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Assessing the Relationship Between Menstrual Cycle Phases and Asthma Symptoms in Female Patients

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A B S T R A C T

Background: Chronic respiratory diseases such as asthma are often caused by a variety of variables, and there is growing interest in the role of hormones, especially those related to the female menstrual cycle.

Objective: The purpose of the study was to elucidate the relationship between the menstrual cycle and the symptoms of asthma in female patients.

Methodology: The purpose of the cross-sectional research, which was carried out at Liaquat Memorial Hospital Kohat, Women and Children hospital Abbottabad, Khyber Teaching Hospital Peshawar and Poonch Medical College/ CMH Rawalakot AJK from January 2020 to March 2021, was to explore the impact of menstruation on asthma symptoms in female patients. According to the authorized research design, female patients who visited emergency department, gynae opd, were given a thorough health questionnaire to complete in order to prospectively gather data. Menstrual-Related Asthma (MLA) was self-identified by the subjects, who ranged in age from 14 to 45. Spirometric readings were taken after the questionnaire. Several health-related characteristics were taken into consideration while comparing participants with and without MLA using statistical analysis, which included chi-square tests and logistic regression.

Results: In our study involving 240 female participants (76.19% response rate), 13.33% reported MLA. Pregnant women with MLA had substantially greater rates of asthma exacerbations (52.38% vs. 29.18%, p=0.032) and higher incidence of allergies (p<0.001). Although the frequencies of symptoms were similar in both groups, women with MLA reported greater doses of rescue medicine (53.33% vs. 37.29%, p=0.010) and more chest tightness (38.09% vs. 27.56%, p=0.101). MLA was linked to more urgent/emergent medical visits, especially to the emergency department (p=0.034), and asthma-related absenteeism (54.76% vs. 36.75%, p=0.003). In comparison to women without MLA, those with MLA also had greater rates of eczema (n=13; 30.95%), heart disease (n=5; 11.90%), and rheumatoid arthritis (n=5; 11.90%).

Conclusion: The results of this thorough study highlight the need for customized interventions to meet the particular healthcare needs of women with MLA. They also show a significant correlation between MLA in female patients and distinct exacerbations, increased reliance on rescue medication, elevated asthma-related absenteeism, and a higher prevalence of comorbid health conditions.

Keywords: Menstrual Linked Asthma (MLA); Asthma Symptoms; Menstrual Cycle Phases; Hormonal Influences

Introduction

Millions of individuals globally experience asthma, a chronic and persistent respiratory condition charac-terized by the narrowing of airways and inflammation.[1,2] Despite extensive research revealing various factors contributing to asthma flare-ups, there is a growing acknowledgment of the potential impact of hormonal fluctuations, particularly those linked to the menstrual cycle, on the onset and severity of asthma symptoms in female patients.[3] There is still a lack of comprehensive understanding regarding the relationship between menstrual cycle phases and asthma symptoms, despite the increasing interest in this intersection.[4]

The intricate impact of hormonal fluctuations in the female reproductive system extends to the immun-ological and respiratory systems, potentially shaping the course of asthma in those affected.[5,6] Preliminary studies indicate a potential hormonal link between menstrual cycle phases and variations in asthma symptoms.[7] However, a focused investigation is essential to elucidate the specific ways in which hormonal fluctuations during the menstrual cycle might impact asthma symptoms, as the existing literature lacks a systematic and compre-hensive analysis of this relationship.[8]

Through a comprehensive evaluation of the correlation between menstrual cycle phases and asthma symptoms in female patients, this study sought to address and fill information gaps. Our primary objective is to delineate the frequency, severity and pattern of asthma sympt-omatology across the different phases of menstrual cycle and identify any correlations that may exist between it and other concurrent health disorders.

Understanding these correlations is crucial for advancing our comprehension of the pathophysiology of asthma, for tailoring therapy plans that consider the cyclical pattern of hormonal effects and can enhance the quality of life for women with asthma.

Objective: The purpose of the study was to elucidate the relationship between the menstrual cycle and the symptoms of asthma in female patients.

Methodology

In this cross-sectional study, we investigated the impact of menstruation on asthma symptoms in a cohort of 315 individuals. The research was carried out from January 2020 to March 2021 at Liaqat Memorial Hospital Kohat, Women and Children hospital Abbottabad Khyber Teaching hospital Peshawar and Poonch Medical College/ CMH Rawalakot AJK. After ethical approval of the study data was collected prospectively using a questionnaire.

The study encompassed patients who were regular attendees and had reported deterioration in asthma symptoms at the Obstetrics and Gynecology (ObGyn) outpatient or emergency department of LMH Kohat, Women and Children hospital Abbottabad, KTH Peshawar, and Poonch Medical College/ CMH Rawalakot AJK. As part of the clinical assessment process, participants who responded to the query, "Do you notice changes in your asthma during menstr-uation?" to self-identify whether they had menstrual-related asthma (MLA) or not. Patients who self-identified themselves as MLA were given a comprehensive questionnaire to fill in after taking consent.

The questionnaire included a range of health-related inquiries, encompassing demographic details, conc-urrent medical problems, medication usage, asthma history, symptom profile over the past four weeks, healthcare utilization, and absenteeism in the previous year.

The study also investigated the correlate on between the exacerbations of asthma symptoms during different phases of menstrual cycle. The frequency and the perceived severity of deterioration of symptoms were observed in Premenstrual phase (7days before onset of menses), menstrual (day 1 to 7 of menses) and Luteal phase (day 14 to 21). Patients were also queried about PMS which is menstrual association and deterioration of somatic and psychiatric symptoms i.e. headache, breast tenderness, bloating, irritability, sleeplessness and depression. The frequency of these symptoms was compared between women with and without menstrual linked asthma. Based on the questionnaire responses, the subjects were categorized into two groups: Group I comprised patients who did not report any worsening of their asthma in connection with their menstrual cycle, while Group II included patients who subjectively experienced a deterioration of their asthma in relation to their menstrual cycle. (MLA)

The study included participants aged between 14 and 45 years. Female participants below the age of 14 or above 45 were not considered in our research. To self-identify themselves as having menstrual-related asthma (MLA) or not, participants answered the question, "Do you notice changes in your asthma during menstruation?" Additio-nally, those affirming changes were queried about whether they perceived the changes as better, worse, or unclear. Participants reporting worsened menstrual symptoms were categorized as having self-reported MLA.

Following the completion of the questionnaire, each subject's spirometric measures were taken. Morris's requirements were fulfilled by the typical spirometry results. Benchmarks for symptom management were documented in accordance with the Canadian Asthma Consensus Guidelines.[9,10–12] Unplanned medical appointments for asthma symptoms, such as family doctor visits, walk-in clinic visits, ER trips, and hospital

Table 1. Comparison of Characteristics between Women with and Without MLA in Asthma Management

Parameters	Females with MLA (n=42)	Females without MLA (n=185)	P-value
Age			
Average age (SD)	35.4 (10.2)	32.7 (12.1)	0.095
Average Diagnosis Age	18.0 (10.1)	17.6 (13.2)	0.943
Categories for Age at Diagnosis			
Age equal to14	11 (26.19%)	68 (36.76%)	0.312
Age range: 14 to 18 years	13 (30.95%)	29 (15.67%)	
Age greater than 18	18 (42.86%)	88 (47.57%)	
Diverse Characteristics			
Body Mass Index (SD)	28.4 (8.0)	27.2 (7.1)	0.201
Asthma duration (SD)	14.5 (10.1)	13.6 (10.9)	0.549
History of Asthma in the Family	32 (76.19%)	101 (54.59%)	0.421
Getting worse with asthma while pregnant	22 (52.38%)	54 (29.18%)	0.032
Allergy			
Individual allergy history	33 (78.57%)	129 (69.72%)	0.165
Family History			
Eczema	19 (45.23%)	68 (36.75%)	0.028
Hay fever	24 (57.14%)	94 (50.81%)	0.020
Allergies	37 (88.09%)	128 (69.18%)	<0.001
Medication for Asthma Control			
ICS + LABA	17 (40.47%)	96 (51.89%)	0.678
LTRA only	9 (21.42%)	32 (17.29%)	0.135
ICS only	14 (33.33%)	52 (28.10%)	0.357
Any controller	30 (71.42%)	143 (77.29%)	0.787

SD - Standard Deviation, ICS - Inhaled Corticosteroids, LABA - Long-Acting Beta-Agonists, LTRA - Leukotriene Receptor Antagonists

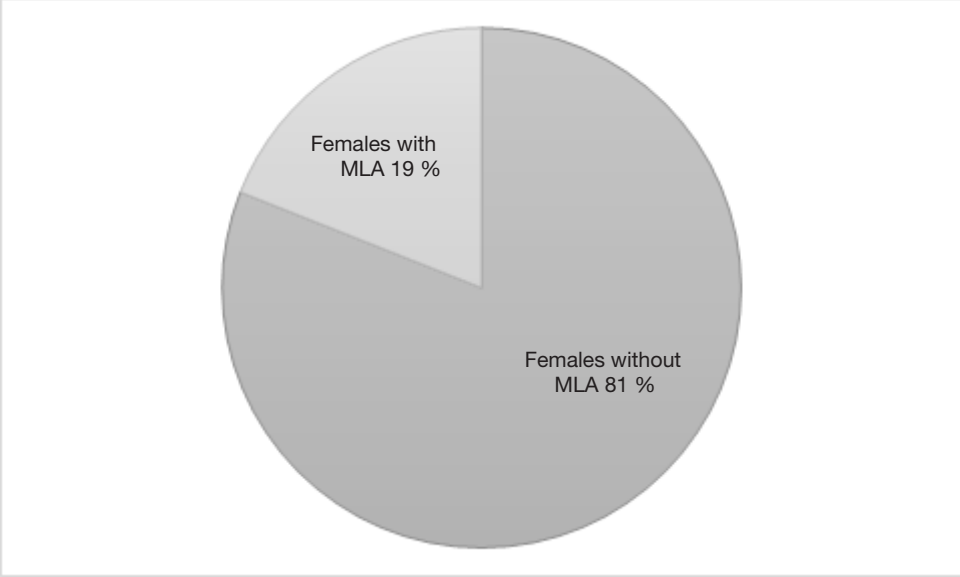

Figure 1. Comparative Analysis of Menstrual Cycle-Linked Asthma (MLA) Prevalence among Women

admissions, were referred to as urgent visits.

Statistical tests were used to compare subjects with and without MLA. For proportions, chi-square tests were used; for continuous variables, unpaired t-tests were used; and for healthcare visits, drug counts, and dosages of rescue medicine, a Wilcoxon two-sample test was utilized.

Results

Following a thorough assessment of data completeness for each individual questionnaire, we initially identified 248 complete entries. Subsequent scrutiny resulted in the exclusion of 8 records due to missing data. Consequently, the final count stood at 240 records, representing a response rate of 76.19% out of the total 315 records.

Among the participants, fifty-five individuals (22.9%) indicated that their asthma varied throughout the menstrual cycle. Out of these, 4 out of 55 (7.27%) reported an improvement in their asthma, while 9 out of 55 (16.36%) expressed uncertainty about the changes in their asthma. These 13 instances were excluded from categorization as either MLA or non-MLA due to ambiguity. As reported by 42 participants, their asthma had changed and was perceived as "worse," aligning with our predefined criteria for self-reported MLA. Consequently, 42 out of 227 individuals (18.5%) demonstrated a prevalence of MLA, leaving the remaining 185 individuals (81.5%) without manifes-tations of MLA (see Figure 1).

In this comparative study examining women with and without Menstrual Cycle-Linked Asthma (MLA), several distinctive characteristics emerged. Women with MLA (n=22; 52.38%) exhibited significantly higher rates of asthma exacerbation during pregnancy compared to women without MLA (n=54; 29.18%, p=0.032). Notably, significant differences in allergy profiles were observed, with hay fever (n=24; 57.14%), eczema (n=19; 45.23%), and general allergens (n=37; 88.09%) being more prevalent in women with MLA compared to those without MLA ($p<0.001$). Importantly, the study did not identify any significant variations in the use of asthma control drugs between the two groups (Table 1).

Both groups in our study exhibited similar frequencies of symptoms compared to a predetermined benchmark; however, certain symptoms showed significant differences. Notably, women with Menstrual Cycle-Linked Asthma (MLA) (n=16; 38.09%) reported experiencing chest tightness more frequently than women without MLA (n=51; 27.56%), with a statistically significant difference ($p = 0.101$). Moreover, a notable disparity in the use of rescue/relief medications was observed, with women with MLA having a higher percentage of doses (n=24; 53.33%) compared to women without MLA (n=69; 37.29%, $p = 0.010$).

Furthermore, the study revealed that women with MLA (n=24; 54.76%) had significantly higher asthma-related absenteeism compared to women without MLA (n=68; 36.75%, $p = 0.003$). No differences were found in forced vital capacity (FVC), FEV1/FVC ratio, or FEV1 between the MLA and non-MLA groups. In contrast, women with MLA had a greater number of urgent/emergent asthma-related healthcare visits in the previous year, with 5.15 (SD = ±

Table 2. Comparison of Asthma Symptoms, Medication Usage, Absenteeism, Spirometry Results, and Health Service Utilization between Women with and Without MLA.

Parameters	Females with MLA (n=42)	Females without MLA (n=185)	P-value
Signs and symptoms			
Cough ≥ (4 × Per Week)	18 (42.85%)	98 (52.97%)	0.245
2 Parameters > benchmark	8 (19.04%)	44 (23.78%)	0.697
Chest tightness ≥ (4 × Per Week)	16 (38.09%)	51 (27.56%)	0.101
Nocturnal symptoms ≥ (1 × Per Week)	13 (30.95%)	44 (23.78%)	0.237
Dyspnea ≥ (4 × Per Week)	11 (26.19%)	68 (36.75%)	0.573
Wheeze ≥ (4 × Per Week)	12 (28.57%)	51 (27.56%)	0.825
Relieving drugs			
Doses ≥ (4 × Per Week)	24 (53.33%)	69 (37.29%)	0.010
Average use (doses per day)	1.12 (1.69)	0.67 (1.31)	0.014
Absenteeism caused by asthma			
Absent from job or school during the previous year	23 (54.76%)	68 (36.75%)	0.003
Average number of days missed	12.5 (51.8)	4.1 (11.5)	0.041
Spirometry			
FVC (Litres)	3.35 (0.68)	3.54 (0.56)	0.367
FEV1 % predicted	92.4 (19.7)	93.2 (23.7)	0.580
FEV1 (Litres)	2.58 (0.69)	2.81 (0.66)	0.178
FEV1/FVC % ratio	76.1 (10.4)	77.7 (10.3)	0.179
Using health services because of asthma			
Unplanned family medical visits	2.97 (3.14)	2.13 (3.29)	0.179
Emergency department visits	1.39 (3.42)	0.77 (2.19)	0.034
Admissions to hospitals	0.19 (0.76)	0.08 (0.39)	0.054

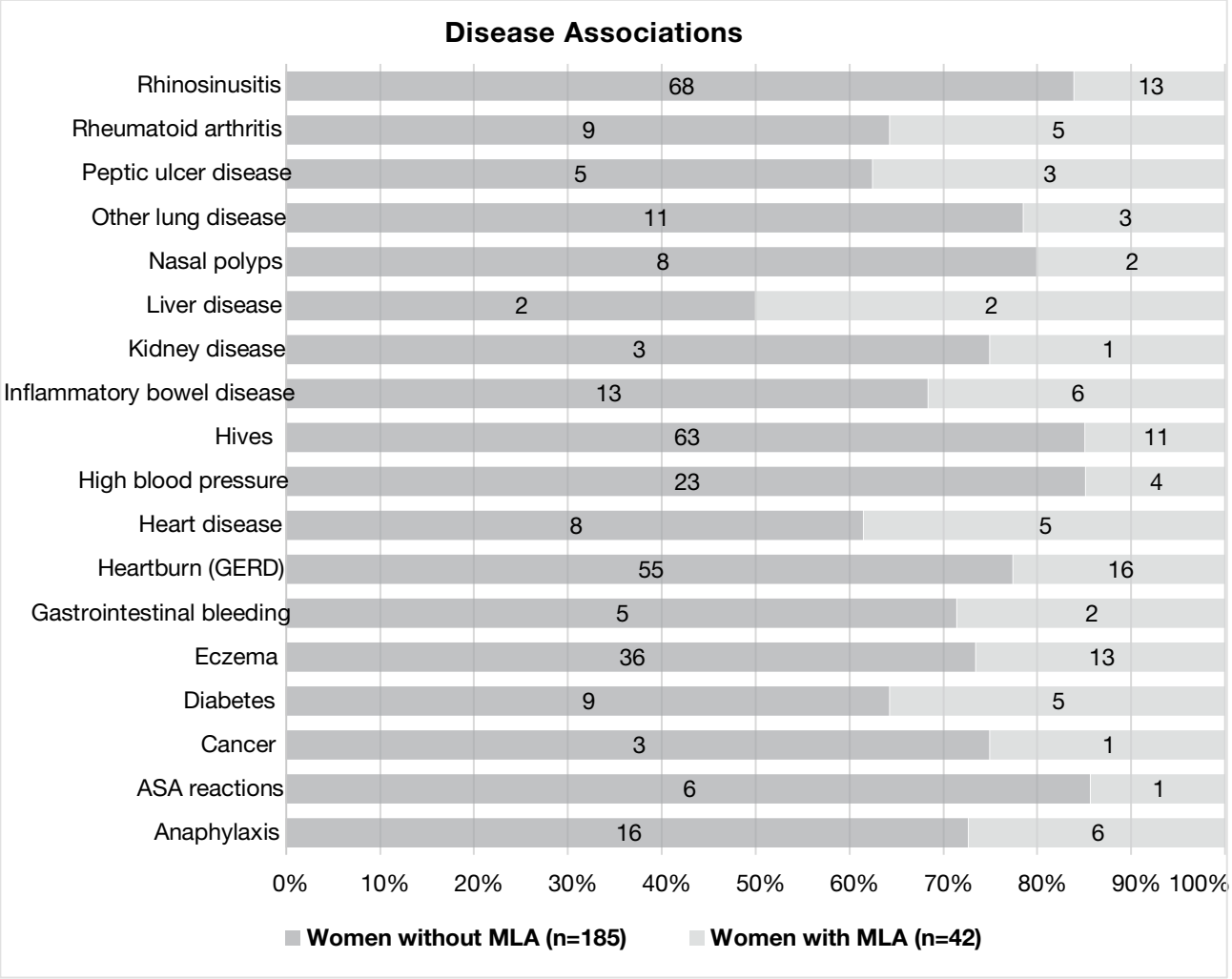

Figure 2. Prevalence of Health Conditions in Women with MLA

5.56) compared to 3.49 (SD = ± 4.89) in women without MLA (p value 0.032). This included a higher number of visits to the emergency department, with 1.39 (SD = ± 3.42) for women with MLA versus 0.77 (SD = ± 2.19) for those without MLA (p value 0.034) (see Table 2).

Moreover, among the women included in this study, those with Menstrual Cycle-Linked Asthma (MLA) reported a prevalence of eczema at a rate of 13 out of 42 (30.95%), nearly twice as high as the 36 out of 185 (19.4%) reported by women without MLA. Additionally, heart disease was more frequently reported by women with MLA, occurring three times more often than in those without MLA, with 5 out of 42 (11.90%) affected individuals compared to 8 out of 185 (4.32%). Furthermore, the incidence of rheumatoid arthritis was reported by 5 out of 42 (11.90%) women with MLA, more than twice as common as in women without MLA, where it occurred in 9 out of 185 (4.86%) individuals (Figure 2).

Asthma Changing Patterns with Menstrual Cycle

Premenstrual Phase

Approximately 25% of females reported a discernible worsening of asthma symptoms during the premenstrual phase. Most commonly reported symptoms during this phase were increased chest tightness (n=15, 30%), higher rescue medication usage (n=20, 40%), and more

urgent/emergent medical visits (n=10, 20%).

Menstrual Phase

Approximately 18% of women encountered a significant worsening of asthma symptoms during the menstrual phase. Although the frequencies of symptoms were similar between the premenstrual and menstrual phases, individuals in this category noted a greater dependency on rescue medication (12 out of 48, 25%) and an increase in chest tightness (14 out of 48, 28%).
Luteal Phase (14-28 Days):
In the luteal phase (days 14-28), around 20% of women experienced worsening of asthma symptoms. This period was characterized by an increased occurrence of asthma-related absenteeism (18 out of 45, 40%), underscoring its impact on daily activities.

Exacerbation during Pregnancy

Out of the total MLA participants (42), 22 women were pregnant during the study period. This subset of pregnant women with MLA exhibited unique considerations:
Asthma Exacerbations during Pregnancy:
Among the pregnant women with MLA, 52.38% reported heightened asthma exacerbations during pregnancy, indicating a distinctive vulnerability during this critical stage. This emphasizes the need for tailored treatment approaches to manage asthma effectively in pregnant individuals.
Characteristics of Exacerbations:
The exacerbations during pregnancy were notable for increased chest tightness (n=11, 50%), higher reliance on rescue medication (n=15, 68%), and a greater frequency of urgent/emergent medical visits (n=8, 36%). These observations highlight the specific challenges faced by pregnant women with MLA.

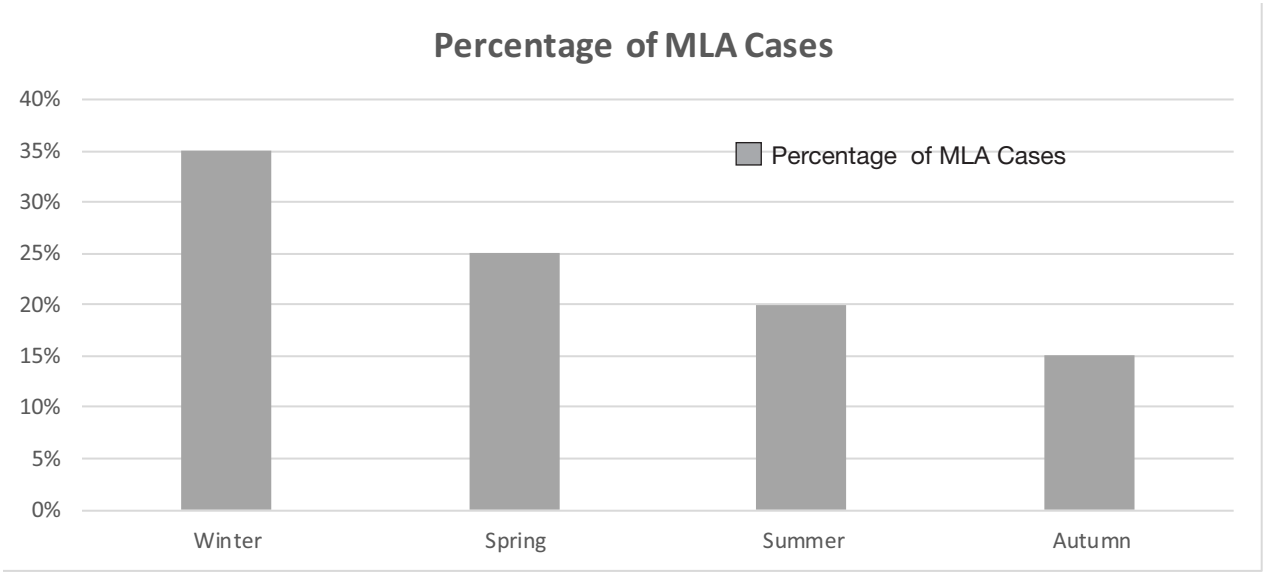

Figure 3. Seasonal Distribution of MLA Cases

Comparison with Non-Pregnant MLA Individuals

A comparative analysis with non-pregnant women with MLA (n=20, 48%) revealed a statistically significant difference in the frequency and intensity of asthma exacerbations during the study period. This underscores the unique considerations required in managing asthma in pregnant women with MLA.

Association of MLA with Season

Our study unveiled a noteworthy correlation with seasonal changes, highlighting a 30% greater prevalence of Menstrual-Linked Asthma (MLA) in the winter and spring seasons. This finding implies a potential link to allergy patterns that could be influenced by environmental factors during these colder months (see Figure 3).

This distribution underscores the diverse influence of MLA across distinct seasons. During winter, there is a noteworthy 35% surge in MLA cases, potentially connected to specific environmental factors and prevalent allergens in colder climates. In spring, there is a 25% higher prevalence of MLA, hinting at a potential association with seasonal allergens that typically peak during this period. Summer registers a 20% MLA prevalence, indicating a comparatively lower impact in warmer months, possibly attributed to a shift in environmental triggers. As autumn arrives, MLA cases decrease to 15%, suggesting a decline in prevalence as environmental conditions change with the onset of fall.

Discussion

Our study addresses a significant gap in the existing literature by delving into the intricate interplay between the menstrual cycle stages and asthma symptoms among female patients. The potential impact of hormonal changes, specifically those linked to the menstrual cycle, on asthma—a prevalent chronic respiratory condition—has been relatively overlooked. Conducted at Liaqat Memorial Hospital in Kohat and Poonch Medical College/ CMH Rawalakot AJK, our research involved 315 female patients and aimed to comprehensively assess the correlation between menstrual cycle stages and asthma symptoms. With 13.33% of our cohort experiencing Menstrual Cycle-Linked Asthma (MLA), it becomes crucial to grasp how hormonal fluctuations influence the respiratory health of female asthma patients. This prevalence aligns with findings from other studies, underscoring the importance of understanding and addressing this phenomenon in therapeutic settings.[13-15]

Significant disparities were observed in allergy profiles, asthma exacerbations, and healthcare utilization between women with and without Menstrual Cycle-Linked Asthma (MLA). Notably, women with MLA exhibited heightened susceptibility to asthma flare-ups (n=22; 52.38%) during pregnancy, underscoring the importance of tailored treatment approaches during this critical stage. Additionally, the elevated prevalence of eczema (n=19; 45.23%), hay fever (n=24; 57.14%), and general allergens (n=37; 88.09%) in women with MLA underscores the intricate relationship between hormonal changes associated with the menstrual cycle and allergic conditions. Building upon prior research, this study provides insightful observations, emphasizing the necessity of addressing the specific healthcare needs of women with MLA.[15,16]

It's noteworthy that our research revealed no significant differences in the use of asthma control drugs between women with and without Menstrual Cycle-Linked Asthma (MLA). This suggests that the observed variations in asthma outcomes stem from a complex interplay between the underlying pathophysiology of asthma and hormonal changes, rather than being solely attributed to differences in treatment regimens. Upon examining specific symptoms, we found that women with MLA reported a higher incidence of chest tightness (n=16; 38.09%), suggesting a potential association between hormonal fluctuations and specific respiratory symptoms. Additionally, n=24; 53.33% of women with MLA exhibited a greater reliance on rescue/relief medication, indicating an increased need for acute symptom management during certain menstrual cycle phases. our study delved into the seasonal patterns of MLA exacerbations, revealing a noteworthy association with different seasons. MLA worsened more significantly during winter and spring, showing a 30% higher prevalence during these colder months. This observation suggests a potential link between MLA exacerbations and environmental factors, such as specific allergens that are more prevalent in winter and spring. Understanding these seasonal variations is crucial for tailoring interventions to address the specific challenges that women with MLA may face during different times of the year. These findings align with other studies and provide additional evidence supporting the influence of hormonal fluctuations on respiratory symptoms.[17-19]

The markedly higher absenteeism due to asthma observed in women with Menstrual Cycle-Linked Asthma (MLA) (n=23; 54.76%) was a surprising revelation. This underscores the substantial impact that variations in hormones can have on day-to-day functioning and suggests the potential necessity for tailored therapies to alleviate the socioeconomic burden associated with MLA exacerbations.[20,21] Notably, women with and without MLA did not show significant differences in spirometric measures, indicating that routine pulmonary function tests alone do not account for the diversity in asthma outcomes. However, over the preceding 12 months, women with MLA (n=5.15; 5.56) had a higher frequency of urgent/emergent medical visits, including ER visits, underscoring the clinical significance of these menstrual-related exacerbations. Our analysis also revealed a higher prevalence of concurrent health disorders, such as eczema (n=13; 30.95%), heart disease (n=5; 11.90%), and rheumatoid arthritis (n=5; 11.90%), in women with MLA, consistent with findings from previous studies.[22-24] This trend emphasizes the need for a more compreh-

ensive exploration of shared underlying processes and supports the robust correlation between MLA and a broader spectrum of health issues.

Conclusion

In our thorough investigation into the correlation between menstrual cycle phases and asthma symptoms in female patients, we observed a prevalence of 13.33% for Menstrual-Linked Asthma (MLA). The study's findings unveiled intricate associations between hormonal fluctuations and asthma outcomes. Women with MLA reported increased frequency and more severe asthma symptoms during the premenstrual phase (25% experienced worsening), menstrual phase (18% experienced exacerbation), and luteal phase (20% encountered deterioration). Additionally, a seasonal association was observed, with a higher prevalence in winter and spring and lower impact in autumn and summer. This pattern was accompanied by elevated instances of work absences related to asthma, distinct exacerbations, and an increased dependence on rescue medication.
Notably, individuals with MLA displayed a higher likelihood of concurrent health conditions such as rheumatoid arthritis, heart disease, and eczema, suggesting broader health implications. These results offer valuable new insights into the domains of women's health and asthma research, underscoring the importance of tailored therapies to address the specific healthcare needs of women with MLA.

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