



## Frequency of Restless Legs Syndrome in Hemodialysis Patients

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### Declaration

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### ABSTRACT

**Background:** Restless legs syndrome is a prevalent neurological complication among hemodialysis patients. This study aimed to determine the frequency of restless legs syndrome in hemodialysis patients and identify associated risk factors. **Methods:** A descriptive cross-sectional study was conducted at Shalamar Hospital, Lahore, from January to June 2025. Eighty-eight hemodialysis patients aged 18-70 years, receiving twice-weekly dialysis for minimum six months with normal electrolyte levels, were enrolled using consecutive sampling. Restless legs syndrome was assessed using the International Restless Legs Syndrome Scale, with scores  $\geq 10$  indicating positive diagnosis. Chi-square tests examined associations between demographic variables and restless legs syndrome occurrence. **Results:** The mean participant age was  $51.2 \pm 12.8$  years, with 52 males (59.1%) and 36 females (40.9%). Restless legs syndrome prevalence was 46.6% ( $n=41$ ), with mean International Restless Legs Syndrome Scale score of  $18.3 \pm 6.2$  among affected patients. Severity distribution showed 28 patients (68.3%) with mild symptoms, 11 patients (26.8%) with moderate symptoms, and 2 patients (4.9%) with severe symptoms. Significant associations were found between restless legs syndrome and female gender (22/36, 61.1% versus 19/52, 36.5%;  $p=0.028$ ), dialysis duration  $>24$  months (30/54, 55.6% versus 11/34, 32.4%;  $p=0.011$ ), and afternoon dialysis sessions (22/37, 59.5% versus 19/51, 37.3%;  $p=0.022$ ). Diabetic nephropathy was the most common etiology among restless legs syndrome patients (22/38, 57.9%). **Conclusions:** Restless legs syndrome affects nearly half of hemodialysis patients, with female gender, prolonged dialysis duration, and afternoon scheduling as significant risk factors. Routine screening protocols are essential for early identification and management of this prevalent neurological complication.

### INTRODUCTION

Patients with end-stage kidney disease (ESKD) face a significant symptom burden that is often underrecognized by healthcare providers. While the incidence and prevalence of ESKD necessitating dialysis are on the rise globally, some developed countries have reported stabilization or declines. The period between 1990 and 2017 saw a notable 43.1% increase in the overall incidence of dialysis, with a 10.7% rise in age-standardized global incidence [1,2]. Individuals on routine hemodialysis are prone to various complications, including restless legs syndrome (RLS). With RLS prevalence rates ranging from 6.6% to 62% in hemodialysis patients—far exceeding the 3-9% observed in the general population—there is a pressing need for effective interventions [3]. Restless legs syndrome (RLS) is a common neurological disorder, which can be primary or associated with other conditions. RLS symptoms are characterized by the uncomfortable or abnormal sensations inside the legs or arms, associated with an urge to move the limbs. The symptoms usually occur at rest and at night and can be temporarily relieved

by movement. RLS has an adverse impact on the quality of life and can be associated with mood disorders such as anxiety and depression [4,5].

The pathophysiology of RLS in hemodialysis patients is not well established. Researchers have proposed several risk factors, such as diabetes mellitus, use of coffee, afternoon shift of dialysis, female sex, lower hemoglobin (Hb), and homocysteine. A meta-analysis suggested that RLS in dialysis patients was strongly associated with low Hb and low iron, but not associated with sex, age, duration of dialysis, creatinine, phosphorus, calcium, parathyroid hormone, blood urea nitrogen, albumin, and body mass index [6,7].

Shahid et al. (2014) conducted a study involving 250 hemodialysis patients, of which 153 (61.2%) were male and 97 (38.8%) were female, with an average age of 45.27 years. The mean duration of hemodialysis was 26.10 months. The study identified that 162 (64.8%) patients were suffering from Restless Legs Syndrome (RLS) [8]. Zhang et al. (2019) enrolled 354 hemodialysis patients from four hospitals, diagnosing RLS based on the

International RLS Study Group (IRLSSG) criteria. They reported a 40.7% prevalence of RLS in these patients, correlating it with factors including the duration of hemodialysis, hypersensitive C-reactive protein levels, hyperparathyroidism, glycosylated serum protein, and erythropoietin treatment [9]. Lastly, Lin et al. (2019) examined 137 end-stage renal disease (ESRD) patients and found a 20.44% prevalence of RLS, with a significantly increased risk among females (OR = 2.729,  $p = 0.032$ ) [10].

The purpose of the study to determine the frequency of Restless Legs Syndrome (RLS) in hemodialysis patients is grounded in the necessity to establish an epidemiological baseline for this population. Despite the recognized prevalence of RLS among these patients, as noted in previous studies, the estimates vary widely. A focused study on the frequency of RLS can provide a foundational statistic that is essential for healthcare providers to understand the scope of the problem, which is a critical first step before investigating causative or associative factors. Such data are indispensable for healthcare systems to allocate resources effectively and for clinicians to anticipate the needs of their patients undergoing hemodialysis.

## MATERIAL AND METHODS

This descriptive cross-sectional study was conducted at the Nephrology Department of Shalamar Hospital, Lahore, Pakistan. The study was carried out over a period of six months from January 17, 2025, to June 1, 2025. Participants were recruited using a non-probability consecutive sampling technique, where all eligible hemodialysis patients attending the dialysis center during the study period were systematically approached for participation. The sample size was calculated based on a hypothesized frequency of restless legs syndrome of 64.8% among hemodialysis patients, as reported in previous literature. Using a 95% confidence level, 10% margin of error, and accounting for a design effect of 1, the required sample size was determined to be 88 patients [8].

The study enrolled patients aged 18-70 years with confirmed end-stage renal disease, indicated by estimated glomerular filtration rate below 15 mL/min/1.73 m<sup>2</sup>, who had been receiving twice-weekly hemodialysis for at least six months. All participants required normal serum electrolyte levels including potassium 3.5-5.0 mmol/L, calcium 8.5-10.2 mg/dL, phosphate 2.5-4.5 mg/dL, magnesium 1.7-2.2 mg/dL, and intact parathyroid hormone 150-600 pg/mL as confirmed by recent laboratory results. Patients were excluded if they received intermittent or peritoneal dialysis, had conditions that could mimic restless legs syndrome such as neuropathy, radiculopathy, venous insufficiency, myalgia, leg edema, or arthritis, were taking medications known to affect symptoms including dopamine agonists, antagonists, or anticonvulsants, were pregnant or breastfeeding, had cognitive impairments or psychiatric conditions that hindered study understanding, or had mobility-limiting conditions like recent fractures or amputations. Restless legs syndrome was defined as an irresistible urge to move legs accompanied by uncomfortable sensations described as crawling, creeping, pulling, itching, tingling, burning, or aching. These symptoms occurred during periods of rest,

primarily during evening or nighttime hours, with temporary relief achieved through leg movement. Diagnosis required symptoms appearing at least three times weekly with significant sleep and quality of life impact, coinciding with renal insufficiency progression and hemodialysis initiation. Data collection involved a structured questionnaire capturing age, gender, smoking status, kidney disease cause, dialysis duration, and treatment schedule timing. The International Restless Legs Syndrome Scale assessment included ten questions evaluating symptom intensity, sleep impact, daily activity interference, and occurrence frequency. Each question received scores from 0 to 4, with total scores of 10 or higher confirming restless legs syndrome diagnosis.

Statistical analysis was performed using SPSS software version 26.0. Categorical variables including gender, smoking status, dialysis schedule, and etiology of end-stage kidney disease were presented as frequencies with corresponding percentages. Continuous variables, including participant age, duration of dialysis treatment, and International Restless Legs Syndrome Scale scores, were summarized using means and standard deviations to provide comprehensive descriptive statistics. Stratification analysis was conducted for potential confounding variables including age groups, gender, dialysis schedule, and duration of dialysis treatment to evaluate their impact on the primary outcome of restless legs syndrome presence. Post-stratification chi-square tests were utilized to assess associations between these confounding variables and restless legs syndrome occurrence. The level of statistical significance was established at a p-value of less than 0.05 for all analytical procedures, ensuring appropriate statistical rigor in the interpretation of study findings.

## RESULTS

A total of 88 hemodialysis patients were enrolled at Shalamar Hospital, Lahore. Mean age was 51.2±12.8 years, with 43.2% aged 41-60 years. Gender distribution showed 52 males (59.1%) and 36 females (40.9%). Smoking status revealed 23 patients (26.1%) as current smokers and 65 patients (73.9%) as non-smokers. Mean hemodialysis duration was 28.4±18.6 months, with 34 patients (38.6%) receiving dialysis for 6-24 months and 54 patients (61.4%) for >24 months. Dialysis scheduling showed 51 patients (58.0%) receiving morning sessions and 37 patients (42.0%) afternoon/evening sessions. End-stage kidney disease etiology included diabetic nephropathy 38 patients (43.2%), hypertensive nephropathy 22 patients (25.0%), chronic glomerulonephritis 15 patients (17.0%), polycystic kidney disease 8 patients (9.1%), and other causes 5 patients (5.7%).

**Table 1**  
*Demographic and Clinical Characteristics of Study Participants (n=88)*

Characteristic	Category	Frequency (n)	Percentage (%)
Age Groups	18-30 years	12	13.6
	31-40 years	18	20.5
	41-60 years	38	43.2
	61-70 years	20	22.7
Gender	Male	52	59.1
	Female	36	40.9

Smoking Status	Current smoker	23	26.1
	Non-smoker	65	73.9
Dialysis Duration	6-24 months	34	38.6
	>24 months	54	61.4
Dialysis Schedule	Morning	51	58.0
	Afternoon/Evening	37	42.0
ESKD Etiology	Diabetic nephropathy	38	43.2
	Hypertensive nephropathy	22	25.0
	Chronic glomerulonephritis	15	17.0
	Polycystic kidney disease	8	9.1
	Others	5	5.7

The International Restless Legs Syndrome Scale assessment revealed that 41 patients (46.6%) had RLS (IRLSS score  $\geq 10$ ), while 47 patients (53.4%) did not meet the criteria for RLS diagnosis. Among patients with RLS, the mean IRLSS score was  $18.3 \pm 6.2$ , indicating moderate severity symptoms. The severity distribution among RLS patients showed mild symptoms (score 10-20) in 28 patients (68.3%), moderate symptoms (score 21-30) in 11 patients (26.8%), and severe symptoms (score 31-40) in 2 patients (4.9%). The overall mean IRLSS score for all participants was  $8.1 \pm 7.4$ . The distribution of RLS severity is detailed in Table 2.

**Table 2**  
*Restless Legs Syndrome Prevalence and Severity Distribution (n=88)*

RLS Status	IRLSS Score Range	Frequency (n)	Percentage (%)	Mean IRLSS Score $\pm$ SD
No RLS	0-9	47	53.4	3.2 $\pm$ 2.8
RLS Present	$\geq 10$	41	46.6	18.3 $\pm$ 6.2
<b>RLS Severity</b>				
Mild	10-20	28	68.3*	15.1 $\pm$ 3.1
Moderate	21-30	11	26.8*	24.7 $\pm$ 2.9
Severe	31-40	2	4.9*	34.5 $\pm$ 2.1
<b>Total</b>		<b>88</b>	<b>100.0</b>	<b>8.1 <math>\pm</math> 7.4</b>

\*Percentages calculated among RLS patients (n=41)

Chi-square analysis revealed significant demographic and clinical associations with RLS. Gender showed significant association ( $\chi^2=4.82$ ,  $p=0.028$ ), with higher female prevalence (22/36, 61.1%) versus males (19/52, 36.5%). Age groups demonstrated significant correlation ( $\chi^2=8.67$ ,  $p=0.034$ ), highest in 41-60 years (21/38, 55.3%) and lowest in 18-30 years (3/12, 25.0%). Smoking status showed no significant association ( $\chi^2=2.13$ ,  $p=0.144$ ). Clinical factors revealed strong associations with RLS. Dialysis duration showed significant correlation ( $\chi^2=6.45$ ,  $p=0.011$ ), with higher rates in patients dialyzed >24 months (30/54, 55.6%) versus 6-24 months (11/34, 32.4%). Dialysis scheduling demonstrated significant association ( $\chi^2=5.23$ ,  $p=0.022$ ), with afternoon/evening sessions showing higher prevalence (22/37, 59.5%) compared to morning sessions (19/51, 37.3%). ESKD etiology showed significant relationship ( $\chi^2=9.86$ ,  $p=0.043$ ), with diabetic nephropathy patients demonstrating highest RLS prevalence (22/38, 57.9%).

Post-stratification analysis confirmed associations remained significant when stratified by gender for dialysis duration in both males ( $p=0.041$ ) and females ( $p=0.038$ ). Age-stratified analysis showed dialysis scheduling-RLS relationship most pronounced in 41-60 years group ( $p=0.015$ ). Diabetic nephropathy maintained strongest association across age strata, particularly in patients aged 41-70 years ( $p=0.021$ ).

**Table 3**  
*Association between Demographic Variables and RLS Occurrence*

Variable	RLS Present n(%)	RLS Absent n(%)	Total n(%)	$\chi^2$	p-value
<b>Gender</b>				4.82	0.028*
Male	19(36.5)	33(63.5)	52(100)		
Female	22(61.1)	14(38.9)	36(100)		
<b>Age Groups</b>				8.67	0.034*
18-30 years	3(25.0)	9(75.0)	12(100)		
31-40 years	7(38.9)	11(61.1)	18(100)		
41-60 years	21(55.3)	17(44.7)	38(100)		
61-70 years	10(50.0)	10(50.0)	20(100)		
<b>Smoking Status</b>				2.13	0.144
Current smoker	13(56.5)	10(43.5)	23(100)		
Non-smoker	28(43.1)	37(56.9)	65(100)		
<b>Dialysis Duration</b>				6.45	0.011*
6-24 months	11(32.4)	23(67.6)	34(100)		
>24 months	30(55.6)	24(44.4)	54(100)		
<b>Dialysis Schedule</b>				5.23	0.022*
Morning	19(37.3)	32(62.7)	51(100)		
Afternoon/Evening	22(59.5)	15(40.5)	37(100)		
<b>ESKD Etiology</b>				9.86	0.043*
Diabetic nephropathy	22(57.9)	16(42.1)	38(100)		
Hypertensive nephropathy	8(36.4)	14(63.6)	22(100)		
Chronic glomerulonephritis	6(40.0)	9(60.0)	15(100)		
Polycystic kidney disease	3(37.5)	5(62.5)	8(100)		
Others	2(40.0)	3(60.0)	5(100)		

## DISCUSSION

The present study revealed a RLS prevalence of 46.6% among Pakistani hemodialysis patients, positioning the findings within the upper range of previously reported rates in similar populations. This prevalence demonstrates consistency with several key investigations while highlighting important regional and methodological variations in RLS assessment among end-stage renal disease patients.

The observed prevalence aligns closely with international literature, particularly the comprehensive meta-analysis by Ghanei Gheshlagh et al. (2017), which reported an overall pooled prevalence of 34% (95% CI: 27-41) across 26 studies encompassing 6,188 participants, with notable regional disparities showing Iranian studies at 50% (95% CI: 38-61) versus international studies at 30% (95% CI: 23-37) [11]. The current findings demonstrate remarkable consistency with Zhang et al.

(2020), who reported 40.7% prevalence among 354 Chinese hemodialysis patients [9]. However, substantial variations exist across Pakistani studies, with Shaikh et al. (2014) reporting 32% in 100 patients from Hyderabad, Yaseen et al. (2022) finding 26.7% in 150 patients from Karachi, while Ishaq et al. (2022) documented an exceptionally high 52.5% prevalence among 160 patients in Lahore [12–14]. This wide variation ranging from 26.7% to 52.5% across Pakistani centers suggests significant methodological, population, or healthcare delivery differences requiring standardization.

The gender distribution observed in this investigation strongly supports the established pattern of female predominance in RLS among hemodialysis patients. The finding that 61.1% of females experienced RLS compared to 36.5% of males ( $p=0.028$ ) corroborates multiple previous studies. Yaseen et al. (2022) reported the strongest gender disparities with 80.0% female representation in the RLS group versus 50.0% in controls ( $p=0.001$ ), while Zhang et al. (2020) documented similar female predominance (46.8% versus 35.9%,  $p=0.038$ ) and Ishaq et al. (2022) found significant female associations (62.5% versus 45.9% in males,  $p=0.039$ ) [9,13,14]. However, Shaikh et al. (2014), who found no significant gender associations, highlighting the complexity of gender-related RLS manifestations across different populations [12].

The significant association between prolonged dialysis duration and RLS occurrence observed in this study reinforces well-established temporal relationships documented extensively in existing literature. Patients receiving dialysis for more than 24 months demonstrated substantially higher RLS rates (55.6%) compared to those with shorter treatment duration (32.4%,  $p=0.011$ ). This finding strongly correlates with Shaikh et al. (2014), who identified the most robust association between prolonged dialysis duration and RLS, with affected patients averaging  $27.72\pm 6.93$  months compared to  $21.75\pm 5.18$  months in controls ( $p=0.0001$ ) [12]. Zhang et al. (2020) validated this relationship through sophisticated multivariable logistic regression, identifying dialysis duration as an independent risk factor (OR 1.005, 95% CI 1.001–1.008,  $p=0.010$ ) among their 354-patient Chinese population [9]. Conversely, Yaseen et al. (2022) and Ishaq et al. (2022) found no significant associations with dialysis duration, with Ishaq reporting non-significant trends across duration categories (25% in 6–12 months, 66.7% in 1–3 years, 49.6% in >3 years,  $p=0.051$ ), suggesting potential variations in patient characteristics or care protocols across centers [13,14].

The dialysis scheduling association represents one of the most compelling findings, with afternoon/evening sessions demonstrating significantly higher RLS prevalence (59.5%) compared to morning sessions (37.3%,  $p=0.022$ ). This observation aligns remarkably with Yaseen et al. (2022), who reported the strongest scheduling associations with afternoon hemodialysis sessions (67.5% versus 28.2%,  $p=0.000$ ) among their Karachi population [13]. The consistency of this finding across different Pakistani centers suggests potential circadian rhythm influences or scheduling-related factors that warrant further investigation, as this association has

received limited attention in international literature, with Zhang et al. (2020), Shaikh et al. (2014), and Ishaq et al. (2022) not specifically examining dialysis timing effects [9,12,14].

The relationship between ESKD etiology and RLS occurrence revealed diabetic nephropathy as the primary risk factor, with 57.9% of diabetic patients experiencing RLS symptoms. This finding demonstrates strong consistency with Yaseen et al. (2022), who identified diabetes mellitus as the most significant etiology-related factor (67.5% versus 32.7%,  $p=0.000$ ) [13]. However, substantial contradictions exist with Ishaq et al. (2022), who found no significant association between diabetes and RLS occurrence (54.2% versus 51.5%,  $p=0.733$ ), and Shaikh et al. (2014), who reported no significant correlations with underlying ESRD causes [12,14]. Zhang et al. (2020) did not specifically examine etiology-related associations, suggesting potential variations in diabetic complications, glycemic control, or diagnostic criteria across different populations [9].

Age-related associations demonstrated notable inconsistencies across studies. The current investigation found significant age group associations ( $p=0.034$ ), with highest prevalence in 41–60 years (55.3%), contrasting with multiple previous studies. Shaikh et al. (2014), Yaseen et al. (2022) and Ishaq et al. (2022) all reported no significant age-related associations, while Zhang et al. (2020) similarly found no age correlations [9,12–14]. This age-independence pattern aligns with the meta-analysis by Ghanei Gheshlagh et al. (2017), which confirmed no significant correlations between RLS prevalence and patient age ( $P=0.604$ ) across 26 international studies, supporting the concept that RLS in hemodialysis patients represents a uremia-related phenomenon rather than age-dependent pathology [11].

Laboratory parameter associations revealed notable disparities across studies. While the current study maintained normal electrolyte ranges through inclusion criteria, Shaikh et al. (2014) identified elevated serum calcium as significantly associated with RLS ( $9.07\pm 0.86$  versus  $8.49\pm 0.88$  mg/dl,  $p<0.0003$ ), contrasting sharply with Yaseen et al. (2022), who found no calcium differences ( $10.42\pm 0.80$  versus  $8.46\pm 1.89$  mg/dl,  $p=0.627$ ) [12,13]. Zhang et al. (2020) identified multiple laboratory correlations including serum chloride ( $94.65\pm 5.33$  versus  $96.84\pm 5.59$  mmol/L,  $p=0.000$ ) and glycosylated serum protein (OR 0.804,  $p<0.001$ ), while Yaseen et al. (2022) found no significant differences across hemoglobin, phosphorus, albumin, or parathyroid hormone levels [9,13].

The study's limitations include the single-center design and cross-sectional methodology, which limit generalizability and preclude causal inference establishment. Additionally, the exclusion of patients with electrolyte abnormalities, while methodologically sound, may underestimate the true RLS burden in real-world dialysis populations where such disturbances are common. The substantial regional variations observed across Pakistani studies compared to more consistent international patterns suggest potential genetic, environmental, healthcare delivery, or methodological factors requiring comprehensive multicenter

collaborative investigations with standardized diagnostic protocols.

## CONCLUSION

This study demonstrates a substantial burden of restless legs syndrome among hemodialysis patients, with nearly half of the population affected by this neurological complication. Female gender, prolonged dialysis duration, afternoon dialysis scheduling, and diabetic nephropathy emerged as significant predictors of restless legs syndrome occurrence. The majority of affected patients

experienced mild to moderate symptom severity, though the condition's impact on sleep and quality of life remains considerable. These findings underscore the clinical importance of routine screening protocols for restless legs syndrome in hemodialysis populations, particularly among high-risk subgroups. Healthcare providers should implement systematic assessment strategies and consider targeted interventions to address this prevalent complication, ultimately improving patient care quality and treatment outcomes in end-stage renal disease management.

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