immunity in asthma.<sup>6</sup>

The association between menstrual cycle and lung functions in normal women has also been recognised.<sup>6</sup> The pathophysiology of this process is still not proved. The purpose of this study was to confirm the probable effects of the female hormones on the bronchial musculature.

## SUBJECTS AND METHODS

The present study involved 40 known asthmatic and 40 non-asthmatic women in menstruating age group. The study design was approved by the Ethical Committee of the Institute. Informed consent was taken from all subjects. Women in age group 15–45 years were included in the study. The patients who had suffered an asthmatic attack in last two months,

women with respiratory illness other than asthma, pregnant women and women on oral contraceptives or other hormonal therapy were excluded from the study.

The Pulmonary Functions were done using a Vitalograph Compact II® fulfilling the accuracy and precision criteria of American Thoracic Society.<sup>7</sup> Three readings were taken at a sitting and the highest reading was used for trend analysis. Spirometry was done for each woman during the first or second day of the menstrual period (menstrual phase), in the middle of the proliferative or follicular phase, and in the middle of the secretory or luteal phase.

Pulmonary functions of all subjects were done in various phases of menstrual cycle. The variations in pulmonary functions were then studied in both asthmatics and non-asthmatics separately. Asthmatic and non-asthmatic subjects were further divided into two groups each. Group-I included 20 non-asthmatic women in age group <30 years; Group-II included 20 non-asthmatic women in age group >30 years; Group-III had 20 asthmatic subjects in age group <30 years; and Group-IV had 20 asthmatic women in age group >30 years.

Vital Capacity (VC), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1<sup>st</sup> second (FEV<sub>1</sub>), FEV<sub>1</sub>/FVC, Peak Expiratory Flow Rate (PEFR), Maximal Expiratory Flow Rate (MEFR,

FEF<sub>200-1200</sub>), Maximal Mid-expiratory Flow Rate (MMFR, FEF<sub>25-75%</sub>) were calculated for each subject. Statistical analysis was done using student's *t*-test. Three pairs were made for analysis of the data as Pair I (Follicular and Menstrual phases), Pair II (Secretory and Menstrual phases), and Pair III (Follicular and Secretory phases).

## RESULTS

Mean values of lung functions in asthmatics and non-asthmatics in 15–30 year age group (group I and II) in three phases of menstrual cycle are shown in Table-1 and 2. The mean values of all the parameters were higher in Group I and III when compared to Group II and IV. The mean values of VC and FVC in all the four groups 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<sub>25-75%</sub>, PEF<sub>200-1200</sub>, in all groups were higher in secretory phase followed by follicular phase and the lowest in menstrual phase.

The statistical significance of the difference in the values is shown in Tables-3 and 4. No significant variation was found in values of FEV<sub>1</sub>/FVC in pairs I and III in all four groups. Statistical analysis of values amongst different pairs is shown in Table-5 and 6.

**Table-1: Mean values of lung functions in asthmatics and non-asthmatics in 15–30 year age group (group I and II) in three phases of menstrual cycle (Mean±SD)**

| Pulmonary Function test         | Follicular phase |                   | Secretory phase |                   | Menstrual phase |                   |
|---------------------------------|------------------|-------------------|-----------------|-------------------|-----------------|-------------------|
|                                 | Group I<br>N=20  | Group III<br>N=20 | Group I<br>N=20 | Group III<br>N=20 | Group I<br>N=20 | Group III<br>N=20 |
| VC (L)                          | 2.82±0.39        | 2.43±0.35         | 2.94±0.37       | 2.53±0.38         | 2.69±0.39       | 2.33±0.34         |
| FVC (L)                         | 2.85±0.39        | 2.44±0.38         | 3.00±0.41       | 2.52±0.37         | 2.67±0.36       | 2.33±0.39         |
| FEV <sub>1</sub> (L)            | 2.67±0.32        | 1.82±0.20         | 2.82±0.33       | 2.00±0.232        | 2.46±0.38       | 1.71±0.25         |
| FEV <sub>1</sub> /FVC (%)       | 94.0±5.05        | 76.5±11.69        | 94.4±6.11       | 80.85±8.9         | 92.2±8.1        | 74.05±11.65       |
| PEFR (L/Min)                    | 328.6±69.8       | 254.9±73.18       | 356±65.58       | 269.7±63.09       | 313±69.83       | 237±77.68         |
| FEF <sub>25-75%</sub> (L/Sec)   | 3.77±0.67        | 2.13±0.24         | 4.04±0.68       | 2.37±0.28         | 3.48±0.75       | 2.03±0.29         |
| PEF <sub>200-1200</sub> (L/Sec) | 5.04±1.03        | 2.83±0.58         | 5.43±1.05       | 2.99±0.58         | 4.76±1.12       | 2.69±0.61         |

**Table-2: Lung functions in asthmatics and non-asthmatics in 31–45 year age group (group III and IV) in three phases of menstrual cycle (Mean±SD)**

| Pulmonary Function test         | Follicular phase |                  | Secretory phase  |                  | Menstrual phase  |                  |
|---------------------------------|------------------|------------------|------------------|------------------|------------------|------------------|
|                                 | Group-II<br>N=20 | Group-IV<br>N=20 | Group-II<br>N=20 | Group-IV<br>N=20 | Group-II<br>N=20 | Group-IV<br>N=20 |
| VC (L)                          | 2.77±0.28        | 2.41±0.38        | 2.89±0.33        | 2.47±0.41        | 2.61±0.28        | 2.29±0.38        |
| FVC (L)                         | 2.75±0.32        | 2.41±0.36        | 2.89±0.36        | 2.44±0.4         | 2.63±0.32        | 2.26±0.32        |
| FEV <sub>1</sub> (L)            | 2.55±0.28        | 1.87±0.30        | 2.71±0.29        | 1.93±0.27        | 2.36±0.33        | 1.76±0.29        |
| FEV <sub>1</sub> /FVC (%)       | 93.25±9.04       | 79.95±10.44      | 94.4±5.71        | 80.85±9.28       | 89.90±7.33       | 80.70±11.86      |
| PEFR (L/Min)                    | 339.80±79.96     | 275.35±68.54     | 363±70.54        | 281.05±50.63     | 323±72.97        | 255±73.63        |
| FEF <sub>25-75%</sub> (L/Sec)   | 3.84±0.73        | 2.13±0.54        | 4.06±0.75        | 2.24±0.37        | 3.56±0.76        | 2.04±0.51        |
| PEF <sub>200-1200</sub> (L/Sec) | 4.91±1.16        | 3.18±0.69        | 5.25±1.05        | 3.24±0.71        | 4.73±1.19        | 2.99±0.68        |

**Table-3: Statistical analysis of lung function tests of asthmatics and non-asthmatics in 15–30 year age group in different phases of menstrual cycle (group I and III)**

| Pulmonary function test         | Phases | t-test  | p     |
|---------------------------------|--------|---------|-------|
| VC (L)                          | F      | -3.292  | 0.002 |
|                                 | S      | -3.424  | 0.002 |
|                                 | M      | -3.075  | 0.004 |
| FVC (L)                         | F      | -3.341  | 0.002 |
|                                 | S      | -3.875  | 0.000 |
|                                 | M      | -2.863  | 0.007 |
| FEV <sub>1</sub> (L)            | F      | -9.967  | 0.000 |
|                                 | S      | -9.9112 | 0.000 |
|                                 | M      | -7.310  | 0.000 |
| FEV <sub>1</sub> /FVC (%)       | F      | -6.146  | 0.000 |
|                                 | S      | -5.612  | 0.000 |
|                                 | M      | -5.720  | 0.000 |
| PEFR (L/Min)                    | F      | -3.269  | 0.002 |
|                                 | S      | -4.241  | 0.000 |
|                                 | M      | -3.269  | 0.002 |
| FEF <sub>25-75%</sub> (L/Sec)   | F      | -10.303 | 0.000 |
|                                 | S      | -10.119 | 0.000 |
|                                 | M      | -8.102  | 0.000 |
| FEF <sub>200-1200</sub> (L/Sec) | F      | -8.363  | 0.000 |
|                                 | S      | -9.111  | 0.000 |
|                                 | M      | -7.295  | 0.000 |

F=Follicular phase, S=Secretory phase, M=Menstrual phase.

**Table-4: Statistical analysis of lung function tests of asthmatics and non-asthmatics in 31–45 year age group in different phases of menstrual cycle (group II and IV)**

| Pulmonary function test         | Phases | t-test | p     |
|---------------------------------|--------|--------|-------|
| VC (L)                          | F      | -3.480 | 0.001 |
|                                 | S      | -3.504 | 0.001 |
|                                 | M      | -3.070 | 0.004 |
| FVC (L)                         | F      | -3.119 | 0.003 |
|                                 | S      | -3.467 | 0.001 |
|                                 | M      | -3.699 | 0.001 |
| FEV <sub>1</sub> (L)            | F      | -7.387 | 0.000 |
|                                 | S      | -8.915 | 0.000 |
|                                 | M      | -6.216 | 0.000 |
| FEV <sub>1</sub> /FVC (%)       | F      | -4.309 | 0.000 |
|                                 | S      | -5.562 | 0.000 |
|                                 | M      | -2.951 | 0.005 |
| PEFR (L/Min)                    | F      | -2.741 | 0.009 |
|                                 | S      | -4.228 | 0.000 |
|                                 | M      | -2.942 | 0.006 |
| FEF <sub>25-75%</sub> (L/Sec)   | F      | -8.371 | 0.000 |
|                                 | S      | -9.745 | 0.000 |
|                                 | M      | -7.432 | 0.000 |
| FEF <sub>200-1200</sub> (L/Sec) | F      | -5.686 | 0.000 |
|                                 | S      | -7.082 | 0.000 |
|                                 | M      | -5.679 | 0.000 |

F=Follicular phase, Se=Secretory phase, M=Menstrual phase

**Table-5: Comparison of PFTs during three phases of menstrual cycle in asthmatics and non-asthmatics in 15–30 year age group**

| Pulmonary function test         | Comparison Groups | t-test    |               | p         |               |
|---------------------------------|-------------------|-----------|---------------|-----------|---------------|
|                                 |                   | Asthmatic | Non-Asthmatic | Asthmatic | Non-Asthmatic |
| VC (L)                          | Pair I            | -6.432    | -3.424        | 0.000     | 0.003         |
|                                 | Pair II           | -7.436    | -3.552        | 0.000     | 0.002         |
|                                 | Pair III          | -4.060    | -3.093        | 0.001     | 0.006         |
| FVC (L)                         | Pair I            | -5.891    | -5.432        | 0.000     | 0.000         |
|                                 | Pair II           | -8.283    | -3.542        | 0.000     | 0.002         |
|                                 | Pair III          | -6.007    | -2.153        | 0.000     | 0.044         |
| FEV <sub>1</sub> (L)            | Pair I            | -6.205    | -4.617        | 0.000     | 0.000         |
|                                 | Pair II           | -8.922    | -5.434        | 0.000     | 0.000         |
|                                 | Pair III          | -5.041    | -4.474        | 0.000     | 0.000         |
| FEV <sub>1</sub> /FVC (%)       | Pair I            | -1.204    | -1.722        | 0.243     | 0.101         |
|                                 | Pair II           | -1.345    | -3.348        | 0.195     | 0.003         |
|                                 | Pair III          | -0.550    | -2.547        | 0.589     | 0.020         |
| PEFR (L/Min)                    | Pair I            | -2.032    | -5.969        | 0.056     | 0.000         |
|                                 | Pair II           | -6.008    | -5.723        | 0.000     | 0.000         |
|                                 | Pair III          | -5.088    | -3.759        | 0.000     | 0.001         |
| FEF <sub>25-75%</sub> (L/Sec)   | Pair I            | -4.352    | -2.759        | 0.000     | 0.012         |
|                                 | Pair II           | -6.567    | -4.250        | 0.000     | 0.000         |
|                                 | Pair III          | -5.638    | -3.521        | 0.000     | 0.002         |
| FEF <sub>200-1200</sub> (L/Sec) | Pair I            | -2.161    | -4.022        | 0.044     | 0.001         |
|                                 | Pair II           | -4.350    | -4.537        | 0.000     | 0.000         |
|                                 | Pair III          | -3.318    | -3.329        | 0.004     | 0.004         |

Pair I: Follicular and Menstrual, Pair II: Secretory and Menstrual, Pair III: Follicular and Secretory

**Table-6: Comparison of PFTs during three phases of menstrual cycle in asthmatics and non-asthmatics in 31–45 year age group**

| Pulmonary function test         | Comparison Groups | t-test    |               | p         |               |
|---------------------------------|-------------------|-----------|---------------|-----------|---------------|
|                                 |                   | Asthmatic | Non-Asthmatic | Asthmatic | Non-Asthmatic |
| VC (L)                          | Pair I            | -6.365    | -4.884        | 0.000     | 0.000         |
|                                 | Pair II           | -8.304    | -2.589        | 0.000     | 0.018         |
|                                 | Pair III          | -4.085    | -0.997        | 0.001     | 0.331         |
| FVC (L)                         | Pair I            | -4.023    | -4.698        | 0.001     | 0.000         |
|                                 | Pair II           | -7.119    | -2.415        | 0.000     | 0.026         |
|                                 | Pair III          | -4.731    | 0.446         | 0.000     | 0.661         |
| FEV <sub>1</sub> (L)            | Pair I            | -5.497    | -4.514        | 0.000     | 0.000         |
|                                 | Pair II           | -10.68    | -3.199        | 0.000     | 0.005         |
|                                 | Pair III          | -6.782    | -1.288        | 0.000     | 0.213         |
| FEV <sub>1</sub> /FVC (%)       | Pair I            | -1.781    | -0.691        | 0.243     | 0.498         |
|                                 | Pair II           | -3.028    | -0.082        | 0.195     | 0.936         |
|                                 | Pair III          | -0.886    | -0.609        | 0.589     | 0.550         |
| PEFR (L/Min)                    | Pair I            | -3.961    | -6.984        | 0.056     | 0.000         |
|                                 | Pair II           | -5.735    | -3.192        | 0.000     | 0.005         |
|                                 | Pair III          | -4.225    | -0.831        | 0.000     | 0.416         |
| FEF <sub>25-75%</sub> (L/Sec)   | Pair I            | -4.245    | -2.045        | 0.000     | 0.050         |
|                                 | Pair II           | -6.178    | -2.872        | 0.000     | 0.010         |
|                                 | Pair III          | -5.887    | -1.215        | 0.000     | 0.239         |
| FEF <sub>200-1200</sub> (L/Sec) | Pair I            | -3.222    | -6.547        | 0.004     | 0.000         |
|                                 | Pair II           | -4.317    | -3.316        | 0.000     | 0.004         |
|                                 | Pair III          | -3.975    | -0.831        | 0.001     | 0.416         |

Pair-I: Follicular and Menstrual, Pair-II: Secretory and Menstrual, Pair-III: Follicular and Secretory

## DISCUSSION

The present study was conducted in an attempt to determine what role the cyclically fluctuating hormone levels during the menstrual cycle might play on the bronchomotor tone and hence the respiratory function tests. Respiratory parameters of women in reproductive age group show significant variation during different phases of menstrual cycle. The results of this study were consistent with the results of previous studies by Rao *et al*<sup>6</sup>. The most probable 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.<sup>8</sup> Progesterone induces hyperventilation through both central medullary and peripheral receptors and by increasing the sensitivity of respiratory receptor during the secretory phase. The fact that progesterone could cause relaxation of smooth muscles was studied by intramuscular injections of progesterone in patients with severe asthma.<sup>9</sup> It was also seen that dose of bronchodilator drugs required reduction in patients that received progesterone by intramuscular route. In the present study also it was observed that with increase or decrease of level of progesterone during various phases of menstrual cycle, the values of pulmonary function tests also increase or decrease correspondingly in women in reproductive age group. Hence this is to be born in mind during management and planning of therapeutic regimens in patients with asthma.

The present study also shows statistically significant increase in pulmonary functions in follicular phase as compared to menstrual ( $p < 0.04$ ). 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. Chandler *et al*<sup>10</sup> observed the relaxant effect of oestrogen on vascular smooth muscle. He observed increase in blood pressure responses in postmenopausal women as compared to women in respiratory age group. They associated estradiol with improvement of asthma symptoms. The present study showed that respiratory parameters of young healthy women and asthmatic women in reproductive age group show significant variation during different phases of menstrual cycle. Similar results were reported by Rumball J<sup>11</sup> and Rao VSJ *et al*<sup>12</sup>. It also showed that the lung function parameters are of lower value in asthmatics as compared to normal women. These results are in agreement with Weinberger SE *et al*<sup>13</sup>, and Pai SR *et al*<sup>14</sup>.

## CONCLUSION

Respiratory parameters of both asthmatic and non-asthmatic women in reproductive age group show significant variation in different phases of menstrual cycle. The smooth muscle relaxant effect of progesterone, and probably of oestrogen too, might contribute to the above result. The lung function parameters in asthmatics were of lower value compared to normal women, might be due to further deterioration of the already compromised respiratory parameters.

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