

Association between Menstruation and Excessive Daytime Sleepiness in Subjects with Restless Leg Syndrome among Intermediate Students in Karachi

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ABSTRACT

Background: Restless Leg Syndrome (RLS) is a neurological disorder characterized by unpleasant or uncomfortable sensations in the legs and an irresistible urge to move them. Menstrual-related distress and RLS symptoms worsen during menstruation, both affecting sleep and mental health, which can contribute to daytime sleepiness. **Objective:** of this study, was to determine the association between Menstruation and Excessive daytime sleepiness in subjects with Restless leg syndrome among intermediate students in Karachi. **Methods:** Cross-sectional study design was used in this research. The study was conducted among different intermediate colleges of Karachi. The study involves 125 participants aged 16 to 20, diagnosed with Restless Leg Syndrome (RLS). The questionnaire incorporates standardized tools to gather data on menstrual symptoms, Excessive daytime sleepiness, and the diagnosis of Restless leg syndrome (RLS) among intermediate-level students. Data were stored and analyzed using IBM- SPSS version 23.0. **Results:** The mean age of the 125 participants was 17 years. The mean age of menarche was 13 years, with a mean menstrual cycle length of 26 days and a mean menstrual duration of 5 days. Among them, 29.6% reported excessive daytime sleepiness during menstruation. Additionally, 59.2% of females experienced mild changes in menstrual distress four days before menstruation, 44.8% experienced moderate changes during menstruation, and 61.6% experienced mild changes during the rest of the cycle. Fisher's exact test revealed a significant association between excessive daytime sleepiness and menstrual distress before menstruation, during menstruation, and during the rest of the cycle. Furthermore, correlation analysis indicated a 38.6% positive correlation between excessive daytime sleepiness and menstrual distress scores. **Conclusion:** The study suggests a noteworthy association between Menstruation and Excessive daytime sleepiness in subjects with Restless leg syndrome among intermediate students in Karachi.

Keywords: Daytime sleepiness, Hypersomnolence, Menstrual cycle, Restlessness, Sleep apnea syndrome, Willis-Ekbom disease

INTRODUCTION

Restless Leg Syndrome (RLS) was introduced by Ekbom ¹ in 1945 to the medical community, yet Sir Tomas Willis had already described its symptoms 300 years prior ². It is also known as Willis-Ekbom Disease. It is a neurological condition where individual experience an overwhelming compulsion to move their limbs due to uncomfortable sensations, which tend to become worse when they are at rest, especially during the night ³ Restless leg syndrome (RLS) significantly impacts sleep quality and can be a disabling condition. However, describing these

symptoms is often challenging for affected individuals. They may resort to humorous descriptions like a creepy or crawly feeling, pain, jitteriness, or sensations of worms, soda bubbling in their veins, and itching bones⁴. This complexity in explaining the sensations can make diagnosis challenging for clinicians, leading to cases being missed or underdiagnosed, despite the condition being quite treatable. In severe cases, these sensations can extend beyond the legs to other body parts like the hips, trunk, hands, or even the face, but the symptoms are usually most severe in the legs, which are often the initial site of discomfort ⁴.

Patients frequently experience trouble falling asleep

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right after getting into bed, as well as difficulties staying asleep. These sleep onset and maintenance issues often lead them to get out of bed and walk or pace to alleviate their symptoms. As a result, they may remain awake and restless until midnight. These disruptions in sleep can result in daytime drowsiness and fatigue⁵.

Restless leg syndrome (RLS) prevalence is notably high during pregnancy⁶. Recent epidemiological studies in various countries have found that the prevalence of Restless Leg Syndrome (RLS) in the general population varies between 3.9% and 15%⁷. Furthermore, it's worth noting that Restless leg syndrome (RLS) is more common in females than in males⁷. A significant number of adolescent girls undergo various forms of stress during their menstrual cycles, and this stress tends to increase with age. Dysmenorrhea, in particular, is a widespread issue among young females. Approximately 10 percent of females experience job disruption due to painful periods, causing them to miss work for about 1 to 3 days⁸.

Menstrual distress encompasses a range of symptoms that affect young women at different stages of their menstrual cycle, including before, during, and after. These symptoms may include sleep disturbances, mental stress, reduced focus, water retention, pain, fatigue, lower back discomfort, breast tenderness, and feelings of isolation, abdominal pain, vomiting, palpitations, and overall fatigue⁹. Menstrual pain can have a detrimental effect on women's sleep quality, as indicated by Yang et al. in 2014¹⁰. Those experiencing menstrual pain are more likely to suffer from daytime sleepiness¹¹.

Daytime sleepiness is recognized as a significant global health concern, with a prevalence of approximately 29.2% among children and adolescents, as reported by Liu et al. in 2019¹². Students who experience daytime sleepiness tend to exhibit higher levels of anxiety and physical health issues compared to those without such sleepiness¹¹. Furthermore, there is a connection between daytime sleepiness and the severity of menstrual pain, as Woosley and Lichstein noted in 2014¹¹. Notably, daytime sleepiness has the potential to contribute to menstrual disorders, which, in turn, can exacerbate menstrual pain, as discussed by Baker et al. in 1999¹¹. Therefore, there is a reciprocal influence between daytime sleepiness and menstrual pain. A study was published in 2019 proposed that Restless leg syndrome (RLS) symptoms aggravate during

menstrual period in 30% of premenopausal RLS patients¹³. Another study suggests that around 23% of patients saw their RLS symptoms worsen during pregnancy, 29% of non-menopausal patients experienced increased RLS severity during menses, and 69% reported symptom aggravation after menopause¹⁴.

Our study Investigate the potential links between menstruations related distress and excessive daytime sleepiness to understand the broader health implications for adolescents' girls diagnosed with restless leg syndrome (RLS). The study addresses the gap in current research by focusing on the intermediate students diagnosed with restless leg syndrome (RLS). The findings could also have implications for educational institutions and health policies tailored to address the unique challenges faced by adolescent students with restless leg syndrome symptoms in the context of sleep disorders and hormonal influences.

METHODOLOGY

A cross sectional study design was used in this research. The study utilized a convenience sampling technique, the study duration was six months. The study settings for this research were educational institutions (intermediate-level schools or colleges) in Karachi, where female students with restless leg syndrome (RLS) symptoms aged 16 to 20 were recruited as participants. Open Epi calculator was used to calculate the sample size. Eight percent margin of error and 95 % Confidence interval for the calculated sample size of (n) 125 for this study¹⁴. The calculated sample size was 117 but for the accuracy of results 125 participants were selected.

Individuals willing to participate in the study aged between 16 to 20 years with diagnosed or self-reported history of restless leg syndrome, should be enrolled in intermediate level schools or colleges in Karachi were included in the study. Individuals younger than 16 years or older than 20 years, students who don't fall within the intermediate education level or those with sever medical or psychological condition that may interfere with study participation or confound the study results were excluded from the study also with secondary causes of restless leg syndrome like pregnancy were excluded. We utilized a questionnaire incorporating standardized tools, including the diagnostic criteria established by the International Restless Leg Syndrome Study Group (IRLSSG) for identifying individuals with restless leg syndrome¹⁵, the Epworth Sleepiness

Scale (ESS) for evaluating daytime sleepiness¹⁶, and the Shortened Menstrual Distress Questionnaire (SMDQ)¹⁷ for capturing data on menstrual distress and symptoms. It stands as the most commonly used self-reported tool for assessing menstrual cycle symptomatology, pinpointing the intensity and type of symptoms women experience during each phase of their menstrual cycle i.e., 4 days before menstruation, during menstruation and rest of the cycle. We also collected demographic details such as name, age, class, and address, ensuring precision in controlled quiet settings. The data, recorded on standardized forms, was treated with strict confidentiality and anonymity, adhering to ethical guidelines and prioritizing participants' rights and well-being throughout the study. The ethical approval for the study was taken from the Research

Ethical Committee (REC) of JPMC, Karachi.

Statistical Analysis

Data were stored and analyzed using IBM- SPSS version 23.0; Mean with standard deviation were reported on baseline characteristics included age, age of period when started, duration of period, scores on Epworth sleepiness scale, SMD at 4 days before period, during period and at rest of cycle. Counts with percentages were reported on international restless leg syndrome study group diagnostic criteria for restless leg syndrome and questions on shortened menstrual distress. Fisher's exact test was used to check the association between menstruation and excessive daytime sleepiness in subject with RLS. Pearson Correlation analysis was

Table 1. Outcomes on Epworth sleepiness scale and shortened menstrual distress questionnaire

Variables	Construct	n	%
ESS	Unlikely for abnormally sleepy	66	52.8
	Average amount of daytime sleepiness	14	11.2
	Excessively sleepy	37	29.6
	Excessively sleepy and should consider seeking medical attention	8	6.4
SMD 4 days before	No experience of symptoms	9	7.2
	Mild change	74	59.2
	Moderate change	35	28.0
	Considerable change	7	5.6
SMD during period	No experience of symptoms	0	0.0
	Mild change	44	35.2
	Moderate change	56	44.8
	Considerable change	24	19.2
	Severe change	1	0.8
SMD rest of cycle	No experience of symptoms	7	5.6
	Mild change	77	61.6
	Moderate change	37	29.6
	Considerable change	4	3.2

performed to study the relationship of ESS and SMDQ scores.

RESULTS

There were one hundred and twenty-five intermediate females, mean age was 17.19 (SD=±1.11), mean age when period started was 13.10 (SD=±1.45), mean weeks from the start of one period to the start of the next one was 3.88 (SD=±2.24) weeks and mean days from the start of one period to the start of next one was 26.12 (SD=±6.38) days, mean duration of period was 5.71 (SD=±1.45) days. Using international restless leg syndrome study group diagnostic criteria for restless leg syndrome all samples were found with RLS, among them 24% were heard of pre-menstrual tension or pre-menstrual syndrome. 91.2% were live with their patents, 4.8% were live own, 1.6% were live with others in residential home and 2.4% were live with others.

Table 1 reports the outcomes on Epworth sleepiness scale (ESS) and shortened menstrual distress questionnaire (SMDQ) tools, using ESS 47.2% were found with abnormally sleepy among them 11.2% were found with average amount of daytime sleepiness, 29.6% were excessively sleepy and 6.4% were found excessively sleepy and should consider seeking medical attention. Using SMD at 4 days before 59.2% were found with mild change, 28.0% were found with moderate change and 5.6% were found with considerable change, SMD outcomes during periods showed 35.2% were found with mild

changes, 44.8% were found with moderate changes ,19.2% were found with considerable changes and 0.8% were found with sever change, whereas SMD outcomes at rest of cycle showed 61.6% were found with mild change, 29.6% were found with moderate change and 3.2% were found with considerable change.

Table 2 reports the association between menstruation and excessive daytime sleepiness in subjects with Restless leg syndrome (RLS), among samples who unlikely for abnormal sleepy 68.2% were found with mild change using SMD 4-days before, 51.5% were found with mild change using SMD during period and 65.2% were found with mild change using SMD at rest of cycle, samples with average amount of daytime sleepiness 64.3% were found with mild change using SMD 4- days before, 57.1% were found with moderate change using SMD during period and 50% were found with mild change using SMD at rest of cycle, among samples with excessively sleepy using ESS 43.2% were found with mild change using SMD 4-days before, 54.1% were found with mild change using SMD during period and 56.8% were found with mild change using SMD at rest of cycle, whereas among samples with excessively sleepy and should consider seeking medical attention 50% were found with mild change using SMD 4-days before, 37.5% were found with mild change using SMD during period and 75% were found with mild change using SMD at rest of cycle, Fishers exact test did give significant association of ESS with SMD before 4 days , during periods and at rest of cycle (p<0.01).V

Table 2. Association between Menstruation and Excessive Daytime Sleepiness in Subjects with Restless leg syndrome (RLS)

SMD outcomes	ESS								p-value	
	Unlikely for abnormally sleepy	Average amount of daytime sleepiness	Excessively sleepy	Excessively sleepy and should consider seeking medicalattention						
	n	%	n	%	n	%	n	%		
SMD 4 days before	No experience of symptoms	8	12.1	0	0.0	1	2.7	0	0.0	<0.001*
	Mild change	45	68.2	9	64.3	16	43.2	4	50.0	
	Moderate change	11	16.7	5	35.7	15	40.5	4	50.0	

SMD outcomes	unlikely for abnormally sleepy	ESS Average amount of daytime sleepiness	Excessively sleepy	Excessively sleepy and should consider seeking medicalattention							p-value
	Considerable change	2	3.0	0	0.0	5	13.5	0	0.0		
SMD during periods	No experience of symptoms	0	0.0	0	0.0	0	0.0	0	0.0	<0.001*	
	Mild change	34	51.5	2	14.3	5	13.5	3	37.5		
	Moderate change	25	37.9	8	57.1	20	54.1	3	37.5		
	Considerable change	7	10.6	4	28.6	11	29.7	2	25.0		
	Severe change	0	0.0	0	0.0	1	2.7	0	0.0		
SMD rest of cycle	No experience of symptoms	7	10.6	0	0.0	0	0.0	0	0.0	0.01*	
	Mild change	43	65.2	7	50.0	21	56.8	6	75.0		
	Moderate change	13	19.7	7	50.0	15	40.5	2	25.0		
	Considerable change	3	4.5	0	0.0	1	2.7	0	0.0		

*p<0.05 was considered statistically significant using Fishers Exact Test

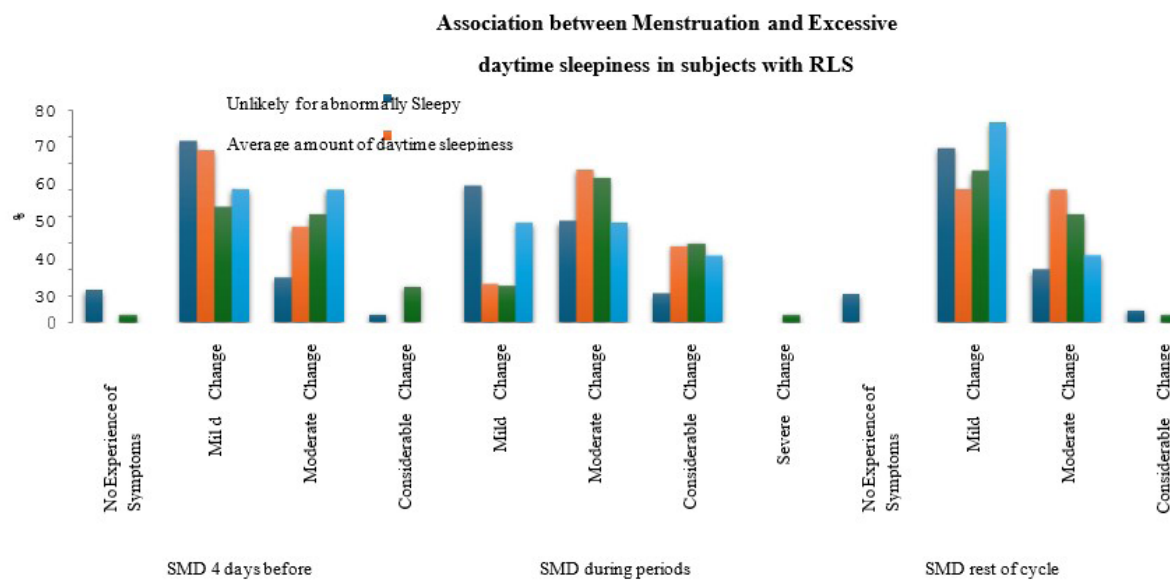


Figure 1. Association between menstruation related distress and excessive daytime sleepiness in subjects with restless leg syndrome

Table-3 showed mean Epworth sleepiness scale (ESS) score was 8.01 (SD=±4.90), mean Shortened menstrual distress (SMD) scores 4-days before were 27.82 (SD=±23.84), mean SMD scores during period were 49.94 (SD=±26.02) and mean SMD scores at rest of cycle were 27.39 (SD=±22.29).

Table 3. Descriptive on Epworth sleepiness scale (ESS) and shortened menstrual questionnaire (SMDQ)

Scales	Mean	SD
Epworth sleepiness scale	8.01	4.90
SMD scores 4 days before	27.82	23.84
SMD scores during periods	49.94	26.02
SMD scores rest of cycle	27.39	22.29

Table 4 reports the correlation analysis of ESS and SMD scores of RLS intermediate female samples, ESS gives 36.4% positive correlation with SMD 4 days before, 38.6% positive correlation with SMD during period and 22.3% positive correlation with SMD at rest of cycle. Correlation of SMD 4 days before with SMD during period was 73.5% and with SMD at rest of cycle was 70.2% whereas correlation of SMD scores during period and at rest of cycle was 61.8%. All these correlations were found statistically significant with $p < 0.05$.

Table 4. Correlation analysis of ESS and SMD scores

Parameters	Epworth Sleepiness Scale (ESS)	SMD scores 4 days before	SMD scores during periods	SMD scores rest of cycle
ESS	R-value: 1 p-value: <0.01*	R-value: 0.364 p-value: <0.01*	R-value: 0.386 p-value: <0.01*	R-value: 0.223 p-value: 0.012*
SMD scores 4 days before	R-value: 0.364 p-value: <0.01*	1 p-value: <0.01*	R-value: 0.735 p-value: <0.01*	R-value: 0.702 p-value: <0.01*

SMD scores during periods	R-value: 0.386 p-value: <0.01*	R-value: 0.735 p-value: <0.01*	1 p-value: <0.01*	R-value: 0.618 p-value: <0.01*
SMD scores rest of cycle	R-value: 0.223 p-value: 0.012*	R-value: 0.702 p-value: <0.01*	R-value: 0.618 p-value: <0.01*	1 p-value: <0.01*

DISCUSSION

The aim of this study was to determine the association between menstruation and excessive daytime sleepiness in subjects with restless leg syndrome (RLS) among intermediate students in Karachi aged between 16 to 20 years. A study was conducted by Rees *et al.* (1995) shows that menarche typically occurs between the ages of 10 and 16 in girls from developed countries, with a historical decline observed in industrialized nations. While the trend of earlier menarche has halted and may even be reversing, research also suggests that delayed menarche is linked to a reduced risk of breast cancer and coronary heart disease, along with lower rates of teen pregnancy. Conversely, a later onset of menarche is positively correlated with an elevated risk of Alzheimer's disease²⁰. Our study indicates a mean age of menarche at 13 years, aligning with the current average.

Damhare *et al.* (2012) research findings highlighted a lack of information regarding menstrual issues among adolescent girls²¹. In alignment with our study results, only 24% of female students possessed knowledge about menstrual issues or premenstrual syndrome. An atypical case report by Suau *et al.* (2016) involves an 18-year-old female experiencing recurrent episodes of hypersomnia temporally connected to her menstrual cycle, termed as menstrual-related hypersomnia (MRH), a rare condition. The patient's symptoms resolve with oral contraceptive treatment, indicating a hormonal influence on the menstrual cycle that often impacts behaviors like sleep patterns²². Likewise, another study conducted by Dong *et al.* (2023) revealed an interplay between menstrual pain and daytime

sleepiness²³. In accordance with my study, there is a notable correlation between menstruation and excessive daytime sleepiness in females with restless leg syndrome.

Jeon *et al.* (2023) research has shown that women experiencing menstrual disturbances often exhibit disrupted sleep, characterized by poor sleep quality, difficulty initiating or maintaining sleep, or short sleep duration²⁴. Similarly, a study was conducted by Wang *et al.* (2019) shows that menstrual irregularities and menstrual pain are linked to an increased risk of daytime sleepiness. The prevalence rates for excessive daytime sleepiness (EDS) were 20.5% mild, 16.7% moderate, and 5.5% severe²⁵. In our study, it was observed that 47.2% of female students with restless leg syndrome (RLS) experienced abnormal sleepiness during their menstrual cycle. Among them, 11.2% had an average level of daytime sleepiness, 29.6% were excessively sleepy, and 6.4% were exceptionally sleepy, indicating the need for medical attention.

A cross-sectional study in Pakistan conducted by Hassan *et al.* (2021) involving school and college students revealed that 77.9% of female students in the selected population experienced moderate menstrual distress, with a mean age of 16 years²⁶. In our study, it was observed that among females with restless leg syndrome (RLS), 59.2% reported mild changes four days before their period, 44.8% experienced moderate changes, and 0.8% had severe changes during menstruation. Additionally, 61.2% reported mild changes during the rest of the menstrual cycle.

The study's exclusive focus on intermediate students in Karachi might limit the generalizability of its findings to other age groups, educational levels, or geographic locations. The study might not account for all relevant variables that could contribute to excessive daytime sleepiness, potentially introducing confounding variables that could impact the study's internal validity. Relying on self-reported data for variables such as restless leg syndrome, menstruation, and sleepiness may introduce recall bias and compromise the accuracy of the information. The calculated sample size is small and is not representative of the broader population, it could limit the study's statistical power and compromise the ability to draw meaningful conclusions.

We recommend similar studies to be conducted in other cities, school and colleges to explore association

between menstruation and excessive daytime sleepiness on larger scale. It was cross-sectional survey so it was not possible to conclude a causative relationship between menstruation and excessive daytime sleepiness. The effect of other confounding factors such as sleep duration, stress level, physical activity, nutritional habits, use of electronic devices, medication use was not considered investigated data depend on questionnaire only and no medical examination and no history was taken. We recommend that future studies should consider longitudinal approach.

CONCLUSION

Menstruation-related distress appears to have a greater impact on sleep quality during the menstruation compared to other phases of the cycle. Consequently, sleep is disrupted during menstruation and cause excessive daytime sleepiness among intermediate students in Karachi who have restless leg syndrome, suggesting a significant link between the menstruation and excessive daytime sleepiness in subjects with restless leg syndrome among intermediate students in Karachi.

Ethical Statement: Research proposal has been reviewed by Ethical Review Committee, JPMC which concluded that your research will not give any harmful impacts on humanity and is in line with our academic objectives. I have confidence in your ability to carry out the research with responsibility and ethically.

Conflicts of Interest: The author declared no conflict of interest.

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Authors' Contribution: ZQ: Conceptualization, methodology and manuscript writing, MA: Supervision, Statistical analysis and interpretation, SK & GA: Data collection and literature review, MF: Manuscript review and editing.

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