Pak. J. Chest Med. 2026;32(02)

Original Article

journal homepage: https:/www.pjcm.net/

Pakistan Journal of Chest Medicine

Official journal of Pakistan Chest Society

Menstrual Cycle-Related Changes in Spirometric Lung Function among Young Women with and without Asthma: Experience from a Tertiary Care Hospital

Tahira Bibi[1], Hifsa Shah[2], Naheed Khan[1], Mehnaz Hafiz[1], Amina Akbar[2] ✉

[1]Department of Gynaecology & Obstetrics, Bacha Khan Medical Complex, Swabi - Pakistan

[2]Department of Medicine, Bacha Khan Medical Complex, Swabi - Pakistan

Corresponding Author:
Amina Akbar
Department of Medicine,
Bacha Khan Medical Complex,
Swabi - Pakistan
Email: dramina.akbar@hotmail.com

Article History:

Received:	Dec 10, 2025
Revised:	Mar 07, 2026
Accepted:	May 20, 2026
Available Online:	Jun 02, 2026

Author Contributions:
AA conceived idea, TB drafted the study, HS NK collected data, MH did statistical analysis and interpretation of data, TB AA critical reviewed manuscript. All approved final version to be published.

Declaration of conflicting interests:
The authors declare that there is no conflict of interest.

How to cite this article:
Bibi T, Shah H, Khan N, Hafiz M, Akbar A. Menstrual Cycle-Related Changes in Spirometric Lung Function among Young Women with and without Asthma: Experience from a Tertiary Care Hospital. Pak J Chest Med. 2026;32(02):85-95.

ABSTRACT

Background: Bronchial asthma is a common chronic respiratory disease characterized by notable sex disparities that become apparent during the reproductive years, indicating a potential role for ovarian hormones in disease manifestation.

Objective: To compare spirometric lung function parameters across different phases of the menstrual cycle among young women with and without asthma, and to determine whether the magnitude and pattern of menstrual cycle-related changes differ between the two groups.

Methodology: This prospective longitudinal comparative study was conducted from January to December 2025. A total of 140 young women were enrolled, comprising 70 asthmatics and 70 age- and BMI-matched non-asthmatic controls. Spirometric assessments, including FEV_1, FVC, FEV_1/FVC ratio, PEFR, and mid-expiratory flow rates (FEF_{25-75}, FEF_{50}, FEF_{75}), were performed during three menstrual cycle phases: menstrual (Days 1-3), follicular (Days 7-10), and luteal (Days 20-23).

Results: Asthmatic women demonstrated significantly lower spirometric parameters across all menstrual cycle phases compared to non-asthmatic controls ($p < 0.001$ for FEV_1, FEV_1/FVC, PEFR, and mid-expiratory flows). Among asthmatic participants, FEV_1 and mid-expiratory flow rates were lowest during the menstrual phase and highest during the luteal phase, whereas FVC and PEFR exhibited the opposite trend. Non-asthmatic controls displayed similar but less pronounced changes. Asthmatic women exhibited substantially greater percentage changes from the menstrual to luteal phase for expiratory flow parameters (FEV_1: +5.6% vs. +2.4%; FEF_{25-75}: +9.5% vs. +4.3%).

Conclusion: Asthmatic women experience greater menstrual cycle-related variation in lung function compared to non-asthmatic controls, with the lowest values observed during the menstrual phase, supporting the concept of perimenstrual asthma.

Keywords: Respiratory Diseases; Asthma; Women; Menstrual Cycle

Introduction

Bronchial asthma is one of the most common chronic lung diseases at the present time and affects approximately 300 million people of all ages around the world. Because of chronic airway inflammation, bronchial hyperreactivity, and variable airway obstruction, asthma places a heavy burden on health care services and reduces the quality of life.[1] According to the epidemiological data, there is a quite marked difference by sex in the frequency of asthma, a difference that is evident even at the adolescent level. Asthma is more common among men before puberty, but after puberty the situation changes with asthma becoming more frequent in women and this higher frequency remains during their reproductive years. Therefore, this sex-specific feature clearly indicates that endogenous sex hormones such as estrogen and progesterone are involved in the development of the disease.[2]

The natural menstrual cycle, characterized by predictable fluctuations in ovarian hormone levels, provides a valuable model for investigating the effects of sex steroids on pulmonary function. During the follicular phase, estrogen concentrations gradually increase, while the luteal phase is marked by elevated progesterone and a secondary rise in estrogen. These hormonal variations influence multiple physiological systems, including the respiratory system. Progesterone, for instance, enhances ventilation by acting on central and peripheral chemoreceptors. Recent molecular studies indicate that sex hormones modulate brain-derived neurotrophic factor (BDNF) expression in airway smooth muscle, thereby affecting airway contraction, remodeling, and inflammation, which are critical factors in asthma pathogenesis.[3] Estrogen receptors, such as ERα, ERβ, and the G protein-coupled estrogen receptor (GPER1), are abundantly expressed in airway epithelium, smooth muscle, and immune cells, where they regulate both genomic and rapid signaling pathways.

While it makes biological sense that the menstrual cycle affects lung function, the literature remains confusing and contradictory. A few studies have shown reduced pulmonary function during the premenstrual or menstrual cycle, which is termed "perimenstrual asthma" (PMA), and is found to affect approximately 10–30% of asthmatic females.[4] However, other studies found a decrease in lung function closer to ovulation, or somewhere within the luteal cycle, with some studies not finding any cyclical variation at all. Similarly, in healthy, non-asthmatic females, the data are unclear, with some papers showing optimal lung function in the luteal cycle and others finding no significant variation. These inconsistencies may arise from methodological differences, including small sample sizes, reliance on peak expiratory flow rate (PEFR) rather than spirometry, and inconsistent phase definitions. PEFR focuses more on the large airways and is effort-dependent, making it less reliable than spirometry for detecting even small changes in peripheral airways, which are particularly affected by asthma.[5]

The mismatch in findings, and the possibility that asthma status might affect how large the menstrual-cycle-related shifts are, point to a need for well-designed, truly comparable studies. Early airway inflammation and hyperreactivity in asthma could increase the impact of hormonal up-and-down shifts on airway size so that asthmatics might show more pronounced cyclical lung-function swings than healthy people. Prior work has also implied that the direction and shape of the change could vary with asthma severity; for instance, moderate persistent asthma might show a bigger amplitude of variation.[6] Still, systematic head-to-head comparisons of how large and what kind of menstrual cycle-related changes occur in women with asthma versus without asthma are pretty scarce, especially within the South Asian population.[7]

This study was designed to address these gaps by conducting a prospective, longitudinal comparative investigation at Bacha Khan Medical Complex, Swabi, following participants over time rather than a single snapshot. The main aim is to see and compare spirometric lung function measures like FEV_1, FVC, the FEV_1/FVC ratio, PEFR, and the mid-expiratory flow rates ($FEF_{25–75}$, FEF_{50}, FEF_{75}) across three separate phases of the menstrual cycle (menstrual, follicular, and luteal). This will be done in young women with well-controlled asthma and in healthy non-asthmatic controls, matched by age and BMI, so the groups are comparable. The secondary aim is more specific: to assess whether the magnitude and general pattern of menstrual-cycle-related shifts differ between the two groups. By employing comprehensive spirometry, ensuring rigorous phase definition, and matching participants for age and BMI, this study aims to provide robust evidence to clarify the interaction between sex hormones, asthma, and pulmonary function. The findings may have important clinical implications for managing asthma in reproductive-aged women, potentially informing tailored therapeutic approaches and optimizing treatment timing in accordance with the menstrual cycle.

Objective

To compare spirometric lung function parameters across different phases of the menstrual cycle among young women with and without asthma, and to determine whether the magnitude and pattern of menstrual cycle-related changes differ between the two groups.

Methodology

This prospective longitudinal comparative study was

conducted at Bacha Khan Medical Complex, Swabi from June 2024 to September 2025. We recruited young women aged 18-35 years attending the Gynecology Department of BKMC. We divided participants into two groups: an asthma group of 70 women with well-controlled asthma and a control group of 70 age- and BMI-matched healthy, non-asthmatic women.

The sample size was based on an earlier published study that examined spirometric lung function across the different phases of the menstrual cycle in young women with and without asthma. In that earlier work, there were 60 participants in each group, for a total of 120 participants, and that part is key. Here, we will use the expected gap in the main spirometric outcome, FEV_1, between the groups. With a 95% confidence level and 80% power, we will determine the required number of participants using a suitable two-group comparison or repeated-measures approach. To account for around 10%–15% attrition (e.g., participants dropping out or not completing every menstrual-cycle assessment), we will increase the final n d accordingly. So, we proposed a recruitment target of about 140 participants, meaning roughly 70 asthmatic and 70 non-asthmatic women.[1]

Women aged between 18 and 35 years, with regular menstrual cycles of 24 to 35 days, and not on hormonal contraceptives, were eligible for inclusion. Subjects in the asthma group must have a documented physician diagnosis of asthma and well-controlled asthma according to the Global Initiative for Asthma (GINA) criteria. We defined well-controlled asthma as answering all four questions on the GINA assessment negatively: no daytime symptoms more than twice a week, no night waking due to asthma, no need for rescue medication more than twice a week, and no limitation of activity due to asthma. We further classified asthma severity based on GINA treatment steps.

Women with irregular menstrual cycles, women using oral contraceptives or other hormonal medication, pregnant or lactating women, and women with a history of upper or lower respiratory tract infection within the last month were excluded. Other exclusions included participants with other significant pulmonary disorders, including chronic obstructive pulmonary disease, pulmonary embolism, interstitial lung disease, or cystic fibrosis, and participants with cardiovascular disease or psychiatric illness that may interfere with participation in the study. Participants with asthma who had an exacerbation requiring systemic corticosteroids in the past month or a change in asthma medication in the past 4 weeks were also excluded.

We used self-reported menstrual history and cycle tracking to determine the menstrual cycle phase. We defined three phases for spirometric assessment: menstrual phase (day 1-3), follicular phase (day 7-10), and luteal phase (day 20-23). All assessments for each participant were timed at the same time of day (± 2 hours) across the three visits to minimize variability. Participants kept a menstrual diary to confirm cycle regularity and accurate phase identification. Women actively bleeding at the time of the initial assessment did not enroll, as this may compromise the ability to capture a complete menstrual cycle during the study period.

Spirometry was performed at each of the three phases of the menstrual cycle using a calibrated spirometer according to the technical standards of the European Respiratory Society and American Thoracic Society (ERS/ATS) for measuring lung volumes. Trained respiratory technicians performed this procedure blinded to participants' group allocation. Participants were asked to refrain from smoking, heavy meals, and strenuous exercise for at least two hours before testing. Asthmatic participants were on a bronchodilator withholding period according to standard guidelines, with short-acting beta-agonists withheld for at least 4 hours and long-acting bronchodilators withheld for at least 12 hours before testing.

Each participant performed at least 3 forced expiratory maneuvers, and we used the best values for analysis. The spirometric parameters that were recorded are: forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, peak expiratory flow rate (PEFR), and mid-expiratory flow rates including $FEF_{25–75}$, FEF_{50}, and FEF_{75}. We assessed repeatability of FEV_1 and FVC measurements by requiring the two largest values to be within 0.100 L or 5% of the highest value, whichever is greater. Baseline spirometry may be supplemented with bronchodilator responsiveness testing, as clinically indicated, to characterize asthma severity in the population studied.

We analyzed the data using SPSS version 26. For demographic and clinical, mean, standard deviation, and frequencies, was found. To compare the asthmatic and non-asthmatic groups at each menstrual cycle stage, we used independent-samples t-tests for continuous measures and chi-square tests for categorical ones. We evaluated changes within each group across the three menstrual cycle phases using repeated-measures ANOVA, similar to repeated observations over time. The size of the menstrual cycle-related shifts was calculated as a percentage change from the menstrual phase to the luteal phase, and then contrasted between groups. A p-value under 0.05 was treated as statistically significant, even if it's just slightly under.

Ethical approval (Ref. No. BC-131/24) was obtained from the Institutional Review Board of BKMC before starting the study, and it followed the principles of the Declaration of Helsinki. Before enrollment, we provided each participant with clear information about the study aims, the full process, and any potential risks. We obtained written informed consent from every participant before they joined. Participants' information was de-identified and kept private throughout the study period. The study ensured every person could withdraw at any time without

any impact on their medical treatment or the care they are receiving.

Results

In this study, a total of 140 young women were included. All participants completed the three scheduled spirometric checkups across different menstrual cycle phases, resulting in a 100% follow-up rate, with no participants lost or dropped out. Age, height, weight, BMI and history of allergies in participants of both groups were approximately same. The asthmatic and non-asthmatic groups were same in terms of age, height, weight, and body mass index (BMI), and there wasn't anything statistically meaningful between them ($p > 0.05$ for every comparison). For the asthmatics, 22.9% reported a history of allergies, while 20.0% in the non-asthmatic group reported one; overall, the difference was not significant ($p = 0.682$) (Table 1).

The average age at menarche was noticeably later among asthmatics than among non-asthmatics (13.1 ± 1.2 years vs 12.2 ± 1.0 years, $p < 0.001$). Still, mean cycle length, menstrual bleeding duration, and dysmenorrhea prevalence were similar overall across both groups ($p > 0.05$) (Table 2).

Among the 70 women with asthma, all participants had well-controlled disease according to the Global Initiative for Asthma (GINA) guidelines at enrollment. Asthma severity, based on treatment requirements, was distributed as follows: 18 participants (25.7%) had intermittent asthma, 17 (24.3%) had mild persistent asthma, and 35 (50.0%) had moderate persistent asthma. None of the participants were classified as having severe asthma, as no individual was receiving high-dose inhaled corticosteroids or anticholinergic medications. Spirometric parameters were collected during three distinct phases of the menstrual cycle: the menstrual phase (Days 1-3), the follicular phase (Days 7-10), and the luteal phase (Days 20-23) (Table 3).

During all three phases in the menstrual cycle, women with asthma showed lower spirometric parameters compared with non-asthmatic women, except for FVC, where the difference looked less dramatic, and maybe only sort of. The biggest gaps between the groups were in the FEV_1/FVC ratio and the mid-expiratory flow rates ($FEF_{25–75}$, FEF_{50}, FEF_{75}), which point toward the obstructive changes typical of asthma.

For the asthmatic group, every spirometric parameter followed a cyclical pattern across menstrual cycle phases; however, these shifts were not statistically significant. In other words, within-group testing gave $p > 0.05$ for every comparison when assessed with repeated-measures ANOVA. Still, the way things varied was not the same for each parameter:

For FEV_1, the FEV_1/FVC ratio, $FEF_{25–75}$, FEF_{50}, and FEF_{75}, the smallest readings occurred in the menstrual phase, then gradually improved through the follicular phase until peak values appeared in the luteal phase. In other words, it was sort of a step-by-step process, not super steady but still clear. The mean FEV_1 values went up by 5.6% from menstrual to luteal (2.34 L to 2.48 L, $p = 0.083$). Also, FEV_1/FVC increased by 7.0% from menstrual to luteal (80.9% to 87.9%, $p = 0.071$).

By comparison, FVC and PEFR in asthmatics followed another rhythm: the highest values were seen during the menstrual phase, while the lowest were noted during the luteal phase. FVC dropped 2.4% from menstrual to luteal (2.89 L to 2.82 L). PEFR fell by 1.2% over the same change (5.82 L/s to 5.75 L/s).

Among non-asthmatic women, spirometric parameters exhibited slight variation across menstrual cycle phases; however, none of these changes reached statistical significance ($p > 0.05$ for all within-group comparisons). Similar to the asthmatic group, FEV_1, FEV_1/FVC ratio, $FEF_{25–75}$, FEF_{50}, and FEF_{75} were lowest during the menstrual phase and highest during the luteal phase. The

Table 1. Demographic and Anthropometric Characteristics of Study Participants

Characteristic	Asthmatics (n=70) Mean ± SD	Non-asthmatics (n=70) Mean ± SD	p-value
Age (years)	22.4 ± 1.7	22.1 ± 1.5	0.412*
Height (cm)	159.2 ± 6.4	157.3 ± 5.8	0.089*
Weight (kg)	53.8 ± 8.1	53.1 ± 8.4	0.623*
BMI (kg/m^2)	21.3 ± 3.8	21.5 ± 2.9	0.742*
History of allergies n (%)	16 (22.9)	14 (20.0)	0.682**

*Independent sample t-test; *Chi-square test

mean FEV_1 increased by approximately 2.4% from the menstrual to the luteal phase (from 2.89 L to 2.96 L). FVC and PEFR in non-asthmatic women followed a comparable trend, with the highest values observed in the menstrual phase and the lowest in the luteal phase, consistent with the pattern seen in asthmatics. The magnitude of these changes appeared smaller in non-asthmatic women (Table 4).

Asthmatic women demonstrated a substantially greater magnitude of change in expiratory flow parameters (FEV_1, FEV_1/FVC, FEF_{25-75}, FEF_{50}, FEF_{75}) between menstrual and luteal phases compared to non-asthmatic women. The largest differences were observed in mid- and end-expiratory flow rates (FEF_{25-75} and FEF_{75}), where asthmatics showed approximately double the percentage change of non-asthmatics. FVC and PEFR showed minimal changes in both groups, with no substantial difference between asthmatic and non-asthmatic women.

We carried out a subgroup analysis to see whether menstrual cycle-related shifts differed when asthma severity was taken into account (intermittent, mild persistent, and moderate persistent). Although the number of participants in each subgroup was not very high, which reduces statistical power, we still observed a trend. Women with moderate persistent asthma had a larger amplitude of FEV_1 variation over the menstrual cycle than women in the intermittent or mild persistent group. Specifically, FEV_1 variation was 7.2% in moderate persistent asthma, versus 4.1% for intermittent asthma and 4.8% for mild persistent asthma.

Discussion

This prospective longitudinal comparative study examined menstrual cycle-related changes in spirometric lung function among 70 young women with 70 well-controlled asthma with age and BMI-matched healthy non-asthmatic controls. In the present study, the asthmatic and non-asthmatic groups were, in general well-matched, with respect to age (22.4 ± 1.7 years vs. 22.1 ± 1.5 years, p = 0.412), height (159.2 ± 6.4 cm vs. 157.3 ± 5.8 cm, p = 0.089), weight (53.8 ± 8.1 kg vs. 53.1 ± 8.4 kg, p = 0.623), and BMI (21.3 ± 3.8 kg/m^2 vs. 21.5 ± 2.9 kg/m^2, p = 0.742). There was no meaningful difference in allergy history between groups (22.9% vs. 20.0%, p = 0.682). The effective pairing of demographic and body-measurement features represents a significant methodological strength, as variations in age and body mass index (BMI) can influence lung function in a predictable manner. Atukorala and colleagues employed a similar approach by matching asthmatic and non-asthmatic participants for age and BMI, reporting comparable values without statistically significant differences between groups.[1] The demographic characteristics observed in the present study are consistent with previous findings in South Asian populations, where younger women in the reproductive phase typically exhibit BMI values within the normal range, as observed among the participants in this study. This matching increases the likelihood that observed differences in spirometric outcomes between groups are attributable to asthma status rather than demographic confounders.[1]

In the present study, the average age at menarche was later in women with asthma compared to women without asthma (13.1 ± 1.2 years vs. 12.2 ± 1.0 years; p < 0.001). This observation is consistent with previous research, which also reported a later age at menarche among asthmatic women, although the magnitude of the difference varied. The delayed menarche observed in women with asthma may be attributable to the chronic inflammation associated with asthma, as persistent inflammation can disrupt physiological processes and alter the timing of puberty.[1] However, other studies have reported conflicting findings. The association between asthma and menarche may vary depending on asthma phenotype. For instance, a large retrospective study of 24,282 US women found that each additional year in age at menarche was associated with a 16% reduction in the risk of childhood-onset asthma. Conversely, early menarche, defined as onset before age 12, was associated with a 56% increased risk of childhood-onset asthma. No association was observed between age at menarche and adult-onset asthma.[8] In contrast, a study from Indonesia reported that girls with asthma had an earlier average age at menarche by 5.2 months.[9] These divergent findings indicate that the relationship between menarche timing and asthma is complex and may be influenced by asthma severity, ethnicity, or other yet unidentified factors.

In contrast to age at menarche, the mean cycle length (29.7 +/- 2.6 days vs. 29.4 +/- 2.3 days, p = 0.578), duration of menstrual bleeding (4.6 +/- 1.0 days vs. 4.4 +/- 0.9 days, p = 0.234), or dysmenorrhea prevalence (58.6% vs. 45.7%, p = 0.128) showed no significant group differences. These observations are similar to findings reported by Atukorala and co-workers,[1] who did not identify significant differences between asthma and control groups in cycle length or bleeding days. Because menstrual cycle lengths and bleeding durations did not differ significantly between groups, the lung functions observed in the asthma group likely did not differ because of differences in cycle length or bleeding-pattern irregularity. In another study, a high prevalence of dysmenorrhea was observed in both groups: 58.6% asthmatics and 45.7% non-asthmatics, which lies within the reported frequency of 45%- 70% among women in South Asian populations.[10]

In the present study, we observed that spirometric parameters were markedly reduced in asthmatic women compared to non-asthmatic women throughout all three phases of the menstrual cycle. The values for FEV at

Table 2. Menstrual Cycle Characteristics of Study Participants

Characteristic	Asthmatics (n=70) Mean ± SD	Non-asthmatics (n=70) Mean ± SD	p-value
Age at menarche (years)	13.1 ± 1.2	12.2 ± 1.0	<0.001***
Cycle length (days)	29.7 ± 2.6	29.4 ± 2.3	0.578*
Duration of bleeding (days)	4.6 ± 1.0	4.4 ± 0.9	0.234*
Dysmenorrhea present n (%)	41 (58.6)	32 (45.7)	0.128**

*Independent sample t-test; **Chi-square test; **p < 0.001

menstrual, follicular, and luteal phases were 2.34 0.42 L, 2.41 0.40 L, and 2.48 0.41 L in the asthmatic individuals as compared with 2.89 0.38 L, 2.92 0.36 L, and 2.96 0.37 L in non-asthmatic patients (P < 0.001). As a result, the FEV/FVC was lower in the asthmatic group (80.9%, 84.6%, and 87.9%) than in the non-asthmatic group (92.6%, 94.5%, and 96.4%) in all three cycles (P < 0.001). Differences between the two groups were more pronounced in the FEV/FVC ratio and in mid-expiratory flow volumes (FEF, FEF, FEF), which are highly indicative of airway obstruction in asthma. Naik et al. reported in their study, that pulmonary parameters such as FEV, FEF, and PEFR were greater in the postovulatory period than in the preovulatory period in women of reproductive age, suggesting that hormonal levels are related to airway smooth muscle function.[11] This steady decrease in the FEV/FVC ratio in asthmatic subjects is characteristic of the airway obstruction that accompanies asthma, and it demonstrates that airway obstruction exists throughout the menstrual cycle. The reduced mid-expiratory flow values of asthmatics (FEF, FEF, FEF) are noteworthy given their well-established correlation with small-airway function and their sensitivity as indicators of peripheral obstruction, which most commonly presents as the initial symptom in asthma. Recent reports suggest that the percentage difference in FEF (FEF%) is a more sensitive indicator of small- and medium-airway obstruction than FEV. Abnormalities in FEF% have been related to increased asthma severity and to persistence of asthma symptoms.

Our asthma group also showed cyclical trends in FEV, FEV/FVC ratio, FEF, and FEF: minimum values occurred during the menstrual period; gradually increased through the follicular phase, and reached a maximum during the luteal phase. Our subject group showed an average increase from the menstrual period to the luteal period of 5.6% in FEV (2.34 L compared to 2.48 L), of 7.0% in FEV/FVC ratio (80.9% compared to 87.9%), of 9.5% in FEF (2.41 L/s compared to 2.64 L/s), of 8.0% in FEF (2.86 L/s compared to 3.09 L/s), and of 11.2% in FEF (1.52 L/s compared to 1.69 L/s). These changes were not statistically significant (p > 0.05). Likewise, Nittner-Marszalska et al. demonstrated no significant change in spirometry variables from the menstrual to the luteal phase among women with stable mild-to-moderate asthma. Still, they noted a tendency toward improved lung volumes and expiratory flow rates during the luteal phase compared with the menstrual phase.[13] These same results across two studies suggest that although the cyclical changes may have clinical significance, they are not statistically significant within controlled asthmatic subjects due to relatively small effect sizes and the effects of between-subject variation.

Farha and coworkers observed that airflow and lung diffusing capacity vary throughout the menstrual cycle, peaking in menses and bottoming out in the early luteal phase.[14] The present study observed similar trends in both FVC and PEFR. The discrepancies between observed fluctuations in FVC and PEFR and those in FEV and mid-expiratory flows may reflect variability in the physiologic mechanisms governing these parameters. While FEV and mid-expiratory flows are influenced predominantly by airway caliber and obstruction, FVC may be influenced by respiratory muscle strength and central neural drive, both of which may vary under the influence of progesterone, known for its stimulatory effects on breathing.[15] Progesterone stimulates ventilation, increasing expiratory capacity and FVC when progesterone is high, but more detailed studies are needed because hormonal interactions affect different parts of respiratory function.

Changes in variables among non-asthmatics within the group of non-asthmatic women, FEV, FEV/FVC ratio, FEF, FEF and FEF demonstrated a pattern that resembled that observed in asthmatics, but changes were in lower degree; the lowest values being obtained in the menstrual period and highest in the luteal phase: mean values of FEV increasing of 2.4% from menstrual to luteal periods (2.89 L to 2.96 L), of 3.8%, 4.3%, 4.6% and 6.0% for FEV/FVC

Table 3. Spirometric Parameters During Menstrual Cycle Phases in Asthmatic and Non-Asthmatic Women

Parameter	Phase	Asthmatics (n=70) Mean ± SD	Non-asthmatics (n=70) Mean ± SD	p-value*
FEV_1 (L)	Menstrual	2.34 ± 0.42	2.89 ± 0.38	<0.001
	Follicular	2.41 ± 0.40	2.92 ± 0.36	<0.001
	Luteal	2.48 ± 0.41	2.96 ± 0.37	<0.001
FVC (L)	Menstrual	2.89 ± 0.48	3.12 ± 0.44	0.008
	Follicular	2.85 ± 0.46	3.09 ± 0.43	0.004
	Luteal	2.82 ± 0.47	3.07 ± 0.42	0.003
FEV_1/FVC (%)	Menstrual	80.9 ± 5.2	92.6 ± 4.1	<0.001
	Follicular	84.6 ± 5.0	94.5 ± 3.8	<0.001
	Luteal	87.9 ± 4.9	96.4 ± 3.6	<0.001
PEFR (L/s)	Menstrual	5.82 ± 0.98	6.74 ± 0.89	<0.001
	Follicular	5.91 ± 0.95	6.81 ± 0.87	<0.001
	Luteal	5.75 ± 0.97	6.69 ± 0.88	<0.001
FEF_{25-75} (L/s)	Menstrual	2.41 ± 0.52	3.28 ± 0.48	<0.001
	Follicular	2.53 ± 0.50	3.35 ± 0.46	<0.001
	Luteal	2.64 ± 0.51	3.42 ± 0.47	<0.001
FEF_{50} (L/s)	Menstrual	2.86 ± 0.55	3.72 ± 0.52	<0.001
	Follicular	2.98 ± 0.53	3.81 ± 0.50	<0.001
	Luteal	3.09 ± 0.54	3.89 ± 0.51	<0.001
FEF_{75} (L/s)	Menstrual	1.52 ± 0.38	2.18 ± 0.35	<0.001
	Follicular	1.61 ± 0.36	2.24 ± 0.34	<0.001
	Luteal	1.69 ± 0.37	2.31 ± 0.33	<0.001

Independent sample t-test comparing asthmatics vs. non-asthmatics at each phase

ratio, FEF, FEF, and FEF, respectively. Likewise, in this group the largest volumes were recorded during menstruation for both FVC and PEFR. At the same time, the lowest values were obtained during the luteal period, showing a decrease of 1.6% and 0.7 in both variables. These changes were not statistically significant ($p>0.05$). Our results in nonasthmatic women agree with previous studies of minimal, non-significant cyclical variability in lung function. Recently, Khan and colleagues found that FVC, FEV, PEFR, and the FEV/FVC ratio in normal adult women are significantly greater during the luteal phase than during the menstrual phase, but between-women variation within cycles is small.[16] In another recent study of normal women, Sieren and colleagues found that individual airway diameters are significantly larger and mean lung density is greater at menses than at the midluteal phase, providing evidence that lung structure is affected by the menstrual cycle when analyzed by techniques capable of greater measurement precision.[17] Furthermore, none of the pulmonary function measures were affected by hormonal phase in a study evaluating primary dysmenorrhea in women, indicating little influence of hormonal fluctuations on measurements of volumetric lung parameters, even in women without asthma.[18]

A key finding of our study is the substantially greater magnitude of change in expiratory flow parameters among asthmatic women compared to non-asthmatic women. Asthmatics demonstrated approximately double the percentage change in FEF_{25-75} and FEF_{75} compared to non-asthmatics (9.5% vs. 4.3% and 11.2% vs. 6.0%, respectively). The difference in change between groups was +3.2% for FEV_1, +3.2% for FEV_1/FVC ratio, +5.2% for FEF_{25-75}, +3.4% for FEF_{50}, and +5.2% for FEF_{75}. In contrast, FVC and PEFR showed minimal changes in both groups with no substantial difference between asthmatic and non-asthmatic women (differences of -0.8% and -0.5%, respectively).

Our finding that asthmatic women show greater menstrual cycle-related variation in lung function than non-asthmatics is supported by previous research. Kaur and colleagues found that asthmatic women showed greater amplitude of variation in spirometric parameters across the menstrual cycle than healthy controls.[2] This observation supports the hypothesis that the pre-existing airway inflammation and hyperreactivity in asthma amplify the effects of hormonal fluctuations on airway caliber. Previous research has shown that women with asthma may lose normal cyclical regulation of β_2-adrenergic receptors, with receptor density down-regulated when exposed to progesterone during the luteal phase.[11]

In contrast, non-asthmatic women show increased receptor density during the luteal phase.[12] This differential response may explain the greater magnitude of cyclical changes observed in asthmatic women. Additionally, estrogen receptors are widely expressed in airway epithelium, smooth muscle, and immune cells, where they modulate inflammatory responses.[8] The withdrawal of estrogen and progesterone during the menstrual phase may lead to loss of their protective effects, resulting in increased airway inflammation and bronchoconstriction, particularly in individuals with pre-existing airway disease.[11]

The largest between-group differences in menstrual cycle-related change were observed in mid-expiratory flow rates (FEF_{25-75} and FEF_{75}), which is clinically significant. These parameters reflect small airway function and are sensitive indicators of peripheral airway obstruction.[5] The greater cyclical variation in these parameters among asthmatics suggests that small airways, which are already compromised in asthma, are particularly susceptible to hormonal influences. This is consistent with the observation that perimenstrual asthma exacerbations often present with symptoms of peripheral airway obstruction, including cough and chest tightness.[13]

Our subgroup analysis by asthma severity, though limited by sample size, showed a trend: women with moderate persistent asthma had greater FEV_1 variation across the menstrual cycle than those with intermittent or mild persistent asthma (FEV_1 variation of 7.2% vs. 4.1% and 4.8%, respectively). This finding suggests that asthma severity may modulate the magnitude of menstrual cycle-related lung function changes, with more severe asthma being associated with greater hormonal susceptibility. This observation is consistent with the findings of Skoczy ski and colleagues,[14] who reported that women with more severe asthma were more likely to experience perimenstrual worsening of symptoms. Pereira Vega and colleagues similarly noted that women with moderate-to-severe asthma had a higher prevalence of perimenstrual asthma compared to those with mild asthma.[15] The mechanism underlying this association may relate to the degree of baseline airway inflammation and hyperresponsiveness, which may be amplified by hormonal fluctuations to a greater extent in more severe disease.[16]

Our findings have important clinical implications for managing asthma in reproductive-aged women. The observation that lung function parameters, particularly FEV_1 and mid-expiratory flow rates, are lowest during the menstrual phase suggests that women with asthma may be at increased risk of exacerbations during this time. This supports the concept of perimenstrual asthma (PMA), which is estimated to affect a significant proportion of asthmatic women.[17] Clinicians should consider menstrual cycle phase when interpreting spirometric results in women of reproductive age and should be alert to the possibility of perimenstrual worsening of symptoms. The greatest variations in mid-expiratory flow rates suggest that small airway function may be particularly affected by hormonal fluctuations, and monitoring these parameters

Table 4. Percentage Change in Spirometric Parameters from Menstrual to Luteal Phase

Parameter	Asthmatics (% Change)	Non-asthmatics (% Change)	Difference in Change (%)
FEV_1	+5.6	+2.4	+3.2
FEV_1/FVC	+7.0	+3.8	+3.2
FEF_{25-75}	+9.5	+4.3	+5.2
FEF_{50}	+8.0	+4.6	+3.4
FEF_{75}	+11.2	+6.0	+5.2
FVC	-2.4	-1.6	-0.8
PEFR	-1.2	-0.7	-0.5

may help identify women at risk of perimenstrual exacerbations.[18]

At a physiological level, the cyclical pattern of lung function is thought to result from the interaction between female hormones and the airways. Progesterone, which is highest at the end of the cycle (the luteal phase), is thought to stimulate central and peripheral chemo-receptor-mediated arousal of respiratory drive and cause bronchodilation.[18,19] Progesterone has also been found to synergize with agonist-induced relaxation of isolated airway smooth muscle.[19] The effect of estrogen is more complicated because it is involved in development and plays a complex role as aas a mediator of both pro- and anti-inflammatory responses.[20] If these hormones are withdrawn during the luteal phase of the menstrual cycle, their beneficial actions may be lost, potentially narrowing the airways. This mechanism is further supported by research showing that sex hormones influence the expression of inflammatory factors and the activity of airway smooth muscle [19,20]. The stronger reaction in people living with asthma than in healthy volunteers indicates that the airway inflammatory environment in asthma worsens the impact of hormone changes, with more severe deterioration in the late luteal phase.[21]

Strengths

This study has several strengths. By matching controls on age and BMI, the study could compare menstrual cycle-related variation between asthmatic and non-asthmatic women and therefore establish the influence of asthma. The full spirometry measuring both expiratory (FEV, FVC, FEV/FVC, PEFR) and inspiratory flows (and expiratory flow not usually measured (FEF, FEF, FEF)) was comprehensive compared to some other studies which merely measured peak flow meter function, which represents predominantly large airway mechanics and is highly effort dependent.

Classification of asthma severity and confirmed good control using GINA asthma staging ensured a uniform asthmatic cohort free from confounding by poorly controlled disease.

Finally, a 0% loss to follow-up supports efficient study design and subject retention.

Limitations

Several limitations are associated with the current study. First, because the study did not assess menstrual cycle phase or correlate hormone levels with spirometric data, its ability to establish direct mechanistic links between specific hormones and changes in lung function is limited. Whilst the cycle phases were confirmed using data on the patients' menstrual history and charted menstrual flow, including menstrual serum blood analysis would have better confirmed cycle phase and allowed correlation analysis.

Secondly, because the study group was relatively healthy and well-controlled asthmatic women, the degree of cycle-related changes observed may have been smaller than in more poorly controlled or severe asthmatic populations.

Third, observing only one menstrual cycle may not capture the considerable cycle-to-cycle variation that is observed in some cases of asthma. Finally, the subgroup analysis by asthma severity was limited by small subgroup sizes, and follow-up studies will require a larger sample to determine the impact of severity.

Conclusion

In conclusion, this study shows that young women with

well-controlled asthma have significantly lower spirometric parameters than healthy non-asthmatic women across all phases of the menstrual cycle, reflecting the underlying obstructive ventilatory defect characteristic of asthma. Both groups show cyclical variations in lung function, with FEV_1 and mid-expiratory flow rates being lowest during the menstrual phase and highest during the luteal phase. In contrast, FVC and PEFR show the opposite pattern. Importantly, asthmatic women show a substantially greater change in expiratory flow parameters than non-asthmatic women, particularly in mid-expiratory flow rates, suggesting that pre-existing airway inflammation in asthma amplifies the effects of hormonal fluctuations on airway caliber. The pattern of lowest values during the menstrual phase supports the concept of perimenstrual asthma. It has important clinical implications for the monitoring and management of asthma in reproductive-aged women. Future studies incorporating hormonal assays and including women across the spectrum of asthma severity are warranted to elucidate further the mechanisms underlying menstrual cycle-related changes in lung function and to identify women at greatest risk of perimenstrual exacerbations.

References

1. Atukorala KR, Silva WA, Amarasiri WA, Fernando DM. Comparison of lung function during different phases of the menstrual cycle among young female asthmatics and non-asthmatics. Int J Multidiscip Stud. 2022;9(1):88-102.
2. Arora D, Kaur P, Arora M, Gupta U. Influence of menstrual cycle on lung functions in asthmatic females. Indian J Fundam Appl Life Sci. 2011;1(4):2231-634562.
3. Wang SY, Freeman MR, Sathish V, Thompson MA, Pabelick CM, Prakash YS. Sex steroids influence brain-derived neurotropic factor secretion from human airway smooth muscle cells. J Cell Physiol. 2016;231(7):1586-1592. DOI:10.1002/jcp.25254.
4. Bukhari N, Hamid BS, Rauf I, Zuhra H, Nargis J, Zaib J. Assessing the relationship between menstrual cycle phases and asthma symptoms in female patients. Pak J Chest Med. 2022;28(2):200-209.
5. Lee B, Rafati Fard AR, Wong E, Tan T, Bloom CI. Oral contraceptives and the risk of asthma attacks: a population-based cohort study. ERJ Open Res. 2025;11(5):01278-2024. DOI:10.1183/23120541.01278-2024.
6. Calcaterra V, Nappi RE, Farolfi A, Tiranini L, Rossi V, Regalbuto C, et al. Perimenstrual asthma in adolescents: a shared condition in pediatric and gynecological endocrinology. Children (Basel). 2022;9(2):233. DOI:10.3390/children9020233.
7. Hu Q, Chen X, Fu W, Fu Y, He K, Huang H, et al. Chinese expert consensus on the diagnosis, treatment, and management of asthma in women across life. J Thorac Dis. 2024;16(1):773-797. DOI:10.21037/jtd-23-1069.
8. Cai L, Li X, Qiu L, Wang Y, Wu L, Wu X, Xu R, Liu Y, Zhou Y. Age at menarche and asthma onset among US girls and women: findings from NHANES, 2001–2018. Ann Epidemiol. 2023 Nov 1;87:25-30. DOI:10.1016/j.annepidem.2023.08.003.
9. Juber NF, Waits A, Dlamini LP, Nguyen T, Masango BZ. Associations between pediatric asthma and age at menarche: evidence from the Indonesian Family Life Survey. J Asthma. 2023;60(1):105-114. DOI:10.1080/02770903.2022.2030750.
10. Raksha HK. Effect of endogenous female hormones on lung functions. J Evol Med Dent. Sci. 2013;2(34):6519-25.
11. Naik SK, Nath SS, Swagatika S, Rath B, Pandey M. Comparison of pulmonary function test between pre-ovulatory and post-ovulatory phases of menstrual cycle. Natl J Physiol Pharm Pharmacol. 2023;13(8):1761-1764.
12. Qin R, An J, Xie J, Huang R, Xie Y, He L, et al. FEF25-75% Is a More Sensitive Measure Reflecting Airway Dysfunction in Patients with Asthma: A Comparison Study Using FEF25-75% and FEV1. J Allergy Clin Immunol Pract. 2021;9(10):3649-3659.e6. DOI:10.1016/j.jaip.2021.06.027.
13. Nittner-Marszalska M, Dor-Wojnarowska A, Wolańczyk-Mędrala A, Rosner-Tenerowicz A, Zimmer M, Dobek J, et al. Studying allergic inflammation and spirometry over menstrual cycles in well-controlled asthmatic women: changes in progesterone and estradiol affect neither FENO levels nor lung function. Nitric Oxide. 2018;75:95-100. DOI:10.1016/j.niox.2018.02.005.
14. Farha S, Asosingh K, Laskowski D, Hammel J, Dweik RA, Wiedemann HP, et al. Effects of the menstrual cycle on lung function variables in women with asthma. Am J Respir Crit Care Med. 2009;180(4):304-10. DOI: https://doi.org/10.1164/rccm.200904-0497OC.
15. Wang S, Cheng Z, Li S, Tian Y, Zhou J, Yang M. The effects of sex hormones on BDNF secretion in airway smooth muscle of patients with obstructive pulmonary disease. Heliyon. 2025;11(4). DOI:10.1016/j.heliyon.2025.e42688.
16. Khan HS, Shaikh SN, Bai K, Canna RA, Shaikh AH. Variations in Pulmonary Function in Relation with the Menstrual Cycle in Healthy Adult Female. Ann Pak Inst Med Sci. 2022;18(1):36-40. DOI:10.48036/apims.v18i1.643.

17. Calcaterra V, Farolfi A, D'Auria E, De Silvestri A, Baldassarre P, Ferrara F, et al. Perimenstrual Asthma and Premenstrual Disorders in Adolescents with Asthma. J Pediatr Adolesc Gynecol. 2024;37(2):132-136. DOI:10.1016/j.jpag.2023.11.001.

18. Calcaterra V, Nappi RE, Farolfi A, Tiranini L, Rossi V, Regalbuto C, et al. Perimenstrual Asthma in Adolescents: A Shared Condition in Pediatric and Gynecological Endocrinology. Children. 2022;9(2): 233. DOI: 10.3390/children9020233.

19. Chiarella SE, Cardet JC, Prakash YS. Sex, Cells, and Asthma. Mayo Clin Proc. 2021;96(7):1955-69. DOI:10.1016/j.mayocp.2020.12.007.

20. Reyes-García J, Montaño LM, Carbajal-García A, Wang Y-X. Sex Hormones and Lung Inflammation. Adv Exp Med Biol. 2021;1304:259-321. DOI:10.1007/978-3-030-68748-9_15.

21. Borkar NA, Ambhore NS, Kalidhindi RSR, Pabelick CM, Prakash YS, Sathish V. Kisspeptins inhibit human airway smooth muscle proliferation. JCI Insight. 2022;7(10):e152762. DOI:10.1172/jci.insight.152762.