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# Prevalence of restless legs syndrome in pregnant women in Oman and its effect on pregnancy and neonatal outcomes

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## Abstract:

**BACKGROUND:** Restless legs syndrome (RLS) is a common sensorimotor disorder during pregnancy. The purpose of this study was to assess the prevalence of RLS and explore the associated risk factors and outcomes in Omani women in the first and third trimester and at 2-week postpartum.

**MATERIALS AND METHODS:** This cross-sectional study included 305 pregnant women visiting four health centers in Muscat between May 2018 and October 2020. A structured questionnaire was used and data were collected through review of electronic records and face-to-face interviews. The International RLS Study Group criteria were used to diagnose RLS. Participants were interviewed during their first trimester, their third trimester, and at their 2-week postpartum visit. Results were presented as means and standard deviations or percentages, as appropriate. To assess the association between RLS and various variables, unpaired t-test or McNemar's test were used, as appropriate.

**RESULTS:** The mean age at baseline was  $29.8 \pm 5.28$  years. The prevalence of RLS was significantly higher in the third trimester (41.0%) than in the first trimester (15.7%) and postpartum period (15.1%) ( $P < 0.001$ ), although there was no significant difference in severity. Family history and personal history of RLS were the only independent correlates of RLS ( $P < 0.001$  and 0.002, respectively). No associations were noted with pregnancy and neonatal outcomes or other comorbidities, including anemia. However, there was a significant relationship between the development of RLS and weight gain during pregnancy ( $P = 0.023$ ).

**CONCLUSION:** One in six pregnant Omani women may be at risk of RLS during the first trimester, while one in 2–3 may be at risk in the third trimester, particularly those with a personal or family history of RLS and those who gain  $>12$  kg during pregnancy.

## Keywords:

Oman, pregnancy, restless legs syndrome, risk factors, sleep disorders

## Introduction

Restless legs syndrome (RLS) or Willis-Ekbom disease is a neurological sensory-motor disorder characterized by an unpleasant crawling or creeping sensation in the legs or an irresistible urge to make leg

movements. Moreover, as these symptoms typically occur at night, it can result in sleep disturbances.<sup>[1]</sup> The syndrome can be classified into primary and secondary types based on the presence or absence of associated conditions. Idiopathic or primary RLS is most common, with 42% of affected individuals who have a first-degree

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relative with the same disorder. In turn, secondary RLS relates to various medical diseases or physiological changes, including pregnancy, iron deficiency, uremia, polyneuropathy, and rheumatoid arthritis.<sup>[2,3]</sup>

The pathophysiology of RLS during pregnancy is still unclear and may be related to deficiency of iron or folate, high levels of estrogen, progesterone, and prolactin, psychomotor disturbances, and radiculopathy or peripheral neuropathy.<sup>[4-9]</sup> Clinically, a diagnosis of RLS relies on four essential criteria that cannot be described by any other disorder: (1) an urge to move the legs (or other parts of the body), usually accompanied or caused by an uncomfortable or unpleasant sensation in the affected limbs; (2) the initiation or worsening of such symptoms during periods of rest or inactivity, such as lying down or sitting; (3) the partial or total relief of these symptoms by movement, such as walking or stretching, at least as long as the activity continues; and (4) a circadian pattern, in which symptoms usually worsen in the evening or at night, or occur solely during these times and not at all during the day.<sup>[3]</sup>

The prevalence of RLS during pregnancy varies from 10.4% to 44% depending on the diagnostic criteria, trimester, and characteristics of the population under study.<sup>[4,5,10-13]</sup> In particular, the prevalence is reportedly lower among pregnant women in the Western Pacific region compared to those in European, Eastern Mediterranean, and American countries.<sup>[14]</sup> The risk of RLS during pregnancy has been found to increase with a positive personal or family history of RLS, anemia, and hormonal changes.<sup>[1,14]</sup> On the other hand, there is inconclusive evidence regarding the relationship with other maternal factors, such as gravidity, multiparity, age, and other medical problems such as diabetes mellitus (DM), hypertension (HTN), depression, and obesity.<sup>[1,4,11,14,15]</sup> Furthermore, there is inadequate evidence to show if RLS has a relationship with mode of delivery, complications, and neonatal outcomes, such as birthweight and preterm birth.<sup>[10,11]</sup>

This research is expected to open the eyes of the healthcare workers and the policymakers on RLS. In addition, it is envisaged that the identification of the risk factors and pregnancy outcomes associated with RLS will help to detect high-risk groups and provide better care to these patients and build up the evidence in this area. Therefore, this study aimed to assess the prevalence and severity of RLS and explore associated clinical and demographic risk factors in pregnant Omani women in the first and third trimester as well as at 2-week postpartum. In addition, the study aimed to discover if the presence of RLS in pregnancy was associated with a higher prevalence of pregnancy-induced HTN (PIH), gestational DM (GDM), and low birthweight.

## Materials and Methods

This prospective observational study was conducted from May 2018 to October 2020 at four of the 32 health centers in Muscat Governorate. The selection of these health centers was done using a simple random sampling strategy involving a lottery method. The selected health centers included the Al-Khoudh, Seeb, Hay aljamea, and Al-Amerat health centers. All pregnant women of Omani nationality who had registered their pregnancy and were receiving care at these health centers before 13 weeks of gestation were included in the study. The necessary sample size was determined as 181 pregnant women according to a precision of 5%, prevalence of 13.6%, and 95% confidence interval (CI).<sup>[16]</sup> However, to avoid missing data, a total of 305 participants were enrolled in the analysis. Ethical approval was obtained from Research and Ethics Committee of Ministry of Health vide letter No. MH/DGPSIM 6/62/2017 dated 11/05/2017 and informed written consent was taken from each participant before data collection.

Three methods were used to collect data. A review of the antenatal and medical electronic records of each patient was conducted, alongside face-to-face interviews. Each participant in the study group was interviewed at three different times: during their first trimester, in their third trimester, and at their 2-week postpartum visit. As the main objective of the study was to find the relationship between RLS and pregnancy, and since the pregnancy effect is more marked in the third trimester than in the second trimester, the prevalence of RLS in the second trimester was not taken. Perhaps future research will consider adding the second trimester. In addition, an Arabic language questionnaire was designed and administered to elicit data regarding the participant's demographic and clinical characteristics, including maternal age, educational level, gravidity, parity, body mass index, history of hyperemesis gravidarum, personal and family history of RLS, and the presence of associated comorbidities such as DM, HTN, and anemia. A diagnosis of anemia was based on the national reference hemoglobin levels of <11 mg/dL.

A diagnosis of RLS was confirmed only in the presence of all four of the criteria designated by the International RLS Study Group as follows: (1) a desire to move the extremities, usually associated with some definable discomfort; (2) evidence of motor restlessness; (3) worsening of the symptoms while at rest, with at least temporary relief granted by activity; and (4) worsening of the symptoms later in the day or at night.<sup>[17]</sup> Subsequently, the International RLS Rating Scale (IRLSRS) was used to evaluate the severity of RLS symptoms in participants with a positive diagnoses of RLS. The IRLSRS is a 10-item scale in which each item is rated in terms of severity from

0 (“none”) to 5 (“very severe”), resulting in a total score range of 0–40. In general, an IRLS score of 1–10 corresponds to mild RLS, while scores of 11–20, 21–30, and 31–40 denote moderate, severe, and very severe RLS, respectively.<sup>[17]</sup>

The Statistical Package for the Social Sciences (SPSS), version 23 (IBM Corp., Armonk, NY, USA), was used to analyze the data. Results were presented as means and standard deviations or numbers and percentages, as appropriate. To assess the possible influence of demographic and other variables on the prevalence of RLS, we used either an unpaired *t*-test or McNemar’s test, as appropriate. The level of statistical significance was set at  $P < 0.05$ .

## Results

A total of 305 pregnant Omani women were included in the study. Table 1 shows the demographic and clinical characteristics of the studied population. The participants ranged in age from 18 to 47 years, with a mean of  $29.8 \pm 5.28$  years. The majority (98.4%) were educated to high school level or higher. Only 1.6% of participants were illiterate. Overweight/obesity was the most frequent comorbidity (56.1%), whereas anemia, chronic DM, and chronic HTN were reported by 24.3%, 1.0%, and 0.7% of participants, respectively, during the first trimester. Approximately one-quarter (23.6%) were primigravida, and the vast majority (99.0%) had singleton pregnancies. A personal history of RLS was found in 19.3% and a family history was reported by 7.5%.

Most participants (91.1%) delivered at  $\geq 37$  weeks of gestation. Most women (84.3%) had spontaneous vaginal deliveries, while the remainder (15.7%) underwent cesarean section (CS) procedures. The majority (92.1%) of women who delivered at  $\geq 37$  gestational weeks had babies with normal birthweights of  $\geq 2.5$  kg. With regard to pregnancy complications and outcomes, no significant relationships were observed between RLS during pregnancy and various pregnancy and neonatal complications such as emergency lower-segment CS (LSCS), prematurity, low birthweight, GDM, and PIH.

The study showed that RLS symptoms were significantly more common in the third trimester than in the first trimester and during the postpartum period (41.0% vs. 15.7% and 15.1%, respectively;  $P < 0.001$ ) [Table 2]. All the pregnant women with RLS during the first trimester continued to experience RLS in the third trimester. Moreover, RLS persisted into the postpartum period for 46 out of 125 pregnant women (36.8%) who had RLS during the third trimester. On the other hand, only 10 out of 48 women (20.1%) had RLS in both the first trimester and the postpartum periods. In terms of severity,

no statistically significant differences were observed between the first and third trimester and between the third trimester and postpartum period ( $P = 0.062$  and  $0.105$ , respectively) [Table 3]. In the third trimester, 66 women (21.6%) gained  $>12$  kg compared to their first trimester; of these, 19 (28.8%) had RLS during the third trimester, the analysis showing a significant relationship between the development of RLS and weight gain ( $P = 0.023$ ). However, there was no statistically significant correlation between weight gain and the difference in the severity of RLS between the first and third trimester ( $r_s = 0.022$ ;  $P = 0.880$ ).

Table 4 presents the findings of the multivariate binary logistic regression analysis to predict the development of RLS by pregnant Omani women. Independent predictors of RLS included age (odds ratio [OR]: 0.929, 95% CI: 0.845–1.022;  $P = 0.129$ ), a family history of RLS (OR: 3.995, 95% CI: 1.580–10.101;  $P = 0.002$ ), and a personal history of RLS (OR: 29.902, 95% CI: 10.706–83.51;  $P < 0.001$ ). Overall, a personal history and family history of RLS were the only statistically significant predictors of RLS. Omani women with a personal history of RLS had a 13-time greater risk of developing RLS during the first trimester.

## Discussion

The main goal of the current study was to assess the prevalence and severity of RLS and explore its associated clinical and demographic risk factors in the first and third trimester and at 2-week postpartum in pregnant women in Oman and find if the presence of RLS in pregnancy was related to pregnancy outcomes. Based on the previous research, the reported prevalence of RLS in pregnancy varies considerably depending on various factors, including the trimester of pregnancy.<sup>[4,5,10-13]</sup> In the Middle East, the prevalence of RLS in pregnant women in Iran and Saudi Arabia was found to be 17.8% and 21.3%, respectively.<sup>[4,5]</sup> Using the same diagnostic criteria, the prevalence of RLS in the present study was 15.7% during the first trimester and 41.0% in the third trimester, with no significant difference between trimesters in terms of severity scores. Hormones are believed to have a role in the presentation and development of RLS during pregnancy; it has been proposed that high levels of prolactin, estradiol, and progesterone during pregnancy may activate RLS.<sup>[18,19]</sup> Another factor that may lead to the development of RLS during pregnancy is deficiencies of iron, folic acid, or both.<sup>[20]</sup> Because the mother is the only source of fetal nutrition, the placenta regulates iron transfer to keep enough supply for the fetus, often regardless of the iron status of the mother. In addition, multigravidity and parity have been linked to the higher risk of anemia and by extension, RLS.<sup>[21,22]</sup> However, although 76.4% of the women in the present study had previously had at least one prior pregnancy,

**Table 1: Associations between restless leg syndrome, sociodemographic and clinical characteristics, and pregnancy complications and outcomes in pregnant Omani women during the first trimester (n=305)**

Variable	Total N (%)	RLS		P-value
		Yes (n=125) N (%)	No (n=180) N (%)	
Age, mean±SD	29.8±5.28	29.72±5.03	29.86±5.46	0.101
BMI, mean±SD		26.6±6.03		
Normal weight	134 (43.9)	61 (45.5)	73 (54.5)	0.154
Overweight/obese	171 (56.1)	64 (37.4)	107 (62.6)	
Family history of RLS				
Yes	23 (7.5)	14 (60.9)	9 (39.1)	0.044*
No	202 (66.2)	74 (36.6)	128 (63.4)	
Unsure	80 (26.2)	37 (46.3)	43 (53.7)	
Gravidity, mean±SD	2.99±1.80	3.10±1.71	2.91±1.85	
Primigravida	72 (23.6)	23 (31.9)	49 (68.1)	0.143
Multigravida (2–5)	208 (68.2)	93 (44.7)	115 (55.3)	
Grand multigravida (>5)	25 (8.2)	9 (36.0)	16 (64.0)	
Parity, mean±SD	1.64±1.51	1.70±1.42	1.59±1.58	0.127
Education level				
Illiterate	5 (1.6)	1 (20.0)	4 (80.0)	0.516
School level	175 (57.4)	70 (40.0)	105 (60.0)	
College or higher	125 (41.0)	54 (43.2)	71 (56.8)	
Personal history of RLS				
Yes	59 (19.3)	47 (79.7)	12 (20.3)	<0.001*
No	246 (80.7)	78 (31.7)	168 (68.3)	
Hyperemesis gravidarum				
Yes	98 (32.1)	46 (46.9)	52 (53.1)	0.092
No	207 (67.9)	79 (38.2)	128 (61.8)	
Previous history of GDM/DM				
Yes	40 (13.1)	14 (35.0)	26 (65.0)	0.409
No	265 (86.9)	111 (41.9)	154 (58.1)	
Previous history of PIH/HTN				
Yes	10 (3.3)	4 (40.0)	6 (60.0)	0.208
No	295 (96.7)	121 (41.0)	174 (59.0)	
Hemoglobin level, mean±SD	10.72±1.03	10.70±1.00	10.73±1.06	0.686
Gestational age at delivery				
Full term	278 (91.1)	111 (39.9)	167 (60.1)	0.229
Preterm	27 (8.9)	14 (51.9)	13 (48.1)	
Birthweight <sup>†</sup>				
Low	22 (7.9)	11 (50.0)	11 (50.0)	0.315
Normal	256 (92.1)	100 (39.1)	156 (60.9)	
Mode of delivery				
SVD	257 (84.3)	110 (42.8)	147 (57.2)	0.312
Elective LSCS	17 (5.6)	5 (29.4)	12 (70.6)	
Emergency LSCS	31 (10.2)	10 (32.3)	21 (67.7)	

\*Statistically significant at  $P<0.05$  using a Chi-squared or independent samples  $t$ -test, <sup>†</sup>Only full-term deliveries ( $n=278$ ). RLS=Restless leg syndrome, SD=Standard deviation, BMI=Body mass index, DM=Diabetes mellitus, GDM=Gestational DM, PIH=Pregnancy-induced hypertension, HTN=Hypertension, SVD=Spontaneous vaginal delivery, LSCS=Lower-segment cesarean section

no association was found between gravidity or parity and RLS.

The present study found a higher prevalence of RLS in Omani pregnant women compared to findings reported regionally in Saudi Arabia (13.6% in the first trimester and 24.1% in the third trimester) and internationally by Chen *et al.*<sup>[4,23]</sup> The higher prevalence of RLS in Oman may relate to the racial

and geographic characteristics of the population and the specific trimester of pregnancy. With regard to the relationship between RLS and period of gestation, the results were comparable to previous studies which showed an increased tendency to develop RLS in the later trimester of pregnancy than the first trimester or postpartum period.<sup>[23,24]</sup> Of the pregnant women who were surveyed, RLS symptoms were significantly more common in the third trimester (41.0%) than

in the first trimester (15.7%) and postpartum period (15.1%) ( $P < 0.001$ ).

The occurrence of RLS in one pregnancy is a significant risk factor for the development of RLS in subsequent pregnancies and potentially even for the development of idiopathic nonpregnancy-related RLS in future.<sup>[25]</sup> In this study, the RLS in one pregnancy was found to increase the risk of RLS in later pregnancies by a factor of eight. Moreover, a personal and family history of RLS was the only independent risk factors for developing RLS in pregnancy. Indeed, many people with primary RLS have a family history of the problem, which may suggest an autosomal-dominant pattern of inheritance. In addition, RLS has been connected to locations on several chromosomes and genes, although the precise genetic basis of the condition has not yet been positively defined.<sup>[26,27]</sup>

**Table 2: Frequency of restless leg syndrome symptoms in the first and third trimesters and at 2-week postpartum in pregnant Omani women (n=305)**

Stage	RLS		P-value
	Yes N (%)	No N (%)	
First trimester	48 (15.7)	257 (84.3)	<0.001*
Third trimester	125 (41.0)	180 (59.0)	
2 weeks postpartum	46 (15.1)	259 (84.9)	

\*Statistically significant at  $P < 0.05$  using McNemar's test. RLS=Restless leg syndrome

In the present study, 66 women (21.6%) gained  $\geq 12$  kg between the first and third trimester. These patients were more prone to developing RLS in the past trimester. However, there was no statistically significant correlation between weight gain and the difference in the severity of RLS between the first and third trimester ( $r_s = 0.022$ ;  $P = 0.880$ ). To the best of the authors' knowledge, no prior research has examined this factor in pregnancy. An earlier study showed that weight gain and higher BMI in early adulthood (age 18–21 years) were related to the development of RLS in the general population.<sup>[28]</sup> The possible explanation of the link between weight gain and RLS is that both may be affected by the dopaminergic system in the CNS.<sup>[29]</sup>

Similarly, data regarding associations between RLS in pregnancy and delivery outcomes are limited. In one study of 1000 American women in the instant postpartum period, 44 reported always experiencing "jumpy or jerky leg movements" during the third trimester of pregnancy; moreover, these movements were linked with an increased incidence of low birth weight and preterm birth.<sup>[30]</sup> Furthermore, in a cohort of over 600 women between 35 and 37 weeks of gestation in New Zealand, pregnancy-onset leg jerking was associated with three times higher odds of fetal distress linked to maternal hypoxia, concerns related to fetal heart rate, or signs of fetal stress.<sup>[31]</sup> However, in our study, no significant relationships were seen between RLS during pregnancy

**Table 3: Severity of restless leg syndrome symptoms in the first and third trimesters and at 2-week postpartum in pregnant Omani women (n=305)**

Stage	RLS severity					P-value
	Total N (%)	Mild N (%)	Moderate N (%)	Severe N (%)	Very severe N (%)	
First trimester	48 (15.7)	9 (18.8)	30 (62.5)	9 (18.8)	0 (0.0)	-
Third trimester	125 (41.0)	15 (12.0)	65 (52.0)	39 (31.2)	6 (4.8)	0.062
2 weeks postpartum	46 (15.1)	7 (15.2)	25 (54.3)	12 (26.1)	3 (6.5)	0.105

\*Statistically significant at  $P < 0.05$  using McNemar's test. RLS=Restless leg syndrome

**Table 4: Multivariate binary logistic regression analysis: Factors related to restless leg syndrome in pregnant Omani women (n=305)**

Variable	$\beta$	P-value	OR	95% CI
Age	0.074	0.129	0.929	0.845 - 1.022
Family history of RLS				
Yes	0.118	0.002*	3.995	1.580 - 10.101
Personal history of RLS				
Yes	3.398	<0.001*	13.103	6.503 - 26.402
BMI at first trimester				
Normal (reference)				
Overweight/obese	0.620	0.186	1.858	0.742 - 4.654
Hb level at first trimester				
Normal (reference)				
Anemic	0.719	0.133	2.052	0.803 - 5.242

\*Statistically significant at  $P < 0.05$  using binary logistic regression. RLS=Restless leg syndrome, OR=Odds ratio, CI=Confidence interval, BMI=Body mass index, Hb=Hemoglobin

and complications and outcomes of pregnancy, including the incidence of emergency LSCS, prematurity, low birthweight, GDM, and PIH, unlike other studies which reported a positive association between RLS and GDM and PIH.<sup>[32]</sup>

This study is subject to certain limitations. As the study was conducted solely at four centers in the Muscat region, more generalizable research is needed from other areas of Oman. Moreover, ferritin levels were not assessed in the current study, a factor which has been shown to have a relationship with RLS in previous research.<sup>[33]</sup> Studies involving a larger sample size and patients from multiple regions of Oman are recommended. In addition, there is a need for further research to evaluate the effect of RLS on the quality of life and sleep of pregnant Omani women.

## Conclusion

Overall, RLS was observed in approximately one in six pregnant Omani women visiting primary health centers during their first trimester and one in 2–3 pregnant women during their third trimester. Women with a personal or family history of RLS or those who gain >12 kg during pregnancy were significantly more likely to develop RLS during pregnancy. However, no associations were found between RLS and other comorbidities, including HTN, DM, anemia, hyperemesis, or obesity. Therefore, it is possible that the role of anemia as a risk factor for RLS in pregnancy may be overestimated. Timely identification of these patients and the establishment of screening programs are important to provide the required care, especially in the third trimester.

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## Conflicts of interest

There are no conflicts of interest.

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