

The Correlation of Restless Leg Syndrome with Endometriosis: A Cross-Sectional Study

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ABSTRACT

Background: Restless leg syndrome (RLS) is a common neurological disorder, but its correlation with endometriosis remains unclear.

Objectives: To evaluate the correlation of RLS with endometriosis.

Materials and methods: A cross-sectional study included 155 patients who were diagnosed with RLS at the Neurology Department, Azadi Teaching Hospital, Kirkuk, Iraq. The study started on 1st June 2020 and ended on 1st March 2023. RLS was diagnosed using the criteria established by the International Restless Leg Syndrome Study Group (IRLSSG). The researchers questioned the patients about their history of endometriosis. Then categorized into two groups. The first group consisted of 72 cases with surgically confirmed endometriosis, whose severity was determined by the Gynecologists following the guidelines of the revised American Society of Reproductive Medicine (rASRM). The remaining 83 cases formed a group comprising individuals with RLS without endometriosis. We collected data from each participant about their age, marital status, smoking habit, and body mass index (BMI).

Results: One hundred fifty five patients with a mean age of 29.19 ± 6.12 years were diagnosed with RLS. There was a statistically significant difference (P -value = 0.029) between the RLS and the age of the patients with endometriosis compared to those without endometriosis. However, there were no significant statistical differences (P -value > 0.05) in marital status, smoking habits, or BMI between the two groups. In terms of RLS severity ratings, patients with endometriosis tended to have more severe rating scales compared to those without this condition. Additionally, a Pearson's correlation test showed a strong positive correlation, between IRLSSG and rASRAM scores (P -value = 0.0001, $r = 0.7$).

Conclusion: RLS was strongly and positively correlated with endometriosis. However, the exact cause and nature of this correlation remained obscure.

Keywords: Restless leg syndrome; Endometriosis; Correlation

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INTRODUCTION

Restless legs syndrome (RLS) is a disorder, often overlooked, characterized by painful sensations primarily in the legs during rest and relieved by movement [1]. RLS can significantly impact one's quality of life by causing pain and disrupting sleep, with a prevalence of 5-15% [2]. The condition tends to be more common among adults with a female predominance and is

divided into two types: primary RLS (also called idiopathic RLS) and secondary RLS which is linked to several factors such as pregnancy, iron deficiency anemia, and chronic renal or neurological disease. Both types had the same symptoms and diagnostic criteria [3]. In addition, endometriosis can affect the nerves by causing pressure effects that lead to pain sensations, and therefore, the overlap of symptoms can make the diagnosis difficult [4].

Endometriosis, a chronic progressive disease with a prevalence of 10%, commonly affects women of reproductive age and regresses with menopause, manifesting through a variety of recurrent symptoms like chronic pelvic pain, painful menstruation, subfertility, and pain during intercourse or defeca-

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tion [5]. Endometriosis commonly affects the ovaries [6], and approximately one out of every nine women receives a diagnosis at delivery, with the highest occurrence occurring between ages 25 and 35 year [7].

There have been several studies that have explored the association between RLS and various health issues such as hypothyroidism, multiple sclerosis, diabetes mellitus, and polycystic ovarian syndrome [8–11]. However, only two studies have investigated the association between RLS and endometriosis. The first study by Tempest et al. [12] distributed a questionnaire to premenopausal women, collecting data on RLS and endometriosis associated symptoms. The study did not provide a specific prevalence rate of RLS in women with endometriosis but mentioned that there was a significantly higher prevalence of symptoms of RLS in cases with endometriosis compared to those without endometriosis. The second investigation was by Sumbodo et al. [13] who did not specifically mention the association of RLS with endometriosis and focused primarily on the relationship between sleep disturbances and endometriosis. Therefore, the objective of this study was to address this gap by determining the correlation of RLS in non-pregnant women with endometriosis.

MATERIALS AND METHODS

After collecting informed consent from all patients, a cross-sectional study was conducted in the Neurological Department at Azadi Teaching Hospital, Kirkuk, Iraq. The study covered the period between 1st June 2020 and 1st March 2023. The current study enrolled 155 consecutive patients with newly diagnosed RLS according to the four-point diagnostic criteria of IRLSSG which include the following: "Desire to move the extremities, usually associated with discomfort or disagreeable sensations in the extremities, motor restlessness, symptoms worse at rest with at least temporary relief by activity, and symptoms worse later in the day or at night".

The Clinical Research Ethics Committee at the College of Medicine, University of Kirkuk approved the study with decision no. 32 on 10.04.2023. The severity of RLS was rated using the IRLSSG rating scale: "(None: 0), (Mild: 1 to 10), (Moderate: 11 to 20), (Severe: 21 to 30), and (Very severe: 31 to 40) points" [14].

All cases were asked for a history of endometriosis, 72 of those surgically confirmed had endometriosis and their severity was labelled by the Gynecologists according to the revised American Society of Reproductive Medicine (rASRM) score [15], which was classified as (1-5 minimal), (6-15 mild), (16-40 moderate) and (> 40 severe endometriosis), while the remaining 83 patients didn't have endometriosis, who were excluded from the study after being referred to Gynecologists who ruled out the diagnosis of endometriosis based on clinical features and in some cases by laparoscopy.

The inclusion criteria were women aged 18 to 42 years with or without endometriosis who accepted participation in the study. The exclusion criteria were women with a history of specific chronic diseases, including anaemia, vitamin D deficiency, parkinsonism, hereditary and/or diabetic neuropathy, spinocerebellar ataxia, thyroid disorders, hypertension, hyperlipidemia, heart disease, stroke, renal disease, osteoarthritis, fibromyalgia, rheumatoid arthritis, varicose veins, diabetes mellitus, and chronic drug users such as hormonal therapy, antidepressants, and antipsychotics, because they could cause RLS and affect the results of the study. Besides, pa-

tients who declined to participate were also excluded from the present study. Data from each patient were registered regarding the age, marital state, smoking, and body mass index (BMI) [calculated by the following equation: weight (kg)/height (m²)] [16]. Statistical analysis was done using IBM SPSS (Statistical Package for the Social Sciences) version 26. The continuous data were presented as mean value \pm standard deviation (SD), and the categorical variables were summarized as numbers (n) and percentages (%). Comparisons between groups were made using Pearson's Chi-squared test for categorical variables. The Pearson correlation coefficient was used to assess the correlation between IRLSSG and rASRM. A P-value of < 0.05 was considered a statistically significant difference.

RESULTS

The study population characteristics based on RLS status with and without endometriosis are outlined in Table 1. Of the 155 newly diagnosed cases of RLS with a mean age of 29.19 ± 6.12 years (ranging from 18 to 42 years), 72 patients had RLS along with endometriosis, while 83 patients had RLS without endometriosis. A significant statistical difference in the age distribution (P-value = 0.029) was observed, with the majority of cases (43.1%) falling within the age range of 25-30 years in the group with RLS and endometriosis. However, we found no significant statistical difference between the two groups concerning marital status, smoking habits, and BMI, with P-values of 0.72, 0.35, and 0.35, respectively.

By using IRLSSG score scales to assess cases of RLS in both groups, a significant difference (P-value = 0.001) was identified, as 44.4% of patients who had endometriosis reported a severe score of RLS, while 31.9% reported very severe symptoms; this is significantly higher than the corresponding figures for those without endometriosis (13.3%), as shown in Table .

The use of the rASRM score to evaluate the severity of endometriosis in individuals with RLS revealed that 25%, 29.17%, 30.56%, and 15.28% had minimal, mild, moderate, and severe scores, respectively, as shown in Figure 1.

The Pearson correlation coefficient test between the IRLSSG rating scales of RLS and the severity of endometriosis (rASRM) indicated a positive correlation, between them (P-value = 0.0001, $r = 0.7$), as indicated in Table and Figure 2.

DISCUSSION

RLS is a common neurological condition that affects approximately 5 to 15 percent of the general population. It can manifest as either primary with origins that are not entirely clear, or secondary, linked to medical and gynecological issues such as iron deficiency anemia, chronic renal failure, peripheral neuropathy, pregnancy, and the use of certain antidepressant medications [2].

Pregnant women are particularly vulnerable to experiencing RLS with rates that indicate the influence of ovarian hormones. However, our study excluded pregnant women to overcome the possible effect of hormonal changes on precipitating RLS and ensure the correlation with endometriosis [17]. The presence of RLS symptoms in patients with gynecological disorders, especially those with endometriosis, is important for many reasons. Firstly, it is possible to identify common etiological factors between the two conditions, leading to novel therapeutic options. For example, iron deficiency anemia is a

Table 1. Sociodemographic characteristics among the study population.

		Endometriosis				P-value*
		Yes		No		
		Number	Percent	Number	Percent	
Age (Years)	< 25	18	25.0%	19	22.9%	0.029
	25-30	31	43.1%	23	27.7%	
	31-35	17	23.6%	20	24.1%	
	>35	6	8.3%	21	25.3%	
Marital state	Married	63	87.5%	71	85.5%	0.72
	Single	9	12.5%	12	14.5%	
Smoking	Yes	5	6.9%	3	3.6%	0.35
	No	67	93.1%	80	96.4%	
BMI(kg/m ²)	Underweight < 18.5	2	2.8%	3	3.6%	0.35
	Normal 18.5-24.9	11	15.3%	10	12.0%	
	Overweight 25-29.9	40	55.6%	37	44.6%	
	Obese > 30	19	26.4%	33	39.8%	

* Pearson’s Chi-squared test, BMI=body mass index.

Table 2. Distribution of the studied groups according to the IRLSSG rating scale.

IRLSSG score	Endometriosis				P-value*
	Yes		No		
	Number	Percent	Number	Percent	
Mild (1-10)	6	8.3%	28	33.7%	0.001
Moderate (11-20)	11	15.3%	33	39.8%	
Severe (21-30)	32	44.4%	11	13.3%	
Very severe (31-40)	23	31.9%	11	13.3%	

* Pearson’s Chi-squared test, IRLSSG = International restless leg syndrome studied group.

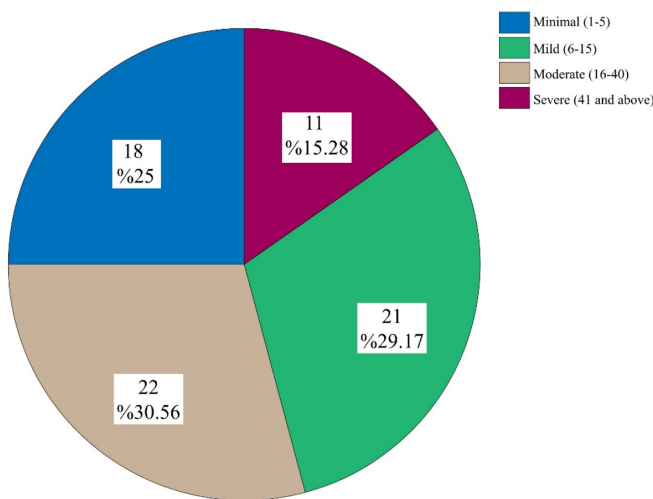


Figure 1. Distribution of RLS patients according to rASRM score of endometriosis. rASRM = revised American Society of Reproductive Medicine.

recognized cause of RLS [18]. In addition, evidence suggests that women with endometriosis have a significantly reduced hemoglobin concentration and average cell volume compared to controls of the same age [12].

In this study, most patients were below 30 years old in cases

Table 3. The correlation of the IRLSSG rating with the severity of endometriosis.

IRLSSG rating scale	rASRM score	
	Pearson’s correlation	0.762*
	Sig. (2-tailed)	0.0001
	N	72

* Strongly positive pearson correlation, IRLSSG = International Restless Legs Syndrome Study Group, rASRM = revised American Society of Reproductive Medicine.

of RLS with endometriosis, which aligns with the findings of Bulun et al.’s study [19]. In addition, about the BMI index and smoking habits, there was no significant association between the two studied groups, which is similar to Pantelis et al.’s study [20] that failed to link BMI to endometriosis, as well as the study of Coiplet et al. [21], which did not find a relationship between smoking and endometriosis. However, this contradicts the study of Srivanitchapoom et al. [22], which identified pregnancy, smoking, and obesity as risk factors for RLS. These discrepancies may be due to differences in sample size or genetic influences on RLS, as well as the occurrence of endometriosis in the different populations examined.

The study found a correlation between the IRLSSG rating scale and the rASRM endometriosis severity score, supporting the research that was conducted by Tempest and col-

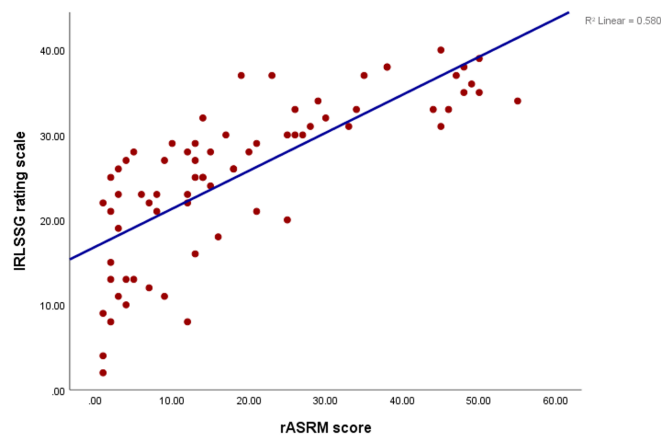


Figure 2. The correlation between restless leg syndrome rating scale and the severity of endometriosis. IRLSSG = International restless leg syndrome Study Group, rASRM = Revised American Society of Reproductive Medicine.

leagues [12]. The current study showed that there was a correlation between RLS in women with surgically confirmed endometriosis, which showed a significant positive correlation between the severity of endometriosis and the RLS rating scale that is comparable to the study of Sumbodo et al. [13].

The correlation between these two conditions might be due to shared factors or hormonal influences affecting both. Our study revealed that 46.3% of participants with RLS also had endometriosis highlighting the importance of this correlation. However, our study had some limitations. Specifically we did not exclude asymptomatic endometriosis cases, which could have influenced our results and potentially underestimated the link between these conditions. Moreover we did not consider parity, as a possible underlying cause of both conditions. Furthermore, the study design is a cross-sectional design over a specific time period imposed constraints on our research scope. Moreover, we did not explore how RLS and endometriosis symptoms coincide during menstruation, where endometriosis symptoms typically worsen. While, our findings indicate a correlation between RLS severity and endometriosis they do not definitively establish whether one condition triggers the other or if there is a shared factor that

causes both conditions. To gain insights into the relationship between these two conditions and ascertain causality, additional future prospective cohort studies are necessary.

CONCLUSION

There was a correlation between RLS and endometriosis, but the cause and nature of this relationship remain unclear. Prospective studies are required to investigate the temporal sequence of events and uncover the underlying mechanisms linking these two conditions.

ETHICAL DECLARATIONS

Acknowledgements

None.

Ethics Approval and Consent to Participate

Ethics approval was obtained from the Clinical Research Ethics Committee, College of Medicine, University of Kirkuk, Kirkuk, Iraq (decision no. 32, date 10.04.2023). Informed consent was obtained from all patients participating in the study.

Consent for Publication

Not applicable (no individual or personal data included).

Availability of Data and Material

Data is available upon reasonable request from the corresponding author.

Competing Interests

The author declares that there is no conflict of interest.

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Authors' Contributions

Taha MA was responsible for the literature review, design of the study, collection of the data, statistical analysis, and writing the manuscript. The author read and approved the final version of the manuscript.

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