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## Restless leg syndrome in patients on hemodialysis

**Mazharulhaq**

Assistant Professor Nephrology, Institute of Kidney Diseases, Hayatabad Peshawar

**Zahid Ahmad**

Assistant Consultant Nephrology, Quaid e Azam International Hospital, Islamabad

**Ayesha Arshad**

Consultant Nephrology, PAF Hospital, Islamabad  
Corresponding author email: [mayeshaarshad88@hotmail.com](mailto:mayeshaarshad88@hotmail.com)

**Kulsoom Ilyas**

Nephrologist / Medical Specialist, Doctors Plus Pharmacy and Diagnostics, Sector A, Bahria Enclave Islamabad

**Behzad Kaleem Baloch**

Assistant Prof Nephrology, Mufti Mehmood Teaching Hospital, Dera Ismail Khan

**Abstract**--Background and Aim: Restless legs syndrome (RLS) is a prevalent neurological disease that is frequently misdiagnosed due to comparable signs and symptoms to other disorders such as diabetes, migraine, and cardiovascular disease. RLS may deteriorate with age, and it is more frequent in women than in males. The incidence of RLS varies from 6.6% to 80% in the general population. The present study aimed to assess the RLS in patients on hemodialysis. Patients and Methods: A questionnaire based study was conducted on 116 consecutive hemodialysis patients in the Department of Neurology and Nephrology of Institute of Kidney Diseases Hayatabad, Peshawar and PAF Hospital, Islamabad for the Duration from June 2022 to December 2022. Patients' history included a history of drug, predialysis duration, and hemodialysis duration. Data was obtained using a standardized questionnaire that includes demographic variables such as personal history, family history, disease history, and smoking history. This self-structured questionnaire also includes the four RLS research group requirements a) leg pain caused by desire to move the legs, b) inactivity or rest worsening symptoms, c) Movement causing relief in symptoms, and d) Symptoms are more bothersome in

the evening and at night than during the day. SPSS version 27 was used for data analysis. Results: The overall mean age of hemodialysis patients (HD) and control was  $32.8 \pm 10.4$  and  $40.6 \pm 10.6$  years respectively. The prevalence of RLS was 8.6% (n=10) among the studied population. There were 64 healthy subjects investigated as a control group. Out of 116 HD cases, there were 96 (82.8%) male and 20 (17.2%) females. The incidence of delayed sleep onset was found in 80% (n=8) cases among HD patients with RLS. Based on John Hopkins Restless Legs Severity Scale (JHRLSS), the incidence of mild, moderate, and severe RLS was 3 (30%), 2 (20%), and 5 (50%) respectively. The grade 3 and grade 4 severity of RLS was found in three and five patients respectively. There were no statistical significance found in duration of hemodialysis, age, predialysis duration, and erythropoietin use in patients with and without RLS. Conclusion: The present study found that the prevalence of RLS was 8.6%. Additionally, the sleep difficulties linked with RLS might be a substantial health risk.

**Keywords**---Hemodialysis, Restless leg syndrome, RLS severity.

## **Introduction**

Restless legs syndrome is a neurological disorder characterized by extremity movement accompanied by unpleasant feeling and sensation that is usually misdiagnosed with other diseases such as migraine, diabetes, and cardiovascular diseases [1]. It is primarily an inevitable disease, but can sometimes occur in conjunction with other medical disorders (secondary RLS), such as iron deficiency and pregnancy. Uremic RLS is a kind of secondary RLS that usually arises in chronic kidney disease. The International RLS Study Group (IRLSSG) agreement establishes the four basic diagnostic criteria for RLS [2]. Continuous (C-RLS) and intermittent (I-RLS) are two different RLS categories based on symptoms evaluated [3]. RLS affects 5-10% of the general population in Western nations, and it is frequently related with a favorable female sex and family history [4, 5]. RLS is more common in ESRD patients undergoing hemodialysis (HD), ranging from 20% to 30% [6, 7].

RLS has a deleterious influence on ESRD patient's outcomes getting long-term HD, with sleep and life quality, and is significantly linked with higher rate of mortality [8-11]. The poor quality of life has been related to the systemic inflammation, but there is paucity of data on RLS with inflammation [12]. RLS is substantially more common in certain conditions, including iron shortage, diabetes, pregnancy, and Parkinsonism [13]. The frequency ranges from 20 to 70% in end-stage renal disease (ESRD) individuals [14, 15]. Therefore, no research on RLS has been published in Pakistan. As a result, the purpose of this study is to assess the incidence and severity of RLS in patients on maintenance hemodialysis.

## Methodology

A questionnaire based study was conducted on 116 consecutive hemodialysis patients in the Department of Neurology and Nephrology of Institute of Kidney Diseases Hayatabad, Peshawar and PAF Hospital, Islamabad for the Duration from June 2022 to December 2022. Patient's history included a history of drug, predialysis duration, and hemodialysis duration. Those with a history of limb weakness, stroke, impaired sensation, or trauma history, as well as any ongoing disease other than chronic illnesses such as renal, diabetes, hypertension, and cardiac disorders were excluded. Data was obtained using a standardized questionnaire that includes demographic variables such as personal history, family history, disease history, and smoking history. This self-structured questionnaire also includes the four RLS research group requirements a) leg pain caused by desire to move the legs, b) inactivity or rest worsening symptoms, c) Movement causing relief in symptoms, and d) Symptoms are more bothersome in the evening and at night than during the day. Individuals with all four characteristics are considered RLS patients. The patients were then questioned about the severity of their symptoms as well as their sleep pattern/sleep disruption. Nevertheless, the severity of symptoms is divided into four categories: mild, moderate, severe, and extremely severe. SPSS 27 versions were used to analyze the gathered data. The qualitative factors were reported as percentages, whereas the quantitative data were expressed as mean standard deviation. A P value of 0.05 is regarded as statistically significant.

## Results

The overall mean age of hemodialysis patients (HD) and control was  $32.8 \pm 10.4$  and  $40.6 \pm 10.6$  years respectively. The prevalence of RLS was 8.6% (n=10) among the studied population. There were 64 healthy subjects investigated as a control group. Out of 116 HD cases, there were 96 (82.8%) male and 20 (17.2%) females. The incidence of delayed sleep onset was found in 80% (n=8) cases among HD patients with RLS. Based on John Hopkins Restless Legs Severity Scale (JHRLSS), the incidence of mild, moderate, and severe RLS was 3 (30%), 2 (20%), and 5 (50%) respectively. The grade 3 and grade 4 severity of RLS was found in three and five patients respectively. There were no statistical significance found in duration of hemodialysis, age, predialysis duration, and erythropoietin use in patients with and without RLS. Comparison of demographic information and physical examination results in hemodialysis and control patients are shown in Table-I. The demographic and physical characteristics of HD (hemodialysis) patients with and without RLS were compared in Table-II. Table-III represents the distribution of various causes for hemodialysis.

Table-I Comparison of demographic information and physical examination results in hemodialysis and control patients

Parameters	Hemodialysis group (N=116)	Control group (N=64)
Age (years)	32.8 ± 10.4	40.6 ± 10.6
<b>Gender N (%)</b>		
Male	104 (89.7)	24 (37.5)
Female	12 (10.3)	40 (62.5)
Pre-HD duration (months)	15.8 ± 20.4	Nil
HD-duration (months)	6.8 ± 10.6	Nil
BMI (kg/m <sup>2</sup> )	20.4 ± 3.8	21.8 ± 5.6
SBP (mm Hg)	144.6 ± 24.6	122.3 ± 10.8
DBP (mm Hg)	86.8 ± 10.3	78.4 ± 4.7

Table-II comparison of demographic and physical characteristics of HD (hemodialysis) patients with and without RLS

Parameters	Hemodialysis group with RLS (N=10)	Hemodialysis group without RLS (N=106)
Age (years)	29.8 ± 9.4	33.6 ± 10.2
<b>Gender N (%)</b>		
Male	8 (80)	88 (83)
Female	2 (20)	18 (17)
Pre-HD duration (months)	12.8 ± 6.9	16.6 ± 20.4
HD-duration (months)	6.8 ± 4.9	7.2 ± 11.7
BMI (kg/m <sup>2</sup> )	18.84 ± 3.46	21.4 ± 3.86
SBP (mm Hg)	151.9 ± 22.9	144.3 ± 24.8
DBP (mm Hg)	91.6 ± 10.7	87.4 ± 9.8
Number of drugs	5.9 ± 1.6	5.8 ± 1.9

Table-III distribution of various causes for hemodialysis

Causes	Prevalence
Chronic glomerulonephritis (CGN)	40%
Chronic interstitial nephritis (CIN)	33%
Hypertension (HTN)	10%
Diabetes mellitus (DM)	8%
Adult polycystic kidney disease (ADPKD)	5%
Chronic rejection (CR)	4%

## Discussion

The present study mainly focused on the incidence of RLS in patients on hemodialysis and found that the prevalence of RLS was 8.6%. Sleep problems associated with RLS may pose a significant health risk. The diagnosis and severity of RLS was measured using IRLSSG criteria and JHRLSS. The healthy

participants were a unique group of healthy prospective renal donors. They were evaluated clinically and biochemically as part of their usual workup, allowing us to determine the prevalence of RLS in a sample of completely healthy people. Because compensated organ donors are illegal in India, they are close relatives such as parents, siblings, or spouses. While RLS was not connected with survival, the intensity of RLS symptoms appears to be related to death. The increasing rate of mortality in hemodialysis patients with RLS was due to various factors regardless of controlling RLS: these factors are lower BMI, age advancement, diabetes, and lower albumin. The dialysis associated higher rate of mortality significantly related to diabetes, age, and nutritional condition [16, 17].

The present study found that hemodialysis patients had higher frequency of RLS than control, it was substantially lower than in other countries [18-21]. There are various plausible explanations for why our hemodialysis patients have a lower prevalence of RLS than those in the West. Our investigations comprised young male patients with CIN, CGN, and HTN.

Sleep disorders is the dominant cause for RLS. In the present investigation, delayed sleep beginning caused 80% cases of RLS as an outcome of their symptoms, which is comparable to the previous study of Brzuszek et al. [22]. The difference in age, erythropoietin usage, dialysis duration, or metabolic profile between individuals with and without RLS was statistically insignificant. This is comparable to a previous research [23].

Another study reported that the uremic RLS pathophysiology to be involved in an inflammatory state. Understanding the relationship between cigarette smoking and restless legs syndrome is essential. Cigarette smoking was linked to the prevalence of RLS in our research. This conclusion is consistent with the findings of previous research [24]. Lee et al. [25] conducted a clinical evaluation and found a high association between RLS syndrome and sleep initiation, difficulty maintaining sleep, increased awakening from sleep, and a lack of rejuvenating sleep [26].

## **Conclusion**

The present study found that the prevalence of RLS was 8.6%. Additionally, the sleep difficulties linked with RLS might be a substantial health risk. Further epidemiological research, however, are needed to determine the prevalence rate, systematic correlations, and severity of RLS in order to reduce cases.

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