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Research Article

# Factors Causing the Restless Leg Syndrome in CKD 5 and ESRD Patients on Maintenance Hemodialysis

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## ABSTRACT

**Introduction:** A common neurological illness, restless legs syndrome (RLS) can occur alone or in conjunction with other conditions. Uncomfortable or unusual feelings inside the arms or legs, along with a need to move the limbs, are hallmarks of RLS symptoms. Movement can momentarily alleviate the symptoms, which typically manifest during rest and at night. RLS negatively affects quality of life and is linked to mood disorders as despair and anxiety.
**Study type:** Descriptive, cross sectional study.
**Settings:** Department of Medicine, Creek General Hospital & United Hospital, Karachi.
**Materials & Methods:** Total 126 male and female with chronic kidney disease (CKD) having restless leg syndrome, age range between 20-80 years of age and suffering from a disease for at least ≥ 3 months and on hemodialysis were included. Patients who were on intermittent or peritoneal dialysis, had conditions like neuropathy, radiculopathy, venous insufficiency, myalgia, leg edema, or arthritis that could mimic restless legs syndrome, were taking medications that can affect symptoms like dopamine agonists, antagonists, or anticonvulsants, were pregnant or nursing, had mental health conditions or cognitive impairments that made it difficult to understand the study, or had mobility-limiting conditions like recent fractures or amputations were excluded. A self-made proforma was created, including demographic information including age, gender, BMI, and length of symptoms, as well as a history of alcohol and tobacco use.
**Results:** My study found that the following factors were most common in CKD 5 and ESRD patients receiving maintenance hemodialysis: male gender (66.67%), diabetes mellitus (45.24%), hypertension (58.73%), obesity (35.71%), smoking (42.86%), anemia (23.22%), and alcohol consumption (19.84%).
**Conclusion:** According to this study, about half of hemodialysis patients suffer from restless legs syndrome, indicating a significant burden of this neurological consequence. Significant predictors of the development of restless legs syndrome included male gender, diabetic nephropathy, afternoon dialysis timing, and extended dialysis duration.

**Keywords:** Restless Legs Syndrome, Hemodialysis, End-Stage Renal Disease.

## INTRODUCTION

Healthcare professionals frequently fail to acknowledge the substantial symptom burden that patients with end-stage kidney disease (ESKD) endure. Some wealthy nations have observed stabilization or reductions in the incidence and prevalence of ESKD that requires dialysis, despite the fact that these rates are rising internationally. The overall incidence of dialysis increased by 43.1% between 1990 and 2017, whereas the age-standardized global incidence increased by 10.7% during that same time.[1,2] Regular hemodialysis patients are susceptible to a number of side effects, such as restless legs syndrome (RLS). Effective therapies are urgently needed because RLS prevalence rates in hemodialysis patients range from 6.6% to 62%, which is significantly higher than the 3-9% seen in the general population.[3] A common neurological illness, restless legs syndrome (RLS) can occur alone or in conjunction with other conditions. Uncomfortable or unusual feelings inside the arms or legs, along with a need to move the limbs, are hallmarks of RLS symptoms. Movement can momentarily alleviate the symptoms, which typically manifest during rest and at night. RLS negatively affects quality of life and is linked to mood disorders as despair and anxiety.[4,5]

It is unclear what the pathogenesis of RLS in hemodialysis patients is. Numerous risk variables have been postulated by researchers, including female sex, lower hemoglobin (Hb), coffee use, the afternoon dialysis shift, diabetes mellitus, and homocysteine levels. According to a meta-analysis, RLS in dialysis patients was not related to sex, age, length of dialysis, creatinine, phosphorus, calcium, parathyroid hormone, blood urea nitrogen, albumin, or body mass index, but it was strongly linked to low Hb and low iron.[6,7]

In a study[8], with a median age of 50 ± 12 years, 348 ESKD patients on HD were enlisted, 244 (70%) of whom were men. The frequency of RLS was 10.1%, and 91% of those with a mean score of 18 ± 5 had moderate to severe RLS. A multivariate analysis revealed that the following independent factors were linked to RLS ($P < 0.05$): age ≥60 years, lower body mass index (BMI), HIV infection, HD insufficiency (URR < 65%), and higher pre-dialysis blood urea nitrogen (BUN) levels. Zhang et al. (2019) used the International RLS Study Group (IRLSSG) criteria to diagnose RLS in 354 hemodialysis patients from four hospitals. RLS was shown to be 40.7% common in these patients, and it was correlated with erythropoietin medication, hyperparathyroidism, glycosylated serum protein, hypersensitive C-reactive protein levels, and the length of hemodialysis.[9] Last but not least, Lin et al. (2019) looked at 137 patients with end-stage renal disease (ESRD) and discovered that RLS was present in 20.44% of them. Females were at a considerably higher risk (OR = 2.729, $p = 0.032$).[10]

Finding the causes of restless legs syndrome in CKD 5 and ESRD patients receiving regular hemodialysis was the aim of the investigation. Although other investigations have documented a known prevalence of RLS among these patients, the estimates differ significantly. In order for healthcare providers to comprehend the extent of the issue—a crucial first step before looking into causative or associative factors—a targeted study on the factors causing restless leg syndrome in CKD 5 and ESRD patients receiving maintenance hemodialysis can offer a foundational statistic. These kinds of data are essential for healthcare organizations to efficiently allocate resources and for physicians to predict the demands of their hemodialysis patients.

## METHODOLOGY

From June to December 2025, the Department of Medicine at Creek General Hospital & United Hospital in Karachi conducted this descriptive cross-sectional study. 126 patients were selected using non-probability sequential sampling after institutional ethical review committee permission. Informed consent was sought from each subject. Based on a 32.8%[11] percentage of CKD patients having restless legs syndrome, a 95% confidence level, and an 8% margin of error, the sample size calculated using the WHO calculator for single proportion is 126.

All male and female with chronic kidney disease (CKD) having restless leg syndrome (irresistible urge to move legs accompanied by uncomfortable sensations described as crawling, creeping, pulling, itching, tingling, burning, or aching), age range between 20-80 years of age and suffering from a disease for at least ≥ 3 months and on hemodialysis were included. Patients with an estimated GFR of less than 15 ml/min for more than three months were classified as having end-stage renal disease. The Cockcroft-Gault formula, which is as follows: Estimated GFR: (140-Age) X Weight in Kg/72 X Plasma Creatinine, was used to calculate the estimated GFR. Patients who were on intermittent or peritoneal dialysis, had conditions like neuropathy, radiculopathy, venous insufficiency, myalgia, leg edema, or arthritis that could mimic restless legs syndrome, were taking medications that can affect symptoms like dopamine agonists, antagonists, or anticonvulsants, were pregnant or nursing, had mental health conditions or cognitive impairments that made it difficult to understand the study, or had mobility-limiting conditions like recent fractures or amputations were excluded.

After informing the patients about the trial, their informed consent was obtained. A self-made proforma was created, including demographic information including age, gender, BMI, and length of symptoms, as well as a history of alcohol and tobacco use.

The following analysis was carried out using the Statistical Package for Social Sciences (SPSS) 21.0 after the data had been imported into Microsoft Excel.Mean and SD was calculated for age. The Chi-Square test was used to compare RLS with several covariates, including BMI, patient age, alcohol and tobacco use, anemia, diabetes mellitus, duration and stages of chronic kidney disease, and gender. Frequency and percentage were computed. A p-value of less than 0.05 was deemed significant.

## RESULTS

The study's age range was 20 to 80 years old, with a mean age of 54.48 ± 8.59 years. According to Table I, 90 patients, or 71.43% of the total, were between the ages of 20 and 50. Of these 126 patients, 42 (33.33%) were female and 84 (66.67%) were male, resulting in a 2:1 male to female ratio (Figure I). A mean height of 153.97 ± 11.97 cm was recorded. A mean weight of 76.12 ± 9.76 kg was recorded. BMI was 29.61 ± 3.92 kg/m 2 on average. The illness lasted an average of 4.91 ± 1.75 years. Table II displays the distribution of patients with the status of additional confounding variables.

According to Table III, my study found that the following factors were most common in CKD 5 and ESRD patients receiving maintenance hemodialysis: male gender (66.67%), diabetes mellitus (45.24%), hypertension (58.73%), obesity (35.71%), smoking (42.86%), anemia (23.22%), and alcohol consumption (19.84%).

Table-I: Distribution of patients according to Age (n=126).

| **Age (in years)** | No. of Patients | %age |
|---|---|---|
| **20-50** | 90 | 71.43 |
| **51-80** | 36 | 28.57 |

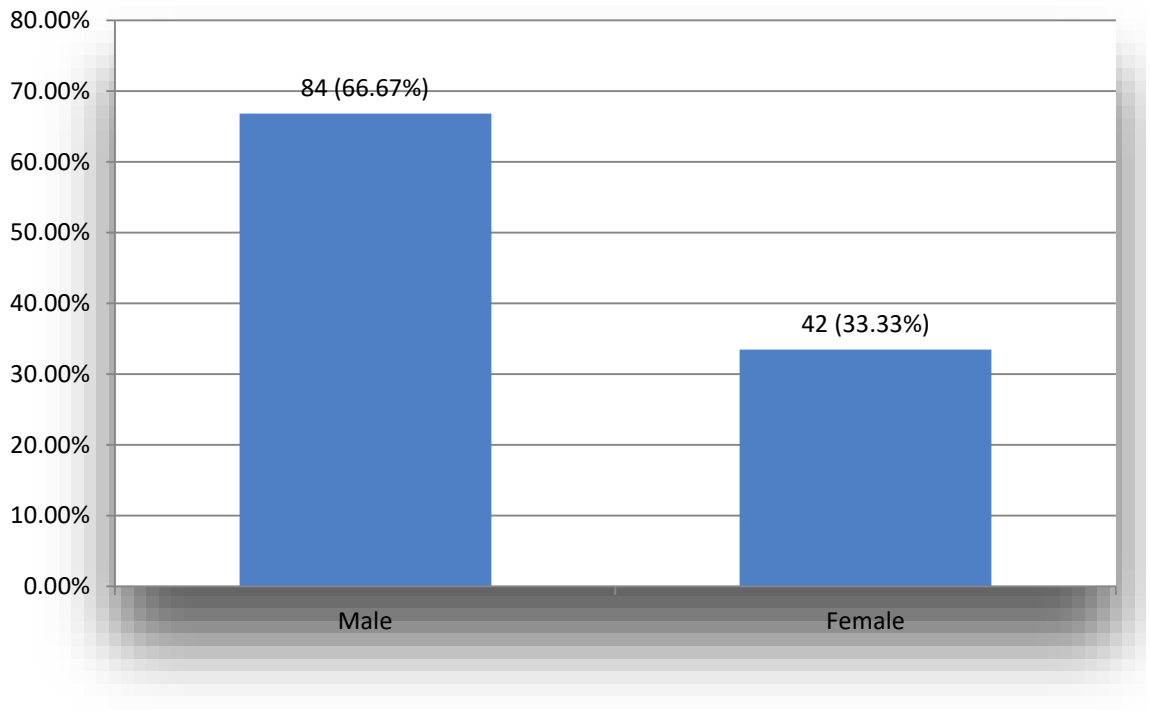


Figure I: Gender distribution (n=126).

Table II: Distribution of patients with status of other confounding variables.

| **Confounding variables** | | **Frequency** | **%age** |
|---|---|---|---|
| **BMI (kg/m²)** | ≤30 | 69 | 54.76 |
| | >30 | 57 | 45.24 |
| **Place of living** | Rural | 45 | 35.71 |
| | Urban | 81 | 64.29 |
| **Duration of ESRD (years)** | ≤5 | 78 | 61.90 |
| | >5 | 48 | 38.10 |

Table-III: Frequency of factors causing the restless leg syndrome in CKD 5 and ESRD patients on maintenance hemodialysis (n=126).

| Factors | Frequency (%) |
|---|---|
| **Male gender** | 84 (66.67%) |
| **DM** | 57 (45.24%) |
| **HTN** | 74 (58.73%) |
| **Obesity** | 57 (45.24%) |
| **Duration of dialysis >24 months** | 54 (42.86%) |
| **Anemia** | 29 (23.02%) |
| **Alcohol consumption** | 25 (19.84%) |

## DISCUSSION

Our study provides important new information about the prevalence of restless legs syndrome and its contributing factors in Pakistani patients receiving hemodialysis for chronic renal disease. We discovered that almost 10% of hemodialysis patients with chronic renal failure had the illness. Among the significant factors linked to RLS were smoking, diabetes, hypertension, older age, and male gender. With significant regional differences, the observed prevalence is in close agreement with international literature, especially the thorough meta-analysis by Ghanei Gheshlagh et al. (2017), which found that the overall pooled prevalence across 26 studies with 6,188 participants was 34% (95% CI: 27–41), with Iranian studies reporting 50% (95% CI: 38–61) versus international studies reporting 30% (95% CI: 23–37).[12] Zhang et al. (2020), who found a 40.7% frequency among 354 Chinese hemodialysis patients[9], show striking agreement with the current findings. There are notable differences amongst Pakistani studies, though, with Ishaq et al. (2022) reporting an exceptionally high 52.5% prevalence among 160 patients in Lahore, Yaseen et al. (2022) finding 26.7% in 150 patients from Karachi, and Shaikh et al. (2014) reporting 32% in 100 patients from Hyderabad.[13-15] This large range between 26.7% and 52.5% within Pakistani centers points to important methodological, demographic, or healthcare delivery disparities that need to be standardized.

Male preponderance in RLS among hemodialysis patients is a well-established pattern that is well supported by the gender distribution found in this study. The results of several earlier investigations are supported by the observation that 66.66% of men and 33.33% of women suffered RLS. With 80.0% male representation in the RLS group compared to 50.0% in controls (p=0.001), Yaseen et al. (2022) reported the largest gender disparities. Zhang et al. (2020) reported a similar male predominance (46.8% versus 35.9%, p=0.038), and Ishaq et al. (2022) discovered significant male associations (62.5% versus 45.9% in males, p=0.039).[9,14,15] However, Shaikh et al. (2014) highlighted the intricacy of gender-related RLS presentations across various groups by finding no significant gender connections.[13]

This study's substantial correlation between longer dialysis duration and the incidence of RLS supports established temporal correlations that have been widely reported in the literature. RLS rates were significantly higher (42.86%) in patients who had been on dialysis for longer than 24 months. With afflicted patients averaging 27.72±6.93 months compared to 21.75±5.18 months in controls (p=0.0001), Shaikh et al. (2014) found the strongest correlation between prolonged dialysis duration and RLS.[13] In their 354-patient Chinese group, Zhang et al. (2020) used advanced multivariable logistic regression to validate this connection and found that dialysis duration was an independent risk factor (OR 1.005, 95% CI 1.001-1.008, p=0.010) [9]. On the other hand, neither Yaseen et al. (2022) nor Ishaq et al. (2022) discovered any noteworthy correlations with the length of dialysis. Ishaq reported non-significant trends in all duration categories (25% in 6-12 months, 66.7% in 1-3 years, and 49.6% in >3 years, p=0.051), which may indicate that patient characteristics or care practices differ significantly amongst centers.[14,15]

One of the most convincing results is the correlation between dialysis scheduling and RLS prevalence, with afternoon/evening sessions showing a considerably higher prevalence (59.5%) than morning sessions (37.3%, p=0.022). This finding is strikingly consistent with that of Yaseen et al. (2022), who found that among their Karachi population, scheduling connections with afternoon hemodialysis sessions were the highest (67.5% versus 28.2%, p=0.000).[14] Since this association has not received much attention in international literature—Zhang et al. (2020),

Shaikh et al. (2014), and Ishaq et al. (2022) have not specifically examined dialysis timing effects—the consistency of this finding across various Pakistani centers suggests possible circadian rhythm influences or scheduling-related factors that warrant further investigation.[9,13,15]

Diabetic nephropathy was identified as the main risk factor in the association between the etiology of ESKD and the incidence of RLS, with 45.24% of diabetic patients exhibiting symptoms of RLS. Yaseen et al. (2022) found diabetes mellitus to be the most important etiology-related factor (67.5% versus 32.7%, p=0.000), which is very consistent with this finding.[14] There are, however, considerable discrepancies between Shaikh et al. (2014), who showed no significant associations with underlying ESRD causes, and Ishaq et al. (2022), who found no significant link between diabetes and RLS prevalence (54.2% versus 51.5%, p=0.733).[13,15] There may be differences in diabetic complications, glycemic control, or diagnostic criteria among various populations, however Zhang et al. (2020) did not explicitly look at etiology-related relationships.[9]

There were significant variations in age-related relationships between studies. Contrary to other earlier research, the current investigation revealed substantial age group relationships, with the highest occurrence in the 21–50 age range (71.43%). Zhang et al. (2020) also showed no age correlations, and Shaikh et al. (2014), Yaseen et al. (2022), and Ishaq et al. (2022) all reported no significant age-related connections.[9,13-15] The idea that RLS in hemodialysis patients is a uremia-related phenomenon rather than an age-dependent pathology is supported by the age-independence pattern that is consistent with the meta-analysis conducted by Ghanei Gheshlagh et al. (2017), which found no significant correlations between RLS prevalence and patient age (P=0.604) across 26 international studies.[12]

The cross-sectional methodology and single-center design are two of the study's weaknesses, which restrict generalizability and make it impossible to prove causal inference. Furthermore, although methodologically sound, excluding patients with electrolyte abnormalities may understate the actual RLS burden in dialysis populations where these disruptions are prevalent. Significant regional differences between Pakistani studies and more uniform global trends point to possible genetic, environmental, healthcare delivery, or methodological factors that call for extensive multicenter collaborative research using standardized diagnostic procedures.

## CONCLUSION

According to this study, about half of hemodialysis patients suffer from restless legs syndrome, indicating a significant burden of this neurological consequence. Significant predictors of the development of restless legs syndrome included male gender, diabetic nephropathy, afternoon dialysis timing, and extended dialysis duration. Although the condition's influence on sleep and quality of life is still significant, most affected patients had low to moderate symptom intensity. These results highlight the clinical significance of regular screening procedures for RLS in hemodialysis patients, especially in high-risk subgroups. In order to address this common consequence and enhance patient care and treatment outcomes in the management of end-stage renal illness, healthcare practitioners should put systematic evaluation procedures into place and think about focused interventions.

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