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Research Article

Construction of an Atopic Symptom Questionnaire and Evaluation of Peri-menstrual Atopy in Women of Reproductive Age

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Abstract

Background: Atopic disorders, such as asthma, atopic dermatitis (AD), and allergic rhinitis (AR), are rising globally. In reproductive-age women, hormonal fluctuations during the menstrual cycle can trigger or worsen symptoms, a condition termed perimenstrual atopy (PMA). Despite its prevalence, PMA remains under-recognized, especially in healthy females, and no standardized tool exists for its comprehensive assessment. ***Objective***: To determine PMA occurrence in females with and without diagnosed atopy and to develop and validate the Atopic Symptom Score Questionnaire (ASQ) for PMA evaluation. ***Methods***: This observational study included 145 reproductive-age females (54 atopic, 91 non-atopic) with regular menstrual cycles. The ASQ was constructed by integrating validated tools for asthma, AD, and AR. Content validity was confirmed by experts, and internal reliability was strong. After pilot testing, the finalized ASQ was administered via face-to-face interviews. Participants rated symptom severity and indicated the timing of symptom onset in relation to menstrual phases. Mean ASQ scores and the frequency of PMA was analyzed, the comparison between atopic and non-atopic groups were conducted. ***Results***: PMA was reported in 29.9% of participants, more often in atopic (40.7%) than non-atopic females (23.3%). The most common symptoms were breathlessness, throat discomfort, and nasal congestion. ASQ scores were significantly higher in atopic individuals (11.5 *vs.* 2.41, $p<0.001$), with most exacerbations during menstrual and premenstrual phases. ***Conclusions***: The ASQ is a valid tool for assessing PMA. PMA is common and underdiagnosed, even among non-atopic females, highlighting the need for greater clinical awareness and standardized evaluation.

Keywords: Atopic symptoms, Menstrual phases, Perimenstrual atopy, Reproductive-age female.

بناء استبيان الأعراض التأتبية وتقييم اللاتوبي في الفترة المحيطة بالحيض لدى النساء في سن الإنجاب

الخلاصة

الخلفية: الاضطرابات التأتبية، مثل الربو والتهاب الجلد التأتبي (AD) والتهاب الأنف التحسسي (AR)، آخذة في الارتفاع على مستوى العالم. في النساء في سن الإنجاب، يمكن أن تؤدي التقلبات الهرمونية أثناء الدورة الشهرية إلى ظهور الأعراض أو تفاقمها، وهي حالة تسمى التأتب في الفترة المحيطة بالحيض (PMA). وعلى الرغم من انتشاره، لا يزال التقييم غير معترف به، خاصة بين الإناث الأصحاء، ولا توجد أداة موحدة لتقييمه الشامل. **الهدف**: تحديد حدوث PMA لدى الإناث مع وبدون تأتب تشخيصي وتطوير والتحقق من صحة استبيان درجات الأعراض التأتبية (ASQ) لتقييم PMA. **الطرائق**: شملت هذه الدراسة القائمة على الملاحظة 145 أنثى في سن الإنجاب (54 تأتبيا ، 91 غير تأبية) مع دورات شهرية منتظمة. تم إنشاء ASQ من خلال دمج أدوات تم التحقق من صحتها للربو و AD و AR. تم تأكيد صلاحية المحتوى من قبل الخبراء، وكانت الموثوقية الداخلية قوية. بعد الاختبار التجريبي، تم إجراء ASQ النهائي من خلال المقابلات وجها لوجه. قام المشاركون بتقييم شدة الأعراض وأشاروا إلى توقيت ظهور الأعراض فيما يتعلق بمراحل الحيض. تم تحليل متوسط درجات ASQ وتكرار PMA، وتم إجراء المقارنة بين المجموعات التأتبية وغير التأتبية. **النتائج**: تم الإبلاغ عن PMA في 29.9٪ من المشاركين، في كثير من الأحيان في التأتب (40.7٪) أكثر من الإناث غير التأتبية (23.3٪). كانت الأعراض الأكثر شيوعا هي ضيق التنفس وعدم الراحة في الحلق واحتقان الأنف. كانت درجات ASQ أعلى بشكل ملحوظ في الأفراد التأتبيين (11.5 مقابل 2.41 ، ص <0.001)، *مع معظم التفاقم خلال مرحلتي الحيض وما قبل الحيض*. **الاستنتاجات**: ASQ هو أداة صالحة لتقييم PMA. PMA شائع وغير مشخص، حتى بين الإناث غير التأتبية، مما يسلط الضوء على الحاجة إلى زيادة الوعي السريري والتقييم الموحد.

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INTRODUCTION

Atopic diseases have intensified worldwide, becoming epidemic in industrialized nations and maintaining ongoing growth in developing countries. Despite stabilizing in some Western areas, their early onset and chronic course continue to cause a major global health challenge [1]. And the psychosocial influence on both patients and their families is considerable. Atopy, defined by the American Academy of Asthma and Immunology as 'the genetic disposition to generate allergic disorders such as asthma, atopic dermatitis (AD), and allergic rhinitis [2]. Although IgE production is a key immunological hallmark, atopic diseases can be found even in the absence of elevated IgE, a class termed as "intrinsic" or non-IgE-mediated atopy [3,4]. This distinction has been supported by observations in eczema and

asthma, where clinical manifestations are frequently identical despite differing IgE profiles. The Handbook of Atopic Eczema reveals that this connection reflects common pathophysiological pathways and a family-linked risk of developing atopic disorders. This overlap underscores the shared pathophysiological pathways and familial tendencies among atopic conditions [5]. In general, women tend to have stronger immune responses, which may help to resist infections. Although this elevation in immune activity also underlies their greater susceptibility to autoimmune diseases. Sex hormones modulate the activity and distribution of mast cells in various tissues, with the presence of sex hormone receptors on the cell surfaces [6]. High estrogen levels enhance adaptive immunity by acting on specific immune cells. Estrogen is believed to be a 'natural modulator' of the immune system, inhibiting allergic responses at high levels. In other studies, associated peak estrogen levels around ovulation are linked to the mast cell degranulation and the promotion of allergic reactions in women of reproductive age. Skin flare-up has been reported during this phase [7]. The skin is highly responsive to these hormones, often reflecting these shifts through differences in sensitivity and inflammatory reactions. Studies indicate that the ratio of progesterone to estrogen can affect how skin cells (epidermal keratinocytes) proliferate, and both hormones may contribute to weakening the skin's barrier function when not in the proper ratio [8]. Decline in progesterone and estrogen during the perimenstrual phase is associated with degranulation of the mast cell, both locally inside the endometrium and systematically, including bronchial tissues [9]. Estrogen receptors are present on the various airway tissues, mast cells, and lymphocytes [10]. In addition, the nasal mucosa becomes hyper-reactive to histamine at peak estrogen level [11]. Hormonal fluctuations during the menstrual cycle, particularly the sharp drop in estrogen and peak in progesterone before menstruation, are thought to trigger this exacerbation, named peri-menstrual atopic symptoms (PMA) [12,13,14]. PMA tends to occur at a time of sharp decline in estrogen levels, and progesterone levels are at their highest. This describes the fact that some asthmatic women experience worsening of their asthma symptoms during the premenstrual or menstrual period of their menstrual cycle [15]. Now, identified as a unique asthma phenotype affecting 19–40% of asthmatic women. PMA is characterized by high symptom severity and lower lung function and is distinguished from traditional allergic asthma with aspirin sensitivity, lower lung capacity, and reduced atopy [9]. Studies have shown that women aged 16 to 35 years have the highest prevalence of PMA and are often unrecognized, leading to insufficient diagnosis and poor management [16]. A standardized definition for PMA remains absent. Murphy *et al*. looked into the following types of PMA definitions: self-reported PMA, increased symptoms, more frequent medication use, lower peak flow, or mixed symptom changes, medication, and peak flow. The difference in the definition of PMA affects the recollection of the data in the research studies and affects the prevalence in different populations [17]. Several questionnaires and scoring systems were used to aid diagnosis or for assessing the severity of asthma, AD, and eczema, each separately. The questionnaire or scoring system includes the Lara Asthma Symptom Scale (LASS) [18] and the Asthma Control Questionnaire (ACQ) [19] for asthma, EASI [20], SCORAD [21], and POEM [22] for AD, and a four-point scale total symptom score (TSS) [23,24] for AR. To date, there is no known scoring system for atopic conditions as a whole. As most of the patients have a combination of atopy, and people with PMA mostly have a combination of symptoms. the development of a scoring system for whole atopy named the atopic symptom score questionnaire (ASQ) is fundamental. This is especially to assess PMA in females with no previous diagnosis of atopy but who have the development of atopic symptoms at certain times of menses that are often overlooked. The study aims to investigate the frequency of PMA among reproductive females with or without atopy and to construct and validate an atopic symptom score questionnaire (ASQ) that is applicable in PMA females with or without an atopy diagnosis. Moreover, the study aims to investigate the rate of individual atopic symptoms to identify the most commonly reported one in PMA females.

METHODS

Study type and setting

This study is an observational study that was conducted at the College of Medicine, University of Sulaimani, and the Asthma and Allergy Center. Ethical approval was obtained by the College of Medicine Ethics Committee (Approval No. 309; Meeting No. 21, dated 22 September 2024) from the University of Sulaimani. Written informed consent was obtained from all participants.

Questionnaire construction and validation

Before the start of receiving participants, a well-structured questionnaire was constructed by the authors, which is derived from the combination of previous questionnaires used separately for each type of atopy: the Lara asthma symptom scale (LASS) [18] and the asthma control questionnaire (ACQ) [19] for asthma; EASI [20], SCORAD [21], and POEM [22] for AD; and the four-point scale total symptom score (TSS) [23,24] with the addition of eye and throat symptoms for AR. The questions were selected based on the questionnaire's suitability for assessing the daily symptom score and for use among both healthy individuals and those with atopy, making it suitable for use outside a clinic and hospital setting. The questionnaire was translated into the native language, and the content validity of the questionnaire was assessed by several experts in the field, including statisticians, immunologists, respiratory medicine specialists, internal medicine specialists, and physiologists, and the questions were modified accordingly. A pilot study was done by distributing

the questionnaire to both atopic and healthy individuals. After filling in the questionnaire, the data were entered into SPSS, and reliability tests were done via Cronbach's alpha. The questionnaire with an acceptable Cronbach's alpha, 0.894, is finalized. The average ASQ score was found using descriptive statistics.

Study design and participant selection

After a pilot study and validation of the questionnaire, the study started with the inclusion of healthy or atopic reproductive-aged females, aged 18-45 years, with a regular menstrual cycle. The finalized, polished questionnaire was filled out for consecutive patients visiting the asthma and allergy center; for atopy individuals, convenient sampling was used for the college staff and students and healthy individuals. Pregnant females or females with irregular cycles, hormonal disturbances, autoimmune disease, systemic disease, or on medication affecting the immune or hormone system were excluded.

Questionnaire content

The questionnaire (ASQ questionnaire; available as supplementary data) includes questions regarding age, date of the interview, the date of the last menstrual period (LMP), and whether they have been diagnosed with atopy, asthma, eczema (AD), or AR previously or not, and the participants have to choose all atopy types that apply to them. This was followed by a question about whether they have had any of the provided (atopic) symptoms within the last 24 hours and a request to rate each of these 17 symptoms on a linear scale from 0 to 3. 0: no symptoms, 1: mild symptoms, 2: moderate symptoms, and 3: severe symptoms. These symptoms include six questions about asthma: coughing, sputum, wheezing, chest tightness, breathlessness, and exercise intolerance from respiratory discomfort. Five questions about eczema: The patient has been asked if he had the following symptoms of eczema: itching, sleep disturbances due to itching, erythema, dryness, or edema. Another six questions about allergic rhinitis (AR): rhinorrhea, nasal congestion, nasal itching, sneezing, eye itching or watery eyes, and throat symptoms (for example, itching and soreness). After a field for total ASQ score, another two questions were asked: Do you think these symptoms appear or change during specific phases of the menstrual cycle? And if the symptoms are menstrual-related, at which phase of the menstrual cycle do they tend to appear or worsen? The participants have to choose one of the three phases of the menstrual cycle administered to them: premenstrual (a few days before menstruation), menstrual (during menstrual bleeding), and periovulatory (a few days after menstrual bleeding stops). The females who answered yes to the first question of "if the symptoms are menstrual-related and appeared or increased with certain phases of the menstrual cycle" were regarded as having perceived perimenstrual atopy (PMA). Those who answered that the provided symptoms are not related to the menstrual cycle phases are defined as non-perceived PMA. Female participants who reported PMA and were interviewed during the specific phase of the menstrual cycle when their symptoms typically worsen were identified and analyzed. If their ASQ scores are one unit above the average for each atopy and healthy individual, their PMA is confirmed and regarded as confirmed PMA.

Statistical analysis

After entering the data into an Excel sheet and coding it is transferred to SPSS 27. Descriptive statistics were performed, and the data were shown either as frequency and percentage for the numerical data, or as mean and standard deviation for continuous data. Comparison of the mean ASQ scores, asthma score, AD score, and AR score between atopy and non-atopy in all participants was done using Students' t-test, and a significant value was set < 0.05. Other group comparisons, such as mean age of individuals with perceived PMA between atopy and non-atopy and mean ASQ scores between atopy and non-atopy in individuals with or without perceived PMA, were analyzed using Students' t-test and demonstrated via stratified box plots. The percentage of PMA between atopy and non-atopy groups was found using a chi-square test and illustrated via a stratified bar chart. Bar charts were also conducted to show the mean ASQ scores indifferent atopy types, including combinations, and the number of days of menstrual cycles with the most frequent PMA.

RESULTS

The total number of participants included in the final analysis is 145 females, comprising 91 healthy, non-atopic females and 54 females with atopy. The number of atopic types, phases of the menstrual cycle, and other characteristics of the studied participants are shown in Table 1. Asthma is the most frequent type of atopy, affecting 25.93% of atopic participants, AD 22.22%, AR 14.81%, AD and AR 12.96%, and asthma and AD and asthma and AR each accounting for 7.41%. Additionally, 9.26% of atopic individuals have a combination of all three types of atopies. The phases of menses with the more frequent PMA are phase 1 (menstrual phase), in which 50% of females with atopy symptom development/exacerbation pointed out that they have it in phase 1, with 42.5% in phase 3 (pre-menstrual), and only 7.5% of them in phase 2 (peri-ovulatory). Among females who were actually in the phases with the perceived PMA at the time of interview, 62.5% of those who confirmed with PMA have perceived PMA, while 42.9% of confirmed PMA are among those who didn't perceive PMA. The mean age of the studied females is 30.63 (8.85). The mean age of females with PMA vs. non-PMA is 34 vs. 27 years in atopic individuals, and in non-atopic females it is 35 vs. 27 years, respectively (Figure 1). Among all participants, 29.9% of them have development of symptoms/symptom exacerbation (perceived PMA) during a certain time of menses, and 40.7% of patients with atopy have symptom exacerbation in comparison

to 23.3% of the non-atopy females, as also revealed in Figure 2 and Table 1.

Table 1: Basic and PMA characteristics of the participants studied (total No. = 145)

Parameters	Total	No.
Mean Age (year)	30.63±8.85	145
Phases of Menstrual cycle		145
Phase 1 (P1)	49(33.8)	
Phase 2 (P2)	41(28.3)	
Phase 3 (P3)	55(37.9)	
Participants		145
Normal (non-atopy)	54(37.5)	
Atopy	91(63.19)	
Atopy types (n=54)		54
Asthma	14(25.93)	
Eczema or Atopic Dermatitis (AD)	12(22.22)	
Allergic Rhinitis (AR)	8(14.81)	
AD + AR	7(12.96)	
Asthma + AD	4(7.41)	
Asthma + AR	4(7.41)	
All three combined (Asthma + AD + AR)	5(9.26)	
Mean ASQ score (n=145)		145
Total	5.79±7.08	
Atopy	11.5±7.63	
Non-Atopy	2.41±3.84	
Symptom exacerbation during certain phase of menstrual cycle (PMA)		144
Yes	43(29.9)	
Atopy	22(40.7)	
Non-Atopy	21(23.3)	
No	101(70.1)	
Atopy	32(59.3)	
Non-Atopy	69(76.7)	
Menstrual phases with symptom exacerbation in PMA group		40
Phase 1 (P1)	20(50)	
Phase 2 (P2)	3(7.5)	
Phase 3 (P3)	17(42.5)	
Presence of perceived PMA in females with the known day of the cycle (n=100)		100
Yes	30 (30)	
No	70(70)	
PMA confirmation among females within the claimed menstrual phase at time of ASQ score filling		30
Perceived PMA	10(62.5)	16
Non-Perceived PMA	6(42.9)	14

Values are presented as frequency (%), and mean±SD.

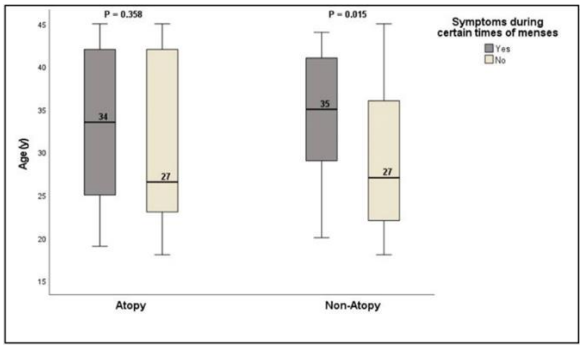

Figure 1. Mean age of individuals experiencing symptom exacerbations during certain phase of menstrual cycle (PMA) in atopic and non-atopic groups.

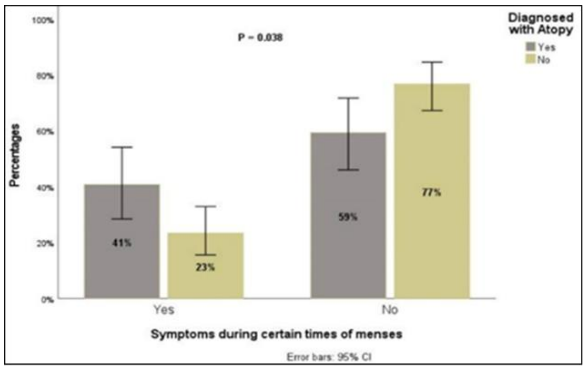

Figure 2. Percentage of exacerbation of symptoms during certain times of menses (PMA) in females with or without atopy.

Mean ASQ scores are 5.79 in total participants, while among atopic compared to non-atopic participants, they are 11.5 vs 2.41, $p < 0.001$. In females with PMA, the ASQ score is 10.5 vs. 3 in atopy and non-atopy individuals (Figure 3a). The mean Asthma score, AD score, and AR score of total participants and comparisons between atopy and non-atopy females are demonstrated in Table 2.

Table 2. Symptom scores comparison between atopy and non-atopy groups

Parameters	Total n= 145	Atopy n= 54	Non-Atopy n= 91	*p*-value
ASQ score	5.79(7.08) 3(0-35)	11.5(7.63) 11(0-35)	2.41(3.84) 1(0-24)	<0.001
Asthma score	2.24(3.57) 1(0-17)	4.31(4.78)	1.01(1.69)	<0.001
AD score	1.22(2.42) 0(0-11)	2.39(3.03)	0.53(1.64)	<0.001
AR score	2.33(3-4) 1(0-15)	4.8(4.15)	0.87(1.62)	<0.001

Values are expressed as mean and median.

When the different atopic type groups are compared, the groups with a combination of Asthma and AD have the highest ASQ scores in comparison to other groups, followed by the AR group. The ASQ scores among all group types are revealed in Figure 3b.

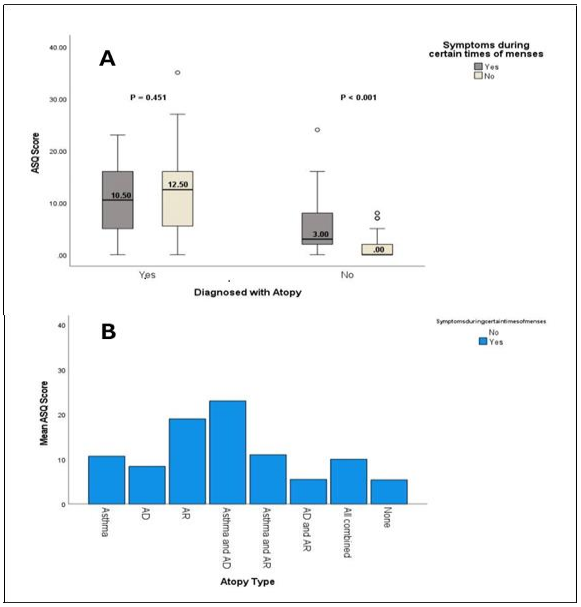

Figure 3: **A**) Comparison of mean ASQ score between females with or without PMA in both atopic and non-atopic groups; **B**) Mean ASQ scores per groups with different type of combinations of atopy.

Figure 4 demonstrates the day of menses with frequent symptom development/exacerbation, in which days 1, 28, and 25 of menses are among the top, and reveals that most of the days are those around menstruation, with the premenstrual and menstruation phases.

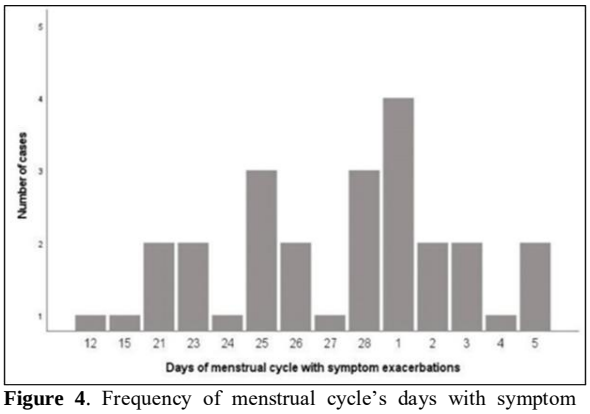

Figure 4. Frequency of menstrual cycle's days with symptom exacerbations.

The frequency and severity of atopic symptoms in PMA females with and without atopy are illustrated in Figure 5. Among females with atopy, the most frequently reported atopic symptom is breathlessness, followed by throat symptoms, nasal congestion, sputum production, and rhinorrhea. For the AD symptoms, itching and dryness at the eczema site are the most frequent symptoms. In contrast, among females without atopy, the most frequent symptoms are rhinorrhea and coughing, followed by exercise intolerance due to breathlessness, itching at the eczema site, eye itching or watery eyes, and sputum production.

DISCUSSION

In the current study, the cyclical variability of atopic symptoms in women during the menstrual cycle is evaluated through constructing, validating, and applying a structured Atopic Symptom Questionnaire (ASQ) to track atopic dermatitis (AD), asthma, and allergic rhinitis (AR) across three phases of the menstrual cycle.

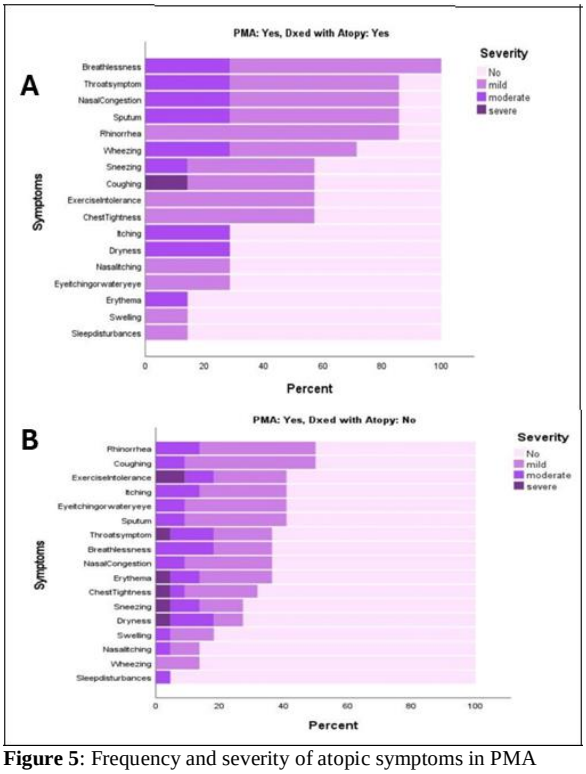

Figure 5: Frequency and severity of atopic symptoms in PMA females; **A**) with atopy; and **B**) without atopy.

Peri-menstrual atopic symptoms (PMA) were recognized in 40.7% of cases, with the highest frequency during the menstrual phase (Phase 1, 50%), followed by the premenstrual phase (Phase 3, 42.5%). Compared to the Skobeloff study, which found that 46% of asthma-related emergency visits occurred during the perimenstrual phase, a recurring pattern becomes clear. In the Skobeloff study, the identification of PMA relied only on the cycle-timing of menstrual-related asthma exacerbation in patients visiting the emergency department (ER) [25], which indicates that only those with severe symptoms were included, potentially excluding females with milder presentations. Both studies highlight the sensitivity of this hormonal phase, which seems to be influenced by falling estradiol levels. While the findings of Skobeloff illustrate how PMA may appear through emergency visits, they lack the symptom-specific detail. Additionally, Skobeloff focused exclusively on asthma, without accounting for other atopic conditions [25]. Likewise, another study conducted among asthma patients presenting to the ER, Brenner *et al*. [26] found that 27% of asthma exacerbations occurred in the perimenstrual phase. PMA was defined by linking each emergency visit to the menstrual phase during which symptoms appeared, calculated from the last menstrual period. Although Brenner *et al*. found a slight rise in asthma symptom exacerbation rates during preovulatory and perimenstrual phases, it concludes that no particular phase consistently drives symptom exacerbation. This differs from our study, which showed clearer phase-linked symptom increases, particularly during the menstrual and

premenstrual phases. Brenner's using a fixed 28-day cycle model, and a slightly older study population (18–54 years) may have introduced variation in cycle length, especially among adults older than 45 years due to menopausal transition. In addition, Skobeloff [25] and Brenner [26] depended on emergency department data where symptoms could be affected by stress or the environment; through structured questionnaires, this study focused on daily symptoms that often don't reach clinical attention. This provided a clearer view of how menstrual phases affect atopic symptoms. Although the Eliasson *et al*. study [27], like our studies, provides clear support for the premenstrual rise in asthma symptoms, with significant aggravation of dyspnea, wheezing, and chest tightness. The menstrual-related exacerbation rate in the study of Eliasson *et al*. (33%) closely reflects the 40.7% rate seen among atopic participants in our findings. In both studies, the clinical impact of symptom flares is evident. Eliasson's findings, in particular, show that individuals with PMA faced over twice the risk of hospitalization. In contrast, Eliasson's study included 57 premenopausal women under the age of 50 using retrospective self-reporting, relying on the ATS-DLD-78-A and a secondary PMA-specific survey, tracking symptom severity using broadly defined menstrual intervals. This methodological difference may help explain the higher PMA rates found in this study. Notably, PMA was identified in 51.9% of asthmatic participants in our study, compared to 33% in Eliasson study, perhaps due to differences in sample composition and the tools used to detect symptom patterns [27]. PMA was far less common in the Suzuki *et al*. study [28], with only 11.3% among menstruating women with asthma, compared to 40.7% in this study. The contrast may be explained by how each study defined PMA, and symptoms were assessed. The current study used ASQ to address symptom variation in real-time across three menstrual phases, while Suzuki relied entirely on a large-scale retrospective survey, where participants self-reported whether their asthma was affected by menstruation. The self-report questionnaire covered symptom frequency, asthma severity, medication use, and emergency history. However, its lack of phase structuring possibly limited its ability to detect cyclical symptom patterns. This reliance on subjective memory may have missed the detection of milder or unrecognized symptoms, an issue noted in earlier studies, where many women with PMA are often unaware of their cyclical symptom changes. In contrast, this study confirmed PMA objectively by linking high ASQ scores at the time of interview to the menstrual phase. Another study found that 37.5% of women with AD noticed increased symptom severity during the cycle, closely aligned with the 40.7% PMA rate seen in our atopic group. The main difference between the two studies is how they identified PMA. The study conducted by Mosbeh and Abdelrahman relied on retrospective interviews among participants aged 20–50. While this method shed light on patient experiences, it lacked clear phase classification and measurable symptoms. Our study, by contrast, used a structured ASQ, allowing for phase-specific tracking and objective confirmation of PMA based on symptom intensity scores during the interview phase. By linking symptoms with defined menstrual phases, this method may detect finer symptom shifts that might be missed through retrospective recall [29]. The finding of Cho *et al*. [30] reinforces the outcomes of our study, reporting a 32% prevalence of menstrual-related worsening in AD symptoms. Both studies reinforce the theory that cyclical hormonal change destabilizes immune balance, particularly in those already prone to atopic conditions. The Grajczyk *et al*. study [31] assessed 40 healthy women (aged 22–32 years), combining self-assessments with nasal airflow and Eustachian tube function tests across the follicular and luteal phases. Though AR and PMA weren't directly assessed, the observed increase in negative middle ear pressure and nasal blockage during the luteal phase strongly resembles the timing and nature of AR symptom flares seen in the current study. Both studies suggest that the hormonal change in the luteal phase could be a phase of heightened airway reactivity. In our study, AR made up 14.81% of atopic cases. What makes this comparison significant is that Grajczyk observed these changes in women with no prior atopic diagnosis, suggesting that cyclical nasal symptoms may not be exclusive to clinical AR [31]. In the present study, 29.2% of AR patients reported PMA. In contrast, Stübner *et al*. [32] examined PMA by testing 23 women with confirmed seasonal AR through nasal provocation tests at midcycle and late luteal phase outside of pollen season. The study observed a shift in allergic response intensity between visits, particularly a rise in sneezing during the progesterone-dominant phase among contraceptive users. Stübner *et al*. did not use a standardized symptom-tracking questionnaire, like the ASQ used in this study. Instead, it relied on acute allergen challenges and immediate symptom scoring on a five-point scale, paired with objective nasal airflow evaluation. It's worth noting that Stübner *et al*. included just 23 participants, all with seasonal AR, and divided the sample between naturally cycling women and those on oral contraceptives [32]. While the study designs vary considerably, both studies support a hormonal link to allergic symptom variability, notably during the luteal phase, but with differing approaches. By linking symptom reporting to defined menstrual phases and using a unified scoring method, our study brings together insights from the prior studies into a clearer, connected picture. Across both respiratory and dermatologic symptoms, the data points repeatedly to the menstrual cycle as a non-negligible factor in modulating atopic symptom expression. This study employed a validated Atopic Symptom Questionnaire (ASQ), refined through expert validation and pilot testing, identifying phase-specific symptom fluctuations across three menstrual phases, with PMA confirmed by higher ASQ scores during targeted phase interviews. Most prior studies have focused on a single atopic condition; however, this study included asthma, atopic dermatitis (AD), and allergic rhinitis (AR) simultaneously, offering a more comprehensive understanding of symptom overlap and perimenstrual atopy. Furthermore, the

current study assessed healthy females who developed menstrual-related atopic symptoms without a prior diagnosis of atopy—an often overlooked population. This approach supports the need for cycle-aware clinical evaluations and more personalized management of atopic symptoms.

Study limitations

This study is limited by its relatively small sample size and cross-sectional design, which prevented continuous symptom tracking across the menstrual cycle. Future research should involve larger, more diverse populations and adopt longitudinal designs to validate these findings. Daily symptom monitoring throughout the menstrual cycle, combined with hormonal profiling and assessment of immune- or allergy-related biomarkers, is recommended.

Conclusion

Peri-menstrual atopy (PMA) was identified in 40.7% of atopic women. Notably, 23.3% of women without a prior atopy diagnosis also reported PMA symptoms, underscoring a substantial but often under-recognized hormonal influence on atopic symptom expression. The highest frequency of symptoms was observed during the menstrual and premenstrual phases. Symptom worsening during these phases was reported by a significant proportion of participants, indicating a cyclical vulnerability that merits greater clinical awareness. This study highlights the importance of considering hormonal fluctuations in the assessment and management of atopic conditions. By employing a validated Atopic Symptom Questionnaire (ASQ), both perceived symptom changes and confirmed PMA were effectively captured. Comparing average ASQ scores between atopic and non-atopic females provided a more reliable means of assessing symptom severity and confirming PMA. These findings may support individualized care strategies aligned with symptom patterns. The findings support the integration of menstrual-cycle–aware approaches into routine clinical evaluation of atopic diseases and suggest that symptom tracking aligned with menstrual phases could enhance diagnostic accuracy and support more personalized treatment strategies.

Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

Supplementary data can be shared by the corresponding author upon reasonable request.

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