Original Article

Prevalence, Risk Factors, and Psychosocial Impact of Restless Legs Syndrome in End-Stage Renal Disease Patients Undergoing Hemodialysis – A Cross-Sectional Study

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Abstract

Background and Objectives: Restless legs syndrome (RLS) is common but often underdiagnosed in patients with end-stage renal disease (ESRD) undergoing hemodialysis, significantly impacting their quality of life. This study investigates the prevalence, risk factors, and psychosocial effects of RLS in this population. **Methods:** A cross-sectional study was conducted among 308 hemodialysis patients at a tertiary care hospital. RLS was diagnosed based on the International Restless Legs Syndrome Study Group criteria. The severity of RLS, sleep quality, and mental health were assessed using the International Restless Legs Syndrome (IRLS) Severity Score, Pittsburgh Sleep Quality Index, and Hospital Anxiety and Depression Scale. Clinical and biochemical parameters were also analyzed. Statistical significance was determined using Chi-squared and unpaired *t*-tests ($P < 0.05$). **Results:** RLS was identified in 46 patients (14.9%). Among them, 56.6% had mild symptoms, 41.3% had moderate symptoms, and 2.1% had severe symptoms. Patients with RLS were younger (50.15 ± 12.19 vs. 57.41 ± 13.43 years, $P = 0.001$) and had lower body weight (57.89 ± 9.64 vs. 62.78 ± 10.58 kg, $P = 0.03$). Anxiety and depression were significantly higher in the RLS group ($P = 0.001$). Poor sleep quality was reported in 97.8% of RLS patients ($P = 0.001$). Hemoglobin ($P = 0.02$) and thyroid-stimulating hormone ($P = 0.03$) levels also differed significantly between groups. **Conclusions:** RLS is highly prevalent in ESRD patients undergoing hemodialysis and is associated with significant psychosocial burden and poor sleep quality.

Keywords: Anxiety, depression, end-stage renal disease, hemodialysis, restless legs syndrome

Introduction

Restless legs syndrome (RLS) is characterized by unpleasant or abnormal sensations in the legs or arms, often accompanied by a strong urge to move the limbs. These sensations typically occur during periods of rest, such as at night, and movement can provide temporary relief. RLS can be either primary (without an underlying cause) or secondary to other conditions.[1]

The prevalence of RLS varies across different populations, with the severity of symptoms required for diagnosis also differing. Mild symptoms of RLS are present in approximately 5%–15% of the general population.[2,3] RLS is frequently associated with various clinical conditions, including peripheral neuropathy, iron deficiency, type 2 diabetes, multiple sclerosis, and uremia. It is commonly linked to insomnia, poor sleep quality, and a decreased quality of life, particularly in patients with end-stage renal disease (ESRD).

The pathophysiology of RLS in chronic kidney disease remains unclear, and several risk factors have been proposed, though studies yield inconsistent results. The type of dialysis (hemodialysis or peritoneal dialysis) does not appear to affect the incidence of RLS, although some recent studies have reported conflicting findings.[4-6]

Despite the recognized epidemiological link between RLS and kidney disease, the connection between these two conditions is often overlooked. RLS in ESRD patients can significantly impair quality of life, likely due to poor sleep quality, insomnia, and depression. Therefore, further research is essential to investigate the prevalence, risk factors, and impact of RLS in ESRD patients.

Methods

Study design

This observational, cross-sectional study aimed to assess the prevalence and associated factors of RLS in patients with ESRD undergoing hemodialysis. The cross-sectional design allowed for data collection at a single time point to explore the relationships between clinical, biochemical, and psychosocial parameters and the presence of RLS. The study was conducted over 6 months, from March 2024 to August 2024, in the Department of Nephrology at a tertiary care hospital.

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Sample size calculation

The sample size was calculated to be 260 using a prevalence estimate of 20.4% from a previous study, a 95% confidence interval, and a margin of error of 0.05. To account for potential non-response, the final sample size was adjusted to 308 participants.

Selection criteria

The study included adult patients diagnosed with ESRD undergoing regular hemodialysis three times per week. All the included patients underwent the same dialysis method. Eligible participants from both genders were aged 18 years or older and provided informed consent. Exclusion criteria included pregnancy, conditions that could confound RLS diagnosis (e.g., Parkinson's disease, type 1 diabetes mellitus, or peripheral neuropathy), or inability to provide informed consent. Exclusion of diagnostic confounders, including conditions such as type 1 diabetes mellitus and peripheral neuropathy, was based on a review of documented medical history. Type 1 diabetes mellitus was excluded by assessing insulin sensitivity, while peripheral neuropathy was ruled out through clinical evaluations.

Outcome measures

The primary outcome was the prevalence of RLS, which was diagnosed based on the International Restless Legs Study Group (IRLSSG) criteria. Secondary outcomes included RLS severity, assessed using the International Restless Legs Syndrome (IRLS) Severity Score Questionnaire, and its impact on psychosocial factors such as sleep quality, anxiety, and depression. Sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI), and anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS). Biochemical parameters, including hemoglobin, calcium, phosphorus, albumin, iron, ferritin, creatinine, blood urea, thyroid-stimulating hormone, and parathyroid hormone (PTH), were also analyzed for potential associations with RLS. For the purposes of these assessments, medical reports from the past 2 months were considered if recent records were available with the patient. For those without recent reports, the necessary investigations were conducted at the time of assessment.

Data collection

Data collection began after obtaining approval from the Institutional Ethical Committee, and written informed consent was obtained from all participants in accordance with the ethical guidelines. A structured questionnaire gathered demographic data (age, gender, weight, height) and clinical information (duration and frequency of dialysis, comorbidities, smoking status, alcohol use, family history of RLS). RLS diagnosis was based on the IRLSSG criteria, and participants satisfying these criteria completed the IRLS Severity Score Questionnaire. Those diagnosed with RLS were also asked to complete the PSQI and HADS questionnaires to assess the impact on sleep quality, anxiety, and depression. Biochemical data were retrieved from recent laboratory reports for accurate analysis.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using International Business Machine Statistical Package for the Social Sciences Statistics, version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics summarized the data, presenting qualitative variables as frequencies and percentages and quantitative variables as means and standard deviations. Relationships between variables were assessed using the Chi-squared test for categorical variables and unpaired *t*-tests for continuous variables. In addition to univariate analysis, multivariate regression analysis was performed to assess the independent associations of sleep quality, depression, and anxiety with the prevalence of RLS, while adjusting for potential confounders. A *P*-value of less than 0.05 was considered statistically significant. This analysis provided insights into the prevalence of RLS and its associations with clinical, biochemical, and psychosocial factors among the study population.

Results

Overall, records of 308 patients (205 males and 103 females) were included in this cross-sectional analysis. Among these 308 patients, 46 patients (14.9%) were diagnosed with RLS. Figures 1 and 2 present the gender and severity distributions of RLS noted in this study, respectively. Table 1 presents a comparison of demographic and clinical variables between individuals with and without RLS. Age and body weight were significantly lower among those with RLS compared to those without RLS. Table 2 Presents the differences in laboratory parameters between RLS-positive and RLS-negative groups in this study. The drug history was obtained during patient interviews, which revealed no use of antidepressants among the participants. However, a few patients were on sedatives.

RLS-positive patients exhibited significantly higher levels of anxiety, depression, and poorer sleep quality, compared to RLS-negative patients [Figure 3]. Among RLS-positive patients, 67.4% had borderline anxiety and 4.3% had abnormal anxiety, compared to 25.2% and 0.8%, respectively, in RLS-negative patients [Table 3]. Similarly, among RLS-positive patients, 60.9% had borderline depression and 26.1% had

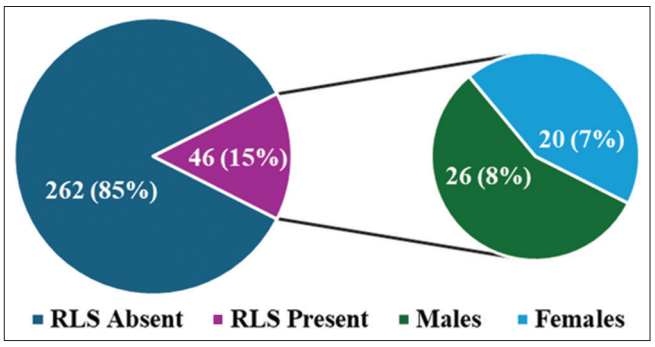

Figure 1: Prevalence and gender distribution of RLS as noted in the study (differences in gender were not statistically significant [$P > 0.05$]). RLS: restless legs syndrome

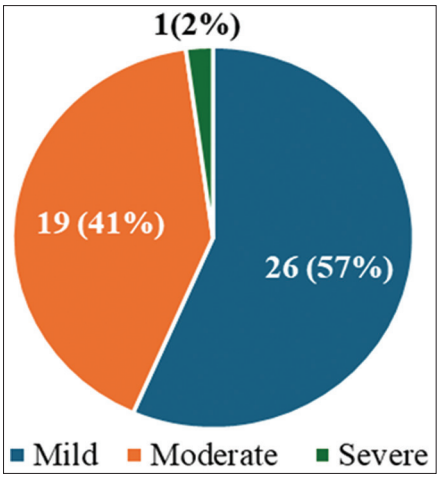

Figure 2: Distribution of RLS severity as noted in the study. RLS: restless legs syndrome

Table 1: Comparison of demographic and clinical variables between individuals with and without RLS

	RLS positive (n=46)	RLS negative (n=262)	*P*-value
Age (years)	50.15±12.19	57.41±13.43	0.001
BMI Kg/m²	22.58±3.60	24.32±3.78	0.004
Hypertension	42 (91.3)	245 (93.5)	0.58
Diabetes	20 (43.5)	148 (56.5)	0.10
Smoking	14 (30.4)	65 (24.8)	0.10
Alcohol	5 (10.9)	49 (18.7)	0.19
Family history (+)	0 (0)	5 (1.9)	0.53
Duration of hemodialysis (Yr)	3.87±3.61	3.27±2.98	0.19

BMI: body mass index, RLS: restless legs syndrome. Data are presented as mean±standard deviation or n (%)

abnormal depression, while these figures were significantly lower in RLS-negative patients [Table 3]. Most RLS-positive patients (97.8%) had abnormal sleep quality scores compared to 60.3% in the RLS-negative group [Table 3]. Univariate regression analysis revealed significant associations of sleep quality, depression, and anxiety with the presence of RLS. Poor sleep quality (Exp (B) = 29.62, $P = 0.001$), depression (Exp (B) = 12.95, $P < 0.001$), and anxiety (Exp (B) = 7.24, $P < 0.001$) were strongly linked to RLS. In the multivariate regression analysis, after adjusting for potential confounders, sleep quality (Exp (B) = 10.93, $P = 0.02$), depression (Exp (B) = 5.14, $P = 0.01$), and anxiety (Exp (B) = 2.78, $P < 0.001$) remained independently associated with RLS, suggesting that these factors significantly contribute to the likelihood of developing RLS.

Discussion

This study aimed to estimate the prevalence of RLS and identify associated factors in individuals with ESRD undergoing hemodialysis at a tertiary care hospital. Among 308 participants, 46 (14.9%) were diagnosed with RLS. This prevalence is lower than the value of 20.4% reported by Lin et al.,[7] but higher than the rates observed in Indian studies, such as 10.3% reported by Ramachandran et al.[8] and 11% reported by Das et al.[9] Globally, RLS prevalence varies, with 26.6% reported in Greece, 25.3% in Taiwan, 22% in Japan, and 15.8% in Iran.[10-13] These differences may be due to variations in study populations, geographic factors, and diagnostic criteria.

In our study, the majority of RLS cases were of mild or moderate severity, with no participants classified as having severe symptoms. Males represented a higher proportion of RLS cases (56.5%) compared to females (43.5%), which contrasts

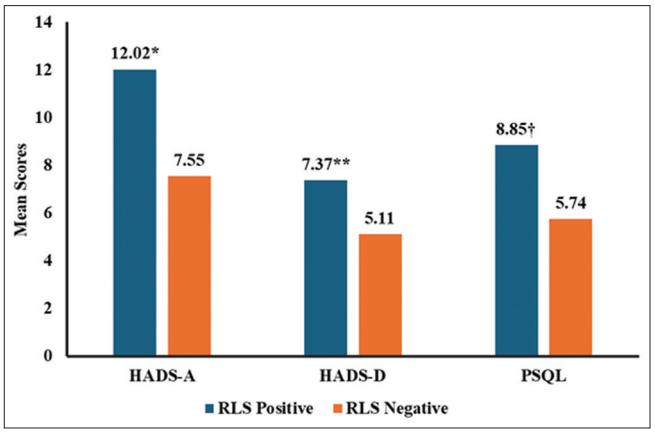

Figure 3: Mean HADS-A, HADS-D and PSQI scores among people with and without RLS. *$P < 0.001$; **$P < 0.001$; †$P < 0.001$. HADS: Hospital Anxiety and Depression Scale, RLS: restless legs syndrome. HADS-A: Hospital Anxiety Depression Scores-Anxiety subscale, HADS-D: Hospital Anxiety Depression Scores-Depression subscale, PSQI: Pittsburg Sleep quality Index

Table 2: Differences in laboratory parameters between RLS-positive and RLS negative groups in this study

	RLS positive (n=46)	RLS negative (n=262)	*P*-value
Pre-creatinine mg/dl	8.83±2.82	8.33±2.36	0.32
Post-creatinine mg/dl	6.52±2.67	6.17±2.15	0.18
BUN mg/dl	60.41±23.92	64.92±24.10	0.24
Post-BUN mg/dl	36.26±19.10	39.69±18.70	0.25
Hb g/dl	8.88±1.56	9.45±1.64	0.02
CA mg/dl	8.24±0.96	8.47±0.78	0.08
PO mg/dl	4.32±1.61	4.36±1.29	0.85
ALB g/dl	3.64±0.99	3.57±0.71	0.56
UA mg/dl	4.59±1.84	4.71±1.67	0.66
Iron ug/dl	49.02±18.88	53.37±21.67	0.20
Ferritin ng/ml	352.17±336.04	344.76±381.0	0.90
TSH mIU/L	3.03±2.44	2.28±1.38	0.03
PTH pg/ml	388.50±313.88	422.83±496.17	0.65

PTH: parathyroid hormone, RLS: restless legs syndrome, TSH: thyroid-stimulating hormone. Data are presented as mean±standard deviation, BUN: Blood Urea, Hb: Hemoglobin, CA: Calcium, PO: phosphorous, ALB: Albumin, UA: Uric Acid, TSH: Thyroid Stimulating Hormone, PTH: Parathyroid Hormone

Table 3: Prevalence of anxiety, depression, and sleep disturbances among individuals with and without RLS

		RLS positive (n=46)	RLS negative (n=262)	*P*-value
Anxiety	Normal, n (%)	13 (28.3)	194 (74)	0.001
	Borderline, n (%)	31 (67.4)	66 (25.2)	
	Abnormal, n (%)	2 (4.3)	2 (0.8)	
Depression	Normal, n (%)	6 (13)	173 (66)	0.001
	Borderline, n (%)	28 (60.9)	86 (32.8)	
	Abnormal, n (%)	12 (26.1)	3 (1.1)	
PSQI	Normal, n (%)	1 (2.2)	104 (39.7)	0.001
	Abnormal, n (%)	45 (97.8)	158 (60.3)	

PSQI: Pittsburg Sleep Quality Index, RLS: restless legs syndrome

with Lin et al.'s[7] finding that females predominated (58.8%). However, this male predominance aligns with Ramachandran et al.'s[8] findings. Hypertension was present in 91.3% of individuals with RLS, and 43.5% had diabetes. Smoking and alcohol use were reported in 30.4% and 10.9% of patients in the RLS group, respectively. Despite previous studies indicating that alcohol consumption increases the risk of RLS in the general population,[14] no significant association was found between alcohol use and RLS in this study.

Biochemically, hemoglobin levels were significantly lower in the RLS group ($P = 0.02$), but no significant differences were observed in other parameters, including serum iron, ferritin, albumin, calcium, and PTH levels. Psychosocially, individuals with RLS exhibited significant differences in anxiety, depression, and sleep quality. In the RLS group, 67.4% had borderline anxiety and 26.1% had borderline depression, compared to lower percentages in the non-RLS group. In addition, poor sleep quality was notably prevalent in the RLS group, with 97.8% reporting abnormal PSQI scores ($P = 0.001$), consistent with the findings of Lin et al.[7]

The mean duration of hemodialysis was higher in the RLS group (3.87 ± 3.61 years) compared to the non-RLS group (3.27 ± 2.98 years), although this differs from Das et al.,[9] who reported a mean duration of 4.18 ± 3.21 years in the RLS group and 1.84 ± 2.9 years in the non-RLS group.

This study has several limitations. The cross-sectional design prevents conclusions about causality or the direction of the observed relationships. In addition, the study's single-center nature limits the generalizability of the findings, and the exclusion of peritoneal dialysis patients restricts comparisons between different dialysis modalities.

Despite these limitations, the study has notable strengths. The large sample size allowed for robust analysis, and the use of validated tools provided comprehensive insights into the psychosocial and clinical impacts of RLS. This study is one of the few conducted in India to assess the quality of life in individuals with ESRD and RLS, offering valuable perspectives on this under-researched population.

Conclusion

This study found a 14.9% prevalence of RLS in individuals with ESRD undergoing hemodialysis. Significant associations were observed between RLS and poor sleep quality, as well as between RLS and increased levels of anxiety and depression. While hemoglobin levels were significantly lower in the RLS group, most other biochemical parameters did not show significant differences between groups. These results underscore the importance of routine screening and early identification of RLS to effectively manage its psychosocial and clinical impact.

Author contributions

AVA: conceptualisation; data curation; formal analysis; investigation; writing-original draft preparation. AM: conceptualisation; project administration; resources; visualisation; writing-review and editing. MJ: supervision; validation; writing-review and editing. ME: supervision; validation; writing-review and editing. PR: supervision; validation; writing-review and editing. PA: supervision; validation; writing-review and editing.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Data availability statement

The data that support the findings of this study are available from the corresponding author (AM) upon reasonable request.

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