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ORIGINAL ARTICLE

The association between iron deficiency anemia and restless leg syndrome in dialysis-dependent patients.

Mehak Zaidi[1], Michelle Ahmad[2], Naeem Ullah[3], Gullali[4], Shaista Qamar[5], Faizan Banaras[6], Amjad Shahzad[7]

ABSTRACT… Objective: To evaluate the association between iron deficiency anemia (IDA) and restless leg syndrome (RLS) in dialysis-dependent patients. **Study Design:** Descriptive Cross-sectional study. **Setting:** Department of Nephrology, Khyber Teaching Hospital, Peshawar. **Period:** 16th July to 30th October 2025. **Methods:** A total of 108 patients undergoing maintenance hemodialysis for at least three months were included. Demographic, clinical, and laboratory parameters were recorded. IDA was defined as serum ferritin <100 ng/mL with transferrin saturation <20%. RLS was diagnosed using the International Restless Legs Syndrome Study Group (IRLSSG) criteria. Statistical analysis was performed using SPSS version 26. Chi-square and independent t-tests were applied, with $p \leq 0.05$ considered significant. **Results:** The mean age was 49.8 ± 13.2 years, with a male predominance (58.3%). IDA was present in 59.3% of patients, and overall RLS prevalence was 41.7%. Patients with IDA had a significantly higher occurrence of RLS compared to those without IDA (62.5% vs. 13.6%, $p < 0.001$). Mean hemoglobin and ferritin levels were lower in the RLS group ($p < 0.01$). Additionally, lower serum albumin and longer dialysis duration were independently associated with increased RLS prevalence. **Conclusion:** IDA is strongly associated with RLS in dialysis-dependent patients, and hypoalbuminemia may further increase risk. Early identification and management of IDA and nutritional deficits may improve patient outcomes.

Key words: Chronic Kidney Disease, Hemodialysis, Hypoalbuminemia, Iron Deficiency Anemia, Restless Leg Syndrome.

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INTRODUCTION

Restless Leg Syndrome (RLS) is a chronic sensorimotor neurological disorder characterized by an uncontrollable urge to move the legs, usually accompanied by discomfort or unpleasant sensations, and typically worsens during rest or at night—greatly disrupting sleep and overall quality of life.[1] Iron deficiency, particularly within central nervous system structures, is a central contributor to RLS pathogenesis through its effects on dopaminergic neurotransmission.[2] Indeed, secondary forms of RLS are prominently seen in conditions characterized by iron deficiency, such as IDA, chronic kidney disease (CKD), and pregnancy.[3]

In the general population, RLS affects approximately 5% to 10% of individuals, whereas the prevalence rises to 25%–43% among patients with IDA.[4] One robust study from Korea documented that among patients with IDA, RLS was present in 40.3%, and most experienced severe to very severe symptoms; these individuals also had notably poorer sleep quality and mood compared to those without RLS.[5]

In patients undergoing hemodialysis, the prevalence of RLS remains substantial. A recent global meta-analysis across 23,248 hemodialysis patients from 21 countries estimated an overall prevalence of 27.2%, which is significantly higher than in the general population.[6] Furthermore, meta-analytical evidence shows that dialysis patients with lower hemoglobin or iron levels are more susceptible to RLS, and diabetes mellitus increases RLS risk by about 24% in Asian cohorts.[7] Biochemical studies in dialysis populations also reveal significant associations between RLS and low hemoglobin, low ferritin, and habitual behaviors such as high coffee intake.[8]

Beyond iron deficiency, chronic inflammation and hypoalbuminemia may contribute to RLS in CKD patients, complicating the picture of its etiology.[9]

1. MBBS, Postgraduate Resident Nephrology, Khyber Teaching Hospital, Peshawar.
2. MBBS, Medical Officer, Khyber Teaching Hospital, Peshawar.
3. MBBS, Medical Officer ICU, Khyber Teaching Hospital, Peshawar.
4. MBBS, Medical Officer ICU, Khyber Teaching Hospital, Peshawar.
5. MBBS, Medical Officer ICU, Khyber Teaching Hospital, Peshawar.
6. MBBS, Postgraduate Resident Nephrology, Khyber Teaching Hospital, Peshawar.
7. MBBS, Intensivist, Medical Intensive Care Unit (ICU), Khyber Teaching Hospital, Peshawar.
Correspondence Address:
Dr. Amjad Shahzad
Intensive Care Unit (ICU), Khyber Teaching Hospital, Peshawar.
Janamjad147@gmail.com

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Studies in non-dialysis CKD patients have indicated that low ferritin and eGFR are independent predictors of RLS in older adults, even when adjusting for inflammatory markers.[10]

Given the high burden of IDA and RLS among dialysis-dependent individuals, particularly in resource-constrained healthcare environments, it is essential to evaluate their association. Identifying modifiable risk factors such as iron deficiency and nutritional status may guide targeted interventions aiming to alleviate RLS symptoms and enhance quality of life. This study therefore aimed to assess the association between IDA and RLS in dialysis-dependent patients, using stringent hematologic definitions and standardized clinical criteria.

METHODS

This descriptive cross-sectional study was conducted in the Nephrology Department of Khyber teaching hospital, Peshawar from 16th July to 30th Oct, 2025. The sample size was determined using the formula:

$n = (Z^2 \times p \times (1 - p)) / d^2$

Where Z = 1.96 (corresponding to the 95% confidence level), p = 41.7% (estimated prevalence of restless leg syndrome in hemodialysis patients)[11], and d = 8% margin of error. The formula is widely recommended for prevalence studies in health research.[12]

Non-probability consecutive sampling was applied. All patients aged 18–70 years on maintenance hemodialysis for at least three months and willing to provide informed consent were included. Patients with known progressive neurological disorders (e.g., Parkinson's disease or peripheral neuropathies), those receiving iron therapy within the past month, pregnant patients, and individuals with acute systemic illnesses were excluded.

Data were documented using a structured proforma, recording demographic variables, comorbid conditions (diabetes, hypertension, and cardiovascular disease), dialysis duration, and laboratory parameters including hemoglobin, serum ferritin, transferrin saturation (TSAT), and serum albumin. Iron deficiency anemia (IDA) was defined as serum ferritin <100 ng/mL with TSAT <20%. Restless leg syndrome (RLS) was diagnosed according to the International Restless Legs Syndrome Study Group (IRLSSG) criteria, administered via face-to-face structured interviews conducted by trained nephrology residents.

Serum inflammatory markers (such as C-reactive protein) and vitamin B12 or folate levels, which may influence both iron status and neurological symptoms, were not assessed in this study and thus could not be analyzed as potential confounders.

All data were entered and analyzed using SPSS version 26. Descriptive statistics—means ± standard deviations (SD) and frequencies with percentages—were calculated. Normality of continuous variables was assessed using the Shapiro–Wilk test. Since the data were normally distributed, independent t-tests were applied to compare group means, and Chi-square tests were used to assess associations between categorical variables. A p-value of ≤0.05 was considered statistically significant. Ethical approval was obtained from the Khyber medical college Peshawar, Ref No: 160/DME/KMC, Date: 17/03/2023.

RESULTS

This table presents the baseline demographic and clinical characteristics of the 108 patients included in the study. The mean age was 49.8 years, indicating a predominance of middle-aged individuals in this cohort. More than half were male, and over half had diabetes mellitus, which is consistent with the known high burden of metabolic comorbidities in dialysis populations. The mean serum ferritin and transferrin saturation (TSAT) values indicate that a substantial proportion had depleted iron stores. Overall, 59.3% of patients met the criteria for iron deficiency anemia (IDA), and 41.7% were diagnosed with restless leg syndrome (RLS), suggesting a considerable overlap of these two conditions.

This table shows how clinical and biochemical characteristics were associated with the presence of RLS. Patients with IDA had a markedly higher prevalence of RLS (62.5%) compared to those without IDA (13.6%) ($p < 0.00001$), highlighting iron deficiency as a key risk factor. Lower serum

albumin (<3.5 g/dL) was significantly associated with RLS, suggesting a possible role of poor nutritional status. Age above 50 years and dialysis duration >24 months also showed higher RLS rates, though the associations were weaker. Gender and diabetes status did not significantly influence RLS prevalence.

TABLE-I

Baseline demographic and clinical characteristics of dialysis-dependent patients

Variable	Frequency (n)	Percentage (%)
Mean Age (years)	49.8 ± 13.2	—
Gender	—	—
Male	63	58.3
Female	45	41.7
Mean BMI (kg/m²)	23.5 ± 4.9	—
Mean Duration of Dialysis (months)	28.1 ± 14.7	—
Diabetes Mellitus	55	50.9
Non-Diabetic	53	49.1
Mean Ferritin (ng/mL)	118.2 ± 55.7	—
Mean TSAT (%)	19.5 ± 6.8	—
Iron Deficiency Anemia	64	59.3
Restless Leg Syndrome	45	41.7

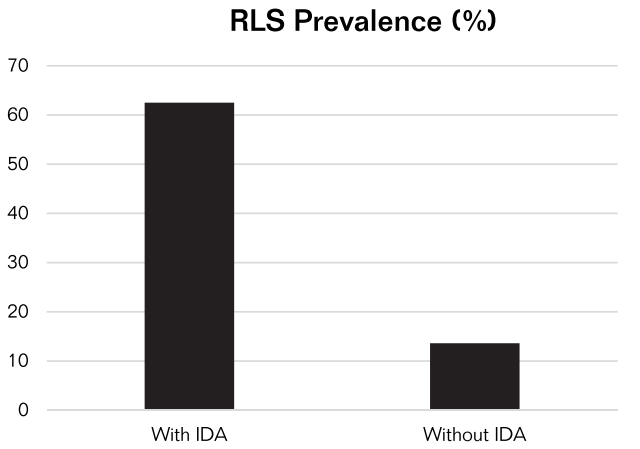
TABLE-II

Prevalence of RLS stratified by demographic and biochemical risk factors

Risk Factor	RLS Prevalence (%)	P-Value
Age > 50 years	48.9	0.042[a]
Age ≤ 50 years	34.0	0.042[a]
Gender	—	—
Male	42.9	0.821[b]
Female	40.0	0.821[b]
Dialysis Duration > 24 months	46.2	0.058[b]
Dialysis Duration ≤ 24 months	36.4	0.058[b]
BMI > 25 kg/m²	35.5	0.153[b]
BMI ≤ 25 kg/m²	45.9	0.153[b]
Serum Albumin < 3.5 g/dL	55.6	0.003[b]
Serum Albumin ≥ 3.5 g/dL	29.8	0.003[b]
Iron Deficiency Anemia	62.5	<0.00001[b]
No Iron Deficiency Anemia	13.6	<0.00001[b]

FIGURE-1

Prevalence of restless leg syndrome (RLS) among dialysis-dependent patients with and without iron deficiency anemia (IDA). Patients with IDA demonstrated a markedly higher RLS prevalence (62.5%) compared to those without IDA (13.6%), highlighting a strong association between iron status and neurological symptoms.



DISCUSSION

In our cohort of dialysis-dependent patients, the prevalence of Restless Legs Syndrome (RLS) was 41.7%, which aligns closely with global and regional findings in similar populations. A systematic meta-analysis of 23,248 hemodialysis patients across 21 countries reported a pooled prevalence of 27.2%, with variation by region—from Africa (39.0%) to Asia (25.7%) and Europe (29.8%)—but significantly higher in smaller studies like ours (under 100 patients), suggesting sampling bias may influence estimates.[13]

Notably, a Saudi Arabian study observed an RLS prevalence of 50.2% among hemodialysis patients, considerably higher than our findings, possibly reflecting genetic or environmental differences, as well as diagnostic methods.[14] Similarly, a multicenter Chinese study reported prevalence rates reaching 62%, emphasizing potential geographic disparities.[15] In contrast, studies from Iran, Japan, and Brazil have shown lower prevalence—ranging from 15.8% to 26.6%—indicative of variability driven by population characteristics and methodology.[16]

The strong association we observed between iron deficiency anemia (IDA) and RLS—where 62.5% of patients with IDA experienced RLS versus only

13.6% without IDA—is consistent with findings from a Korean cross-sectional study reporting a 40.3% RLS prevalence among patients with IDA, most exhibiting moderate to very severe symptoms.[17] Furthermore, in community-based samples of IDA patients (non-dialysis), RLS prevalence was nearly 24%, a ninefold increase over the general population, with significant sleep and energy impairment.[18] These results collectively support the role of systemic iron deficiency in RLS pathogenesis.

Our study also highlighted hypoalbuminemia as a novel associated risk factor—patients with albumin below 3.5 g/dL showed significantly higher RLS rates (55.6%) compared to those with normal albumin levels (29.8%). This aligns with evidence from CKD-related populations indicating that malnutrition-inflammation may contribute to neurological symptoms, though most studies focus on ferritin and hemoglobin rather than broader nutritional markers.[19]

Unlike some international cohorts, we found no significant gender difference in RLS prevalence—an observation similar to findings from a Saudi dialysis center[14] and several studies in European cohorts.[13] This may suggest that in dialysis populations, traditional sex differences in RLS prevalence could be attenuated by shared risk factors such as uremia and iron metabolism disturbances.

In terms of dialysis duration, although not statistically significant, patients with more than two years on dialysis had numerically higher RLS prevalence (46.2% vs. 36.4%), suggesting a trend toward cumulative risk—consistent with BMC Neurology findings where longer dialysis vintage was occasionally linked to greater RLS risk, albeit inconsistently across studies.[16]

These findings collectively underscore the multifactorial nature of RLS in the dialysis-dependent population—where iron deficiency clearly plays a central role, but nutritional status and chronicity of dialysis may also contribute.

Strengths of our study include stringent use of IRLSSG diagnostic criteria, comprehensive iron status assessment, and inclusion of nutritional markers like serum albumin. However, limitations deserve mention: our single-center design limits generalizability; we lacked inflammatory marker data such as CRP or hepcidin, which may influence iron mobilization and RLS, and we did not perform polysomnography to objectively confirm RLS severity.

CONCLUSION

In this study of dialysis-dependent patients, restless leg syndrome was found in over two-fifths of participants, with a markedly higher prevalence among those with iron deficiency anemia. The strong association between depleted iron stores and RLS underscores the importance of routine iron status assessment in the dialysis population. Hypoalbuminemia also emerged as a significant correlate, suggesting that poor nutritional status may exacerbate neurological symptoms. Regular screening for RLS, coupled with targeted correction of iron deficiency and nutritional optimization, may improve patient comfort, sleep quality, and overall quality of life. Multicenter prospective studies are warranted to further explore causal pathways and to evaluate the efficacy of iron and nutritional interventions in reducing RLS burden.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Mehak Zaidi:** Conception.
2	**Michelle Ahmad:** Drafting.
3	**Naeem Ullah:** Data collection.
4	**Gullali:** Interpretation of data.
5	**Shaista Qamar:** Data entry.
6	**Faizan Banaras:** Critical revision.
7	**Amjad Shahzad:** Data analysis.