Article published online: 2021-08-12

ORIGINAL ARTICLE

The prevalence of restless leg syndrome among pregnant Saudi women

Mohmd Khan, Noha Mobeireek[1], Yassar Al-Jahdali[1], Nujood Al-Dubyan[1], Anwar Ahmed[2], Majed Al-Gamedi, Abdullah Al-Harbi, Hamdan Al-Jahdali

Department of Medicine, Pulmonary Division, Sleep Disorders Center, King Abdulaziz Medical City, King Saud University for Health Sciences, [1]College of Medicine, King Saud University for Health Sciences, [2]Department of Epidemiology and Biostatistics, King Abdullah International Medical Research Center, College of Public Health and Health Informatics, King Saud University for Health Sciences, Riyadh, Saudi Arabia

Access this article online

Website: www.avicennajmed.com

DOI: 10.4103/ajm.AJM_123_17

Quick Response Code:

ABSTRACT

Objectives: Restless legs syndrome (RLS) is common among pregnant women, but it has not been documented in pregnant Saudi Arabian women. The main purpose of this study was to estimate the extent of the prevalence of RLS and identify both the associated factors and the associated risk factors among pregnant Saudi women. **Methods:** A cross-sectional study was conducted among pregnant women visiting obstetric clinics at King Abdulaziz Medical City in Riyadh (KAMC-Riyadh) over the period from June 1 to November 1, 2014. We interviewed the participants and collected demographic data, number of pregnancies, duration of pregnancy, comorbidities, and symptoms of RLS. The diagnosis of RLS is based on the four criteria designated by the International RLS Study Group. **Results:** The total number of participants enrolled was 517, and the mean age was 30.11 ± 5.42 years. The prevalence of RLS was 21.3% (110/517) (95% confidence interval [CI]: 17.83%-25.06%). RLS symptoms were more common among women in the third trimester (24.1%) compared to the second trimester (14.3%) and first trimester (13.6%), $P = 0.043$. The stepwise multivariate logistic model identified insomnia (odds ratio [OR]: 3.6, 95% CI: 2.167–6.017, $P = 0.001$), and poor sleep quality (OR: 4.9, 95% CI: 1.473-16.454, $P = 0.010$) were associated with RLS. **Conclusion:** RLS occurs in two of ten pregnant women visiting obstetric clinics at KAMC-Riyadh and is strongly associated with insomnia and poor sleep quality. Studies are needed to explore the causality of these associations.

Key words: Body mass index, Epworth Sleepiness Scale, excessive daytime sleepiness, Pitts, restless legs syndrome, the International Restless Legs Syndrome Study Group

INTRODUCTION

Restless leg syndrome (RLS), also known as Willis-Ekbom Disease, is a sensorimotor sleep disorder that causes discomfort or a "creepy-crawly" sensation in the legs during rest and is relieved by activity. The clinical course of RLS is variable from mild to severe, but the symptoms tend to fluctuate over time. The disorder could be either primary or secondary. Primary RLS is idiopathic, and 42% of patients have a first-degree relative with this disorder.[1,2] Secondary RLS is accompanied by pregnancy or other medical conditions such as renal insufficiency, iron deficiency anemia, Parkinson's disease, and diabetic neuropathy.[3]

The pathophysiology of the syndrome is thought to be related to iron deficiency in the brain that affects the

Address for correspondence: Prof. Hamdan Al-Jahdali, Department of Medicine, Pulmonary Division, Sleep Disorders Center, King Abdulaziz Medical City, King Saud University for Health Sciences, Riyadh, Saudi Arabia.
E-mail: Jahdalih@gmail.com

Cite this article as: Khan M, Mobeireek N, Al-Jahdali Y, Al-Dubyan N, Ahmed A, Al-Gamedi M, *et al*. The prevalence of restless leg syndrome among pregnant Saudi women. Avicenna J Med 2018;8:18-23.

dopaminergic pathways.[4,5] There are also assumptions that genetics could play a role in the etiology.[2] The disease, which could be autosomal, recessive, or dominant, affects the chromosomes 12q, 14q, 9p, 20p, 4q, and 17p2.[2,6] The availability of serotonin transporters in the brainstem could also contribute to the disease; the less serotonin transporters there are, the more serotonin transmission there is in the brain, and this exacerbates RLS symptoms.[7]

The diagnosis of RLS depends on four well-defined criteria: (i) the urge to move the legs whether it was with or without the abnormal sensation, (ii) worsening of symptoms with rest, (iii) improvement with activity, and (iv) worsening of symptoms at night.[8]

The prevalence of restless leg syndrome is variable, and it ranges from 1% to 17%.[9-19] A local study among Saudi participants suggests that the prevalence of RLS in adult Saudis attending healthcare is 5.2%, while it is 8.4% among middle-age school employees and 14.7% among the general population.[18,20,21]

The prevalence of RLS in pregnancy is reported to range from 11 to 30%.[10,19,22-30] RLS is most common in the third trimester of pregnancy, and it usually improves after delivery.[28,31] However, this condition has not been described in the pregnant Saudi population. This will be the first study of its kind to determine the prevalence of RLS in the pregnant population and the risk factors for RLS among pregnant Saudi women.

METHODS

A cross-sectional study was conducted to assess the presence of restless leg syndrome in consecutive pregnant women who attended obstetric clinics at King Abdul-Aziz Medical City in Riyadh (KAMC-Riyadh) between June and November 2014. This study was reviewed and approved by the Institutional Review Board. The coinvestigator conducted the study by conducting personal interviews with the participants, using prestructured questionnaires. These questionnaires include demographic information, characteristics such as age, gender, educational level, duration of pregnancy, number of pregnancies, and parities. Furthermore, we asked about associated comorbidities. The diagnosis of RLS was based on the four criteria designated by the International RLS Study Group (IRLSSG).[8]

These four diagnostic criteria are: (i) A desire to move the extremities usually associated with some definable discomfort, (ii) Motor restlessness, (iii) Worsening of symptoms while at rest with at least temporary relief by activity, and (iv) Worsening of symptoms later in the day or at night. A diagnosis of RLS is confirmed only in the presence of all four criteria. We also assessed RLS severity using the IRLSSG.[32] The RLS severity was defined by 10 items with each rated on a scale of 5 points: None to very severe. We also assessed daytime sleepiness using the Epworth Sleepiness Scale (ESS). An ESS score of more than 10 would indicate excessive daytime sleepiness (EDS).[33,34] Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI).[35] These questionnaires have been validated and used in previous studies.[18,20,21,34,36] Exclusion criteria were pregnant women with a history of neuropathy and a prepregnancy diagnosis of RLS or other sleep disorders. The sample size was calculated according to a precision of 2%, prevalence of 5%[18] and 95% confidence interval (CI), while the minimum required sample size was 457 subjects. A total of 517 of 600 pregnant women gave informed consent and enrolled in the analysis, with a response rate of 86%.

Statistical analysis

The data were presented as the mean and standard deviation or number and percent, as appropriate. To assess the possible influence of demographic and other variables on the prevalence of RLS, we used either the unpaired *t*-test or the Mann–Whitney U-test for nonparametric data, as appropriate. A stepwise multivariate logistic regression analysis was used to assess the risk of RLS while controlling for other characteristics. The variables associated at $P < 0.05$ level in bivariate analysis were included in the final multivariate model.

RESULTS

The sample mean age was 30.11 ± 5.42 years (age range: 17–47 years) with 58% of participants younger than 30 years of age and 37% in the 31–39 year age group. The mean ESS was 7.8 ± 4.8 (score range: 0–24). The mean PSQI was 42.4 ± 10.4 (score range: 4–72).

Education-wise, 83% of the patients had high school or higher education. The majority of the participants were in the third trimester (72%) of pregnancy. Regular and daily tea and coffee intake was reported as 48% and 75%, respectively. The most common comorbidities reported were anemia 19%, asthma 11%, diabetes 7%, and hypertension 5%, with other demographic characteristics shown in Table 1.

The prevalence of RLS was 21.3% (95% CI: 17.83%–25.06%). As shown in Figure 1, RLS symptoms were more common among women in the third trimester (24.1%) compared to the second (14.3%) or first trimester (13.6%), $P = 0.012$. When we compared the risk factors and clinical characteristics of participants with RLS to those without, there was no

Table 1: Sample characteristics and restless leg syndrome among pregnant Saudi women

Characteristics	Overall	No	Yes	*P*
Demographic (mean±SD)				
Age (17-47 years)	30.1±5.4	30.1±5.4	30.1±5.6	0.947
Education level university or more, *n* (%)				
No	236 (46.9)	187 (79.2)	49 (20.8)	0.573
Yes	267 (53.1)	206 (77.2)	61 (22.8)	
Co-morbidities and potential risk factors, *n* (%)				
Coffee intake				
No	128 (24.8)	104 (81.3)	24 (18.8)	0.421
Yes	389 (75.2)	303 (77.9)	86 (22.1)	
Tea intake				
No	268 (51.8)	217 (81)	51 (19)	0.195
Yes	249 (48.2)	190 (76.3)	59 (23.7)	
Third trimester				
No	143 (27.7)	123 (86)	20 (14)	0.012*
Yes	374 (72.3)	284 (75.9)	90 (24.1)	
Obese				
No	238 (47.3)	185 (77.7)	53 (22.3)	0.757
Yes	265 (52.7)	209 (78.9)	56 (21.1)	
Abortion				
No	234 (55.2)	185 (79.1)	49 (20.9)	0.917
Yes	190 (44.8)	151 (79.5)	39 (20.5)	
DM				
No	482 (93.2)	380 (78.8)	102 (21.2)	0.813
Yes	35 (6.8)	27 (77.1)	8 (22.9)	
HTN				
No	493 (95.4)	391 (79.3)	102 (20.7)	0.139
Yes	24 (4.6)	16 (66.7)	8 (33.3)	
Depression				
No	502 (97.1)	397 (79.1)	105 (20.9)	0.332
Yes	15 (2.9)	10 (66.7)	5 (33.3)	
Bronchial asthma				
No	462 (89.4)	369 (79.9)	93 (20.1)	0.065
Yes	55 (10.6)	38 (69.1)	17 (30.9)	
Gravida (1-18) (mean±SD)	3.8±2.6	3.8±2.5	4±2.9	0.441
Parity (0-16) (mean±SD)	3±2	2.9±2	3.2±2.3	0.26
Symptoms of sleep disorders, *n* (%)				
EDS				
No	351 (67.9)	285 (81.2)	66 (18.8)	0.046*
Yes	166 (32.1)	122 (73.5)	44 (26.5)	
Insomnia				
No	371 (71.8)	317 (85.4)	54 (14.6)	0.001*
Yes	146 (28.2)	90 (61.6)	56 (38.4)	
PSQI				
Good sleep	95 (18.4)	86 (90.5)	9 (9.5)	0.002*
Poor sleep	422 (81.6)	321 (76.1)	101 (23.9)	
Berlin				
Low risk	325 (62.9)	266 (81.8)	59 (18.2)	0.024*
High risk	192 (37.1)	141 (73.4)	51 (26.6)	

*Significant at α=0.05. DM: Diabetes mellitus, HTN: Hypertension, EDS: Excessive daytime sleepiness, PSQI: Pittsburgh Sleep Quality Index, SD: Standard deviation

significant difference regarding age, number of pregnancies, or educational level. There was no significant association between RLS and gravid $P = 0.441$ or parities $P = 0.26$. We also did not find any association between drinking habit of coffee or tea and RLS $P = 0.421$ and 0.195, respectively. There was also no association between RLS and other medical problems; obesity, diabetes, hypertension, depression or age, $P = 075$, 0.813, 0.139, 0.332, 0.94, respectively.

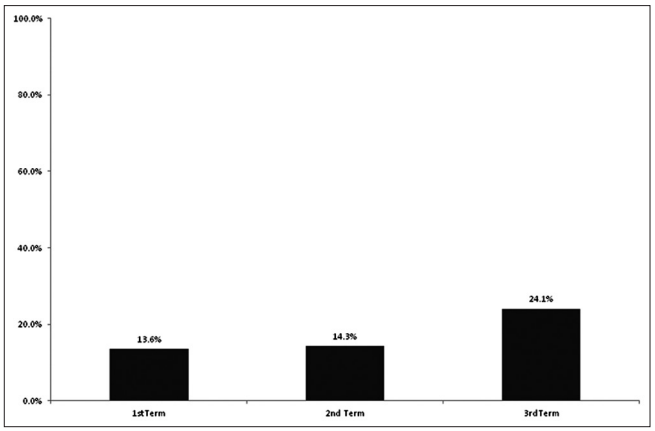

Figure 1: Restless legs syndrome in relation to pregnancy term

Poor sleep quality as measured by PSQI and EDS as measured by ESS (>10) were significantly high among pregnant women with RLS, 23.9% ($P = 0.002$) and 26.5% ($P = 0.046$) [Figures 2 and 3].

The stepwise multivariate logistic model [Table 2] identified insomnia (odds ratio [OR]: 3.6, 95% CI: 2.167–6.017, $P = 0.001$), and poor sleep quality (OR: 4.9, 95% CI: 1.473–16.454, $P = 0.010$) were associated with RLS. Table 3 shows that RLS severity was associated with bronchial asthma (OR: 4.3, 95% CI: 1.130–16.684, $P = 0.032$).

DISCUSSION

The reported prevalence of RLS in pregnancy varies and ranges from 1% to 30%.[10,19,22-25,28,29,31] The variation in reported prevalence in the literature is due to various factors including study populations, ethnicity, and methodology used to collect information, diagnostic criteria used for the definition of RLS, and the gestational age at study time.

Significantly, the number of criteria used for the diagnosis of RLS also differed among studies.[10,19,22-30] The prevalence of RLS in our study was found to be 21.3% which is similar in range to other published studies. A study from Turkey reported a prevalence of 10%,[24] while a study from Pakistan[19] reported a prevalence of 30%. In this study, RLS was 13.6% in the first trimester, 14.3% in the second, and 24.1% in the third, which is similar to many other studies.[23,28,37,38]

A potential mechanism for the higher prevalence of RLS in pregnancy may be threefold to fourfold increase in iron requirements in pregnancy.[10,27] As the mother is the sole

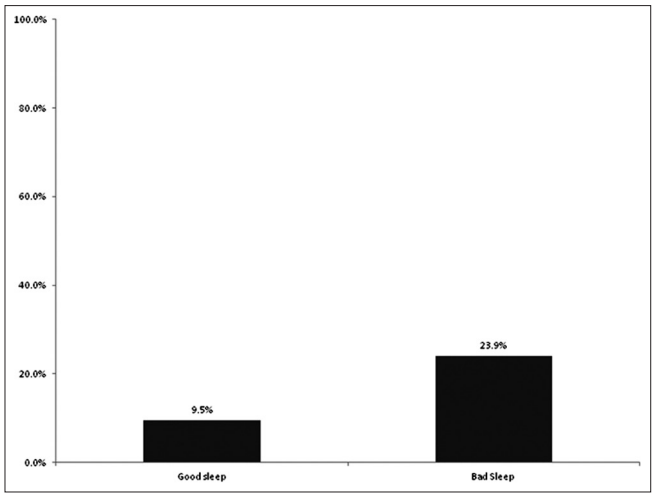

Figure 2: Restless legs syndrome in relation to sleep quality

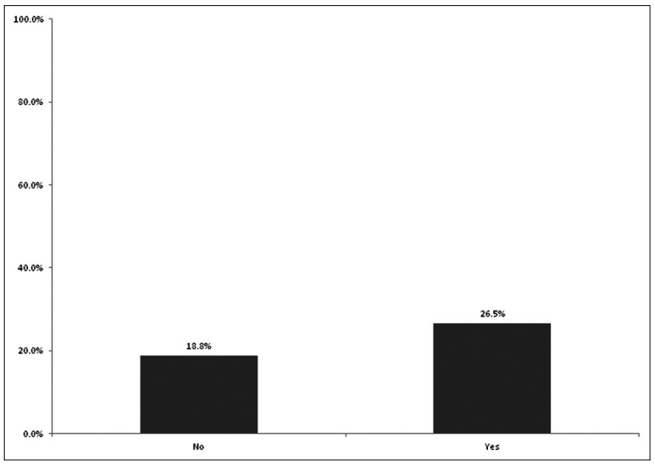

Figure 3: Restless legs syndrome in relation to risk for excessive daytime sleepiness

Table 2: Factors associated with restless leg syndrome among pregnant Saudi women (*n*=517)

	Reference	Univariate analysis			Multivariate analysis		
		P	OR	95% CI for OR	*P*	OR	95% CI for OR
Age		0.947	1.0	0.961-1.038			
Gravida		0.441	1.0	0.948-1.131			
Parity		0.260	1.1	0.954-1.189			
Third trimester	No	0.012*	1.9	1.149-3.307			
Obese	No	0.757	0.9	0.612-1.43			
University education or more	No	0.573	1.1	0.739-1.728			
Coffee intake	No	0.421	1.2	0.743-2.037			
Tea intake	No	0.195	1.3	0.866-2.016			
Abortion	No	0.917	1.0	0.608-1.564			
DM	No	0.813	1.1	0.487-2.503			
HTN	No	0.139	1.9	0.798-4.603			
Depression	No	0.332	1.9	0.633-5.65			
Bronchial asthma	No	0.065	1.8	0.959-3.285			
EDS	No	0.046*	1.6	1.007-2.41			
Insomnia	No	0.001*	3.7	2.35-5.678	0.001*	3.6	2.167-6.017
Poor sleep	No	0.002*	3.0	1.46-6.19			
Berlin	No	0.024*	1.6	1.064-2.499	0.010*	4.9	1.473-16.454

*Significant at α=0.05. DM: Diabetes mellitus, HTN: Hypertension, EDS: Excessive daytime sleepiness, OR: Odds ratio, CI: Confidence interval

Table 3: Factors associated with severity of restless leg syndrome among pregnant Saudi women with restless leg syndrome (*n*=110)

	Reference	Univariate analysis			Multivariate analysis		
		P	OR	95% CI for OR	*P*	OR	95% CI for OR
Age		0.864	1.0	0.929-1.064			
Gravida		0.880	1.0	0.857-1.141			
Parity		0.966	1.0	0.836-1.206			
Third trimester	No	0.347	1.6	0.598-4.303			
Obese	No	0.337	1.5	0.68-3.094			
University	No	0.780	1.1	0.523-2.369			
Coffee intake	No	0.776	0.9	0.348-2.198			
Tea intake	No	0.930	1.0	0.455-2.054			
Abortion	No	0.942	1.0	0.444-2.398			
DM	No	0.055	8.0	0.954-67.78			
HTN	No	0.451	1.8	0.401-7.798			
Depression	No	0.197	4.3	0.467-39.97			
Bronchial asthma	No	0.022*	4.0	1.225-13.34	0.032*	4.3	1.130-16.684
EDS	No	0.506	1.3	0.601-2.804			
Insomnia	No	0.152	1.7	0.816-3.716			
Poor sleep	No	0.107	3.8	0.751-19.15			
Berlin	No	0.392	1.4	0.653-2.963			

*Significant at α=0.05. DM: Diabetes mellitus, HTN: Hypertension, EDS: Excessive daytime sleepiness, OR: Odds ratio, CI: Confidence interval

source of nutrients to the fetus, the placenta upregulates its iron transfer systems to maintain an adequate supply for the fetus, which often occurs at the expense of the mother's stores. This upregulation is more pronounced under conditions of maternal iron deficiency. Iron deficiency in the brain has been demonstrated in MRI studies with RLS patients, where reduced cerebrospinal fluid concentrations of ferritin and transferrin have also been found.[4,39] Multiple gravid and parties associated with risk for anemia and therefore risk of developing RLS.[40] In our sample, 82.4% of the women had multiple pregnancies, but we did not find any association between number of gravid or parities and RLS. This could be because all participants were followed at antenatal care from early pregnancy and any commodities include anemia identified and treated early. However, the diagnosis of anemia in our study was not confirmed by laboratory tests and only based on history taken from the patients and iron supplement information. Therefore, we do not include anemia as a risk factor for RLS in our participants. In this study, age has no effect on the prevalence of RLS which similar to our previous study in general population where age has no effect on the prevalence of RLS.[21] On concurrence with our previous study in general population in this study, we did not find any association between coffee, tea intake, diabetes, hypertension, obesity, and asthma.[21]

There are other impacts of RLS on quality of sleep in our study. Some women with RLS reported higher sleep latency, EDS, lower total sleep time, frequent insomnia, and poor sleep quality as measured by PSQI, as compared with unaffected pregnant subjects.[27,31,37] In our study, we found that 23.9% of pregnant women with RLS had poor quality of sleep. This is similar to other studies but is much lower than the study conducted by Chen *et al*. among the Taiwan population.[31] Sleep disruption or deprivation during pregnancy is considered a significant risk factor for the occurrence of mood disturbances and recurrence of depression.[41-43] However, we did not assess for depression in this study, as this was beyond the scope of our study.

The strength of our current study is the large number of patients, an interview-based data collection according to international RLS standards, and being the first study of its kind in the pregnant Saudi population. We also recognized the potential weakness of being a single-center study as well as the lack of a control group (e.g., nonpregnant women population). Early detection and adequate treatment of severe RLS is very important to prevent maternal discomfort, poor sleep, and possible health risks. The questionnaire method is a simple, reliable diagnostic tool for diagnosis of RLS.

CONCLUSION

RLS occurs in two of ten pregnant women visiting obstetric clinics at KAMC-Riyadh and is associated with insomnia and poor sleep quality. Future studies are needed to explore the causality of these associations.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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