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A Survey on Menstrual Cycle Related Changes in Respiratory Function Among Women: A Cross-Sectional Analysis.

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Abstract

Background: ***Aim:*** This study aimed to survey perceived and objective changes in respiratory function specifically dyspnea, peak expiratory flow (PEF), and breathing pattern—across the early follicular (EF) and mid-luteal (ML) phases in healthy eumenorrheic women. ***Methods:*** A prospective within-subject survey was conducted on 48 naturally cycling women (age 19–34 years). Participants underwent two assessments: during EF (days 2–4) and ML (days 20–24), confirmed by serum progesterone. Outcome measures included the Modified Medical Research Council (mMRC) dyspnea scale, baseline PEF via handheld peak flow meter, respiratory rate (RR), and a self-administered 10-item Respiratory Symptom Perception Score (RSPS). Data were analyzed using paired t-tests and Wilcoxon signed-rank tests. ***Results:*** Mean PEF was significantly lower in the ML phase (385.4 ± 31.2 L/min) compared to EF (402.7 ± 29.8 L/min); mean difference -17.3 L/min (95% CI: -22.1 to -12.5; $p<0.001$). Dyspnea scores (mMRC) increased during ML: 68.8% of women reported grade 1 or higher vs. 29.2% in EF ($p<0.001$). Respiratory rate was unchanged (14.1 vs. 14.0 breaths/min; $p=0.64$). The RSPS showed significantly higher perception of "chest tightness" and "need to sigh" during ML ($p<0.01$). Notably, 72.9% of participants were unaware of cycle-related breathing changes prior to the survey. ***Conclusion:*** Significant, measurable reductions in peak expiratory flow and increased dyspnea perception occur during the mid-luteal phase compared to the early follicular phase. These findings suggest that menstrual cycle phase should be considered in respiratory assessments, particularly for women with pre-existing lung conditions or during clinical trials involving pulmonary function tests.

Keywords: Menstrual cycle, respiratory function, peak expiratory flow, dyspnea, progesterone, women's health.

INTRODUCTION

Respiratory function is not a static physiological parameter; rather, it is dynamically modulated by a complex interplay of neural, mechanical, and humoral factors. Among these, sex hormones—particularly estrogen and progesterone—have emerged as significant, yet often overlooked, regulators of pulmonary mechanics and ventilatory control.1,2 These hormones exert their effects through specific receptors identified in bronchial smooth muscle, airway epithelium, vagal afferent nerves, central chemoreceptors within the medulla oblongata, and even the diaphragm.3-5 Consequently, the normal menstrual cycle, characterized by predictable, cyclical fluctuations in estradiol and progesterone, provides an ideal endogenous model to investigate hormone-driven respiratory plasticity in healthy women.6

The menstrual cycle is conventionally divided into two principal phases relative to ovulation: the early follicular (EF) phase (days 2–4), associated with nadir levels of both estrogen and progesterone, and the mid-luteal (ML) phase (days 20–24), marked by a sustained elevation of progesterone and a secondary, moderate rise in estrogen.7 Progesterone, in particular, is a known respiratory stimulant: it increases central chemosensitivity to carbon dioxide (CO_2), leading to hyperventilation, a reduced partial pressure of arterial CO_2 ($PaCO_2$), and a compensatory increase in tidal volume.8 While these changes are typically well-tolerated, they can manifest subjectively as air hunger, sighing, or a sensation of "not getting enough air," especially during rest or light activity.9 Estrogen, conversely, appears to have a protective role in airway physiology, including enhancement of β_2-adrenergic receptor expression and reduction of airway smooth muscle proliferation.10,11 However, the net effect of combined hormonal elevation during the luteal phase remains incompletely characterized.

Despite a growing body of literature on sex differences in respiratory disease, several critical gaps persist.12 First, most prior studies have focused on women with pre-existing conditions—most notably, asthma—where perimenstrual worsening (so-called "perimenstrual asthma") is well-documented.13,14 Far fewer investigations have examined the baseline respiratory fluctuations in healthy, asymptomatic women, making it difficult to distinguish pathological from physiological cycle-related changes.15 Second, among existing studies on healthy women, sample sizes have often been small (typically n < 20), and many have not used biochemical confirmation of ovulation (e.g., serum progesterone), introducing the risk of including anovulatory cycles where hormonal profiles are atypical.16 Third, the majority of research has emphasized minute ventilation and chemosensitivity, with comparatively little attention paid to expiratory flow mechanics—such as peak expiratory flow (PEF) or forced expiratory volume in one second (FEV_1)—which are clinically relevant for conditions involving airflow limitation.10,11 Fourth, while subjective symptoms like dyspnea are frequently reported anecdotally by women, there is a paucity of standardized survey data quantifying the prevalence, severity, and awareness of such symptoms across the cycle.17

The clinical implications of these gaps are non-trivial. If healthy women exhibit measurable changes in respiratory function, then clinicians interpreting pulmonary function tests (PFTs) or assessing dyspnea of unknown origin should ideally account for menstrual cycle phase.18 Moreover, women with underlying respiratory diseases (e.g., asthma, cystic fibrosis, or post-COVID interstitial lung disease) might experience exaggerated cycle-related effects, and the failure to recognize this could lead to misdiagnosis, inappropriate medication adjustments, or unnecessary testing.13,14 Finally, the lack of public and even professional awareness means that many women may silently tolerate cyclic respiratory symptoms, attributing them to stress, deconditioning, or anxiety, rather than a predictable biological phenomenon.9

Therefore, the present study was designed to survey perceived and objective changes in respiratory function—specifically dyspnea, peak expiratory flow (PEF), and breathing pattern—across the early follicular (EF) and mid-luteal (ML) phases in healthy eumenorrheic women.

We hypothesized that the mid-luteal phase would be associated with a small but statistically significant reduction in PEF and a higher prevalence of dyspnea compared to the early follicular phase.

MATERIALS AND METHODS

Study design, setting and population

A prospective observational study design was conducted at the department of Respiratory Medicine associated with department of Obstetrics & Gynaecology. The target population consisted of healthy, naturally menstruating women aged 18–40 years.

Inclusion Criteria:

- Female sex, age 18–40 years
- Self-reported regular menstrual cycles lasting 24–35 days for the preceding 6 months
- Not using any hormonal contraceptives (oral pills, implants, intrauterine devices, vaginal rings) for at least 3 months prior to enrollment
- Willing to attend two assessment visits scheduled according to menstrual cycle phase
- Able to provide written informed consent

Exclusion Criteria:

- Known history of any respiratory disease: asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease, bronchiectasis, or prior pulmonary embolism
- Active respiratory infection (cold, flu, bronchitis, pneumonia) within 4 weeks prior to either assessment
- Current smoking or history of smoking >5 pack-years
- Body mass index (BMI) >30 kg/m² (obesity class I or higher)
- Pregnancy, lactation, or attempted pregnancy during study period
- Diagnosed polycystic ovary syndrome (PCOS), thyroid dysfunction, or other endocrine disorders affecting menstrual regularity
- Use of systemic steroids, beta-blockers, or any medication known to affect respiratory or menstrual function
- Inability to perform peak flow maneuvers correctly after instruction.

Sample Size Calculation

Sample size was determined a priori using G*Power software (version 3.1.9.7) for a paired t-test (two-tailed). Input parameters: anticipated mean difference in peak expiratory flow (PEF) between cycle phases = 10 L/min (based on pilot data from 8 women, unpublished), estimated standard deviation of differences = 15 L/min, desired power = 80%, alpha = 0.05. The calculated minimum sample size was 32 participants. Accounting for an anticipated 20% dropout rate due to

anovulatory cycles or missed visits, the target enrollment was set at 40. However, to improve precision for subgroup analyses (e.g., symptom severity strata), the final sample size was set at 48 participants, which also allowed for robust nonparametric testing.

Procedure for Data Collection

Recruitment and Screening (Week 0):

- Potential participants responded to study advertisements and underwent a telephone screening for initial eligibility.
- Eligible candidates attended a screening visit where written informed consent was obtained. A detailed medical and menstrual history was recorded. BMI was measured.
- Participants were instructed on how to use urine luteinizing hormone (LH) detection kits (Clearblue® Digital Ovulation Test) to identify the LH surge.

Phase 1 Assessment – Early Follicular (Cycle Days 2–4):

- Participants were contacted on day 1 of menstruation (self-reported). Assessment scheduled for day 2, 3, or 4.
- Upon arrival: seated rest for 10 minutes.
-

Data collected:

- o Demographics and menstrual cycle characteristics via questionnaire.
- o Baseline respiratory rate (60-second count, unannounced to avoid voluntary alteration).
- o Peak expiratory flow: best of three attempts using a Mini-Wright peak flow meter (EU scale), with 1-minute rest between attempts. Maneuver standardized according to ATS guidelines.
- o mMRC dyspnea scale administered verbally.
- o RSPS (10-item) self-administered (5 minutes).
- Total visit duration: 30 minutes.

Interim Monitoring (Days 10–20):

- Participants used LH urine tests daily starting day 10. The day after the first positive LH test was designated as ovulation day (day 0).
- Research team was notified within 24 hours of positive LH test.

Phase 2 Assessment – Mid-Luteal (Cycle Days 20–24, i.e., 7–9 days post-LH surge):

- Scheduled precisely 7–9 days after confirmed LH surge to coincide with peak serum progesterone.
- Upon arrival: same resting conditions as Phase 1.
- **Data collected:**

- o Repeat measurements of respiratory rate, PEF, mMRC, and RSPS using identical protocols.
- o Venous blood sample (5 mL) drawn for serum progesterone measurement (to confirm ovulation; threshold >5 ng/mL). Samples centrifuged within 1 hour and stored at -20°C until batch analysis via electrochemiluminescence immunoassay.
- Total visit duration: 35 minutes.

Data Quality Assurance:

- The same research assistant performed all PEF measurements to ensure consistency.
- Peak flow meters were calibrated weekly using a standard syringe.
- Participants who reported intercurrent illness or medication use between visits were rescheduled to the next cycle (maximum two cycles allowed).

Statistical Analysis

Data were exported to IBM SPSS Statistics (version 27.0) for analysis. Statistical significance set at $p < 0.05$ (two-tailed).

RESULTS

Table 1: Baseline Demographic and Cycle Characteristics of Participants (N=48)

Characteristic	Mean ± SD or n (%)	Range
Age (years)	26.8 ± 4.1	19 – 34
Body mass index (kg/m²)	22.4 ± 2.7	18.1 – 29.8
Age at menarche (years)	12.9 ± 1.3	10 – 16
Typical menstrual cycle length (days)	28.5 ± 2.2	25 – 33
Typical menstrual bleed duration (days)	5.1 ± 1.0	3 – 7
Nulliparous	41 (85.4)	—
Regular physical activity (≥150 min/week)	29 (60.4)	—
Self-reported premenstrual syndrome (PMS)	33 (68.8)	—
Serum progesterone – mid-luteal (ng/mL)	12.4 ± 3.6	6.8 – 21.2

The 48 participants had a mean age of 26.8 years (range 19–34) and normal BMI (22.4 kg/m²). All had regular cycles (mean length 28.5 days) and ovulatory mid-luteal progesterone levels (mean 12.4 ng/mL, range 6.8–21.2). Most were nulliparous (85.4%) and physically active (60.4%). Notably, 68.8% reported premenstrual syndrome symptoms, and only 27.1% were aware of potential cycle-breathing links at baseline.

Table 2: Comparison of Respiratory Parameters Between Early Follicular (EF) and Mid-Luteal (ML) Phases (N=48)

Parameter	Early Follicular (EF)	Mid-Luteal (ML)	Mean / Median Difference	95% CI for difference	p-value
Peak Expiratory Flow (PEF) (L/min)	402.7 ± 29.8	385.4 ± 31.2	-17.3 (mean)	-22.1 to -12.5	<0.001
Respiratory rate (breaths/min)	14.1 ± 1.2	14.0 ± 1.3	-0.1 (mean)	-0.5 to 0.3	0.64
mMRC dyspnea score (median [IQR])	0 (0 – 0)	1 (0 – 1)	+1 (median)	—	<0.001
RSPS total score (0–30)	3.5 (2.0 – 5.0)	9.0 (6.0 – 12.0)	+5.5 (median)	—	<0.001

Peak expiratory flow (PEF) declined significantly from early follicular (402.7 L/min) to mid-luteal (385.4 L/min), a mean difference of -17.3 L/min (95% CI: -22.1 to -12.5, p<0.001). Respiratory rate showed no change (14.1 vs. 14.0 breaths/min, p=0.64). The median mMRC dyspnea score increased from 0 to 1 (p<0.001), and the median RSPS total score rose from 3.5 to 9.0 (p<0.001), indicating substantially higher symptom burden in the luteal phase.

Table 3: Distribution of mMRC Dyspnea Grades Across Menstrual Cycle Phases (N=48)

mMRC Grade	Description	Early Follicular (EF) n (%)	Mid-Luteal (ML) n (%)
0	No dyspnea except with strenuous exercise	34 (70.8)	15 (31.2)
1	Shortness of breath when hurrying on level ground or walking up a slight hill	12 (25.0)	27 (56.2)
2	Walks slower than 同齢人 on level ground because of dyspnea, or stops to breathe when walking at own pace	2 (4.2)	6 (12.5)
3	Stops for breath after walking ~100 m or after a few minutes on level ground	0 (0)	0 (0)
4	Too breathless to leave the house, or breathless when dressing/undressing	0 (0)	0 (0)

The proportion of women with grade 0 (no dyspnea) dropped sharply from 70.8% in early follicular to 31.2% in mid-luteal. Correspondingly, grade 1 dyspnea increased from 25.0% to 56.2%, and grade 2 from 4.2% to 12.5% (McNemar's test, p<0.001). No participant reported severe dyspnea (grades 3 or 4) in either phase.

Table 4: Individual Item Analysis of Respiratory Symptom Perception Score (RSPS) (N=48)

Symptom Item	Early Follicular (EF) Median (IQR)	Mid-Luteal (ML) Median (IQR)	p-value
Chest tightness or heaviness	0 (0 – 1)	2 (1 – 2)	<0.001
Feeling of needing to take a deeper breath	1 (0 – 1)	2 (1 – 3)	<0.001
Sighing more than usual	0 (0 – 1)	2 (1 – 2)	<0.001
Shortness of breath at rest	0 (0 – 0)	1 (0 – 1)	<0.001
Rapid or shallow breathing	0 (0 – 1)	1 (0 – 2)	0.001
Difficulty taking a full breath	0 (0 – 0)	1 (0 – 2)	<0.001
Wheezing	0 (0 – 0)	0 (0 – 0)	0.75
Cough	0 (0 – 1)	0 (0 – 1)	0.37
Throat tightness	0 (0 – 0)	1 (0 – 1)	0.003
Palpitations associated with breathing effort	0 (0 – 0)	1 (0 – 1)	0.002

The most pronounced luteal-phase increases were for chest tightness (median 0→2, p<0.001), need to take a deeper breath (1→2, p<0.001), and sighing (0→2, p<0.001). Shortness of breath at rest, difficulty taking a full breath, and rapid shallow

breathing also increased significantly (p≤0.001). In contrast, wheezing and cough showed no phase-related changes (p=0.75 and p=0.37, respectively), suggesting these are not cycle-sensitive in healthy women.

Table 5: Individual Changes in Peak Expiratory Flow (PEF) Between Phases (N=48)

PEF Change Category	n (%)	Mean PEF change (L/min) ± SD
Decrease in ML (any decline)	44 (91.7)	-19.8 ± 10.2
No change (±5 L/min)	2 (4.2)	+1.0 ± 3.0
Increase in ML (any rise)	2 (4.2)	+8.5 ± 2.1
Clinically meaningful decline (≥10 L/min)	29 (60.4)	-22.4 ± 9.7
Decline ≥15 L/min	18 (37.5)	-26.1 ± 8.3

A decline in PEF occurred in 91.7% of women (44/48). A clinically meaningful decline (≥10 L/min) was seen in 60.4% (29/48), with a mean decline of -22.4 L/min in this subgroup. A decline of ≥15 L/min occurred in 37.5% (18/48). Only two women (4.2%) showed a small increase in PEF during the luteal phase.

Table 6: Awareness and Perceived Impact of Menstrual Cycle on Breathing (N=48)

Survey Question	Yes n (%)	No n (%)
Pre-study awareness: "Before this study, were you aware that your breathing might change with your menstrual cycle?"	13 (27.1)	35 (72.9)
Post-study recognition: "After completing both assessments, do you believe your breathing changes across your cycle?"	42 (87.5)	6 (12.5)
Would you consider cycle phase when evaluating your respiratory health in the future?"	44 (91.7)	4 (8.3)
Have you ever mentioned breathing symptoms to a healthcare provider in relation to your menstrual cycle?"	3 (6.2)	45 (93.8)

Only 27.1% (13/48) were aware of cycle-related breathing changes before the study. After participation, 87.5% (42/48) recognized such changes, and 91.7% (44/48) stated they would consider cycle phase in future respiratory health assessments. Strikingly, only 6.2% (3/48) had ever mentioned breathing symptoms to a healthcare provider in relation to their cycle (p<0.001 for pre-post awareness change).

Table 7: Correlation Matrix of Key Variables (Mid-Luteal Phase Only, N=48)

Variable	PEF (L/min)	mMRC score	RSPS total	Progesterone (ng/mL)	Age (years)
PEF (L/min)	1.00	—	—	—	—
mMRC score	-0.38*	1.00	—	—	—
RSPS total	-0.32*	0.61**	1.00	—	—
Progesterone (ng/mL)	-0.19	0.24	0.28	1.00	—
Age (years)	-0.11	0.05	0.08	-0.02	1.00

During the mid-luteal phase, PEF showed moderate negative correlations with mMRC dyspnea (ρ=-0.38, p<0.05) and RSPS total score (ρ=-0.32, p<0.05). mMRC and RSPS were strongly positively correlated (ρ=0.61, p<0.001). Progesterone levels did not significantly correlate with any respiratory variable (ρ ranging from -0.19 to 0.28, all p>0.05), suggesting that within ovulatory ranges, progesterone concentration alone does not linearly predict symptom severity. Age showed no correlation with any outcome.

DISCUSSION

The present survey of 48 healthy, ovulating women demonstrated that the mid-luteal phase of the menstrual cycle is associated with both objective and subjective alterations in respiratory function compared to the early follicular phase. Specifically, peak expiratory flow (PEF) declined by a mean of 17.3 L/min (4.3%), while dyspnea perception and symptom burden increased substantially, as reflected by mMRC and RSPS scores. Notably, nearly two-thirds of participants (60.4%) experienced a clinically meaningful decline in PEF (≥10 L/min), and over two-thirds (68.8%) reported at least mild dyspnea during the luteal phase. Despite these measurable changes, the majority of women (72.9%) were unaware of any cycle-related breathing variation prior to study participation. These findings have important implications for clinical respiratory assessment and women's health education.18

The observed luteal-phase decline in PEF aligns with findings from previous studies that have examined cyclical variations in expiratory flow. In a well-controlled study by Farha and colleagues (2014) involving 17 healthy women, forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were found to be significantly lower during the mid-luteal phase compared to the early follicular phase, with mean declines of approximately 3–5%.10 Our finding of a 4.3% decline in PEF is remarkably consistent with these values, suggesting that the effect size is reproducible across

different measures of expiratory flow. Similarly, a study by Macsali et al. (2011) using data from the European Community Respiratory Health Survey reported that naturally cycling women had lower lung function during the luteal phase, although the study relied on retrospective phase assignment rather than hormonal confirmation.16 A larger population-based study by Real and colleagues (2008) similarly noted cyclical variations in peak flow among healthy women, further supporting our observations.15

The subjective symptom findings of the present study corroborate earlier work by Tan and colleagues (1997), who documented increased reports of chest tightness and breathlessness during the luteal phase in women with and without asthma.13 However, our study extends these observations to a larger, hormonally confirmed sample of completely healthy women without any prior respiratory diagnosis. Notably, the strong correlation we observed between PEF decline and mMRC/RSPS scores (ρ = -0.38 and -0.32, respectively) indicates that subjective awareness of breathing difficulty is at least partially grounded in objective physiological changes, rather than being purely psychosomatic.9

In contrast, a smaller study by Chandler et al. (1997) involving only 12 healthy women reported no significant cyclical changes in spirometric parameters.14 The discrepancy may be attributed to their smaller sample size (n=12 vs. n=48), lack of biochemical confirmation of ovulation, or differences in the timing of luteal assessment. Our use of serum progesterone measurement (mean 12.4 ng/mL) ensured that all participants were truly in the mid-luteal phase with adequate progesterone elevation, thereby reducing misclassification bias.7

The reduction in peak expiratory flow during the luteal phase is likely multifactorial. Progesterone, which rises sharply after ovulation, has been shown to cause fluid retention and mild submucosal edema in the airway wall, potentially reducing luminal diameter and increasing resistance to expiratory flow.1,2 Additionally, progesterone may alter smooth muscle contractility, though the net effect remains debated.[3] Estrogen, which also peaks during the luteal phase (though less prominently than progesterone), may have opposing protective effects on airway patency; the net result appears to be a mild but consistent decrement in expiratory flow.10,11

Progesterone is a well-established respiratory stimulant that increases central chemosensitivity to carbon dioxide, leading to chronic mild hyperventilation and reduced $PaCO_2$.8 This state of relative hypocapnia can trigger sensations of air hunger or "needing to take a deeper breath," which were among the most highly endorsed symptoms in our RSPS analysis (median score 2 out of 3 during luteal phase). The unchanged respiratory rate (14.1 vs. 14.0 breaths/min) suggests that the increased dyspnea is not due to tachypnea per se, but rather to altered neuromechanical coupling or increased respiratory effort perception.9 The strong correlation between RSPS and mMRC (ρ=0.61) supports the internal consistency of these subjective measures.

Interestingly, wheezing and cough did not differ between phases. This is reassuring, as it suggests that healthy women do not experience bronchoconstriction or airway irritability across the cycle. It also provides a useful contrast: in women with asthma, cyclical worsening of wheezing is well-documented, indicating that the healthy airway is relatively resistant to hormone-induced bronchospasm.13 A study by Pefkaros and colleagues (2015) similarly reported no cyclical changes in cough reflex sensitivity in healthy women, aligning with our findings.17.

CONCLUSION

In conclusion, this survey of 48 healthy eumenorrheic women provides robust evidence that the mid-luteal phase is characterized by a small but statistically significant decline in peak expiratory flow (mean -17.3 L/min) and a clinically meaningful increase in dyspnea perception, with 68.8% of women reporting at least mild breathlessness. The majority of women were unaware of these changes prior to study participation, highlighting a critical gap in both public and professional education. Clinicians should consider menstrual cycle phase when evaluating respiratory symptoms or interpreting pulmonary function tests in premenopausal women. A simple question—"Do your breathing symptoms change with your menstrual cycle?"—may yield valuable diagnostic information and improve patient-centered care.

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