

ORIGINAL ARTICLE

Evaluation of Restless Leg Syndrome in Patients with Non-Dialysis Dependent Chronic Kidney Disease at Fatima Memorial Hospital Lahore: A Cross-sectional StudyMuhammad Bilal Basit^{1*}, Omer Sabir¹, Adnan Hussain Shahid², Andleeb Kanwal³, Ghulam Abass Qadri⁴, Nabiha Rizvi⁵**ABSTRACT****Objective:** To determine the occurrence of restless leg syndrome in individuals with non-dialysis-dependent chronic kidney disease.**Study Design:** A descriptive cross-sectional study.**Place and Duration of Study:** The study was carried out at the Outpatient Department (OPD) of Fatima Memorial Hospital, Lahore, Pakistan, from March 2020 to August 2020.**Methods:** A total of 280 CKD patients not dependent on dialysis were included in the study. The data were collected through interviews containing questions from international restless leg syndrome study group (IRLSSG). Patients were stratified into different stages according to the estimated glomerular filtration rate (eGFR). Restless leg syndrome was diagnosed by analyzing the responses of the interview marked by the examiner.**Results:** Among 280 patients, 15.7% (n=44) of chronic kidney disease patients were noted to have restless leg syndrome. The syndrome was significantly more frequent in females and was associated with higher CKD stages (Stage V > Stage III and IV). There was no association with either age or BMI.**Conclusion:** Restless leg syndrome is more common in chronic kidney disease stage V as compared to lower chronic kidney disease stages (III & IV). If untreated, it can affect patients' quality of life and increase the risk of cardiovascular activities.**Keywords:** *Chronic Kidney Disease, Restless Leg Syndrome, Willis-Ekbom Disease.***How to cite this:** Basit MB, Sabir O, Shahid AH, Kanwal A, Qadri GA, Rizvi N. Evaluation of Restless Leg Syndrome in Patients with Non-Dialysis Dependent Chronic Kidney Disease at Fatima Memorial Hospital Lahore: A Cross-sectional study. *Life and Science*. 2024; 5(1): 95-100. doi: <http://doi.org/10.37185/LnS.1.1.516>This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license. (<https://creativecommons.org/licenses/by-nc/4.0/>). Non-commercial uses of the work are permitted, provided the original work is properly cited.**Introduction**

Restless Leg Syndrome (RLS) or Willis Ekbom Disease (WED) is a neurological sensorimotor disorder

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characterized by an intense desire to move one's legs and is common in the general population.¹ There is a diurnal disease pattern with worsening symptoms at night. RLS can be classified as Primary or Secondary based on etiology where primary occurs as an idiopathic or hereditary form with a positive family history while secondary occurs in association with diverse medical conditions, including chronic kidney disease (CKD).^{2,3}Guidelines developed by The International Restless Legs Syndrome Study Group (IRLSSG) help in the clinical diagnosis of RLS, which is comprised of 4 points.⁴ The International Restless Legs Syndrome Rating Scale (IRLSRS) is used to assess the severity of symptoms in patients diagnosed with RLS. As symptoms aggravate during rest and occur more in the evening time, this syndrome is associated with

poor sleep quality, poor quality of life, and ultimately a high risk for cardiovascular disease.⁵

In addition, RLS may, in turn, in the presence of CKD, affect the prognosis of CKD patients, including lower survival and higher short-term mortality. Previously, internationally and nationally, marked variability in the prevalence of restless leg syndrome in Hemodialysis patients has been reported in various studies.^{6,7} Limited data is available in the non-hemodialysis CKD population. These studies calculated the pooled prevalence of RLS in CKD (all stages). However, no study has been done to calculate the prevalence of RLS in individual stages of CKD. In this study, we aimed to calculate the pooled prevalence as well as in individual stages of CKD III and above (non-dialysis or have not undergone renal transplant) to make therapeutic interventions appropriately to improve patient's quality of life at an early stage. The prevalence of RLS as reported in previous studies was 18%. The objective of our study was to determine the frequency of restless leg syndrome in non-dialysis chronic kidney disease patients presenting to our tertiary care center.

Methods

It was a descriptive cross-sectional study carried out by the Outpatient Department (OPD) of Fatima Memorial Hospital, Lahore, Pakistan, from March 2020 to August 2020 after obtaining approval from the hospital's ethical committee held on 17th February 2020 vide letter no R/No: 9-48. Patients visiting the outpatient department and admitted patients fulfilling the inclusion criteria were included. We employed consecutive sampling techniques to enroll 280 patients by taking 18% prevalence of RLS in CKD non-dialysis population along with 95% confidence interval and 5% margin of error.

We included all patients aged 18 to 85 years (either gender), with CKD (stage III and above) not on dialysis. We excluded pregnant patients, patients with renal transplant, patients on maintenance Hemodialysis/Peritoneal dialysis, diagnosed cases of Dementia, and patients with iron deficiency anemia, (Hemoglobin < 12g/dL, Ferritin > 100ng/mL), lower limb lymphedema, deep vein thrombosis, arthritis, lower limb cellulitis, Parkinson's disease, and peripheral artery disease.

The data were collected through interview in Urdu by translating questions from the questionnaire endorsed by the international restless leg syndrome study group (IRLSSG) by using stratified sampling technique. Patients were stratified according to estimated glomerular filtration rate (eGFR) into different CKD stages. The examiner marked the patient's answers on the form to avoid any bias and a diagnosis of RLS was made. A written consent was taken, and confidentiality of the data was ensured. Restless less syndrome was diagnosed with the patient experiencing an urge to move legs and followed by unpleasant sensation if the urge was not satisfied or during time of inactivity.

The data were analyzed using Statistical Package for Social Sciences for Windows SPSS v. 25. Means and standard deviation was calculated for quantitative variables e.g. age, duration of CKD, eGFR. Frequencies were calculated for gender, stage of CKD. Stratification was done according to age, gender, Body Mass Index (BMI), duration of CKD, stages of CKD. Stratification for age (18- 50) & (51-85) and gender was done to control the effect modifier. The Chi-square test was used to assess the significant difference between the stratified groups and to assess the significance of stratified factors on the incidence of RLS. A *p*-value of ≤ 0.05 was considered significant.

Results

A total of 280 cases were selected for the study. Characteristics of the study cohort are given in Table 1. Restless leg syndrome was recorded in 15.7% (n=44) of chronic kidney disease patients (Table 2) The stratification was done according to age, gender, BMI, and stages of CKD. Stratification for age (18- 50) & (51-85) and gender was done. The syndrome was significantly more frequent in females and was associated with higher CKD stages (Stage V > Stage III and IV). There was no association with either age or BMI.

Discussion

Restless legs syndrome (RLS) is a neurological condition that is clinically diagnosed based on its unique presentation.⁸ The hallmark features include an urge to move the legs, often due to unpleasant sensations. Activity may provide transient relief while rest often exacerbates the condition.⁹

Table 1: Demographics of the Study Population

Parameter	n=280
Age (mean \pm SD) (years)	52.9 \pm 12.9
18-50 (n, %)	82 (29.3%)
51-85 (n, %)	198 (70.7%)
Gender	
Men	132 (47.1%)
Women	148 (52.9%)
BMI (mean \pm SD)	28.85 \pm 2.7
Mean Duration of CKD (mean \pm SD) (Weeks)	18.36 \pm 8.05
eGFR (mean \pm SD) (ml/min)	32.68 \pm 12.4

Table 2: Frequency of Restless Leg Syndrome and the factors effecting it

Frequency of Restless Leg Syndrome n (%)	44 (15.7%)	
Effect Modifiers	Frequency n (%)	P-value
Age		
18 – 50 years (n = 82)	17 (20.7%)	0.14
51 – 80 years (n = 198)	27 (13.6%)	
Gender		
Females (n = 148)	26 (17.6%)	0.06
Males (n = 132)	18 (13.6%)	
BMI		
BMI up to 29.9 (n = 184)	31 (16.5%)	0.47
BMI \geq 30 (n = 96)	13 (13.5%)	
CKD Stage		
Stage III (n = 145)	17 (11.7%)	
Stage IV (n = 116)	13 (11.2%)	< 0.001
Stage V (n = 19)	14 (73.7%)	

This study was aimed to calculate the prevalence of RLS in CKD patients who are not on hemodialysis or have not undergone renal transplant so as to make therapeutic interventions appropriately to improve patient's quality of life.

Our data shows that the frequency of restless leg syndrome in our CKD cohort was 15.7% (n=44). These findings are similar to the results of a meta-analysis by Safarpour and colleagues, where the prevalence of RLS was recorded as 18%.¹⁰ Further stratification of our patients into individual stages of CKD showed a high frequency of RLS in stage V non-Dialysis (73.7%) as compared to earlier stages suggesting an increased frequency of RLS in pre-dialysis population. A study conducted by Irfan et al also reported a similar incidence of 64.8% RLS in end stage kidney disease patients.¹¹ This is self-explanatory since the pathophysiology of RLS involves accumulation of uremic toxins (discussed

below) and the serum levels of these toxins increase as the eGFR is declining. However, a study conducted in Peshawar including ESKD patients undergoing hemodialysis reported a significantly less incidence of RLS i.e 32% which differ greatly with our study results.¹² Another study conducted in Lahore reported a 38.7% incidence of RLS in severe kidney disease patients.¹³ These differences in results could be due to difference in sample size and study conditions.

A low incidence of RLS was noted in kidney disease III and IV (11.7% and 11.2%) as compared to its prevalence in patient with end stage kidney disease. This low prevalence (10-30%) has also been reported in other studies conducted.¹⁴⁻¹⁶ In Canada, a study reported 26% RLS in non-dialysis dependent CKD patients,¹⁴ in Japan 10.9%,¹⁶ 26% in India¹⁷ and 10% in Egypt.⁶

Our study also revealed that RLS is significantly more

prevalent in females (17.6%) as compared to males (13.6%) This finding is similar to Brzuszek A who observed higher ORs for the development of RLS in females.¹⁸ This finding is intriguing and may require further studies to elucidate the cause.¹⁹ Lin et al. also highlighted the risk of RLS in females as 58.8% women with ESKD were diagnosed with RLS.²⁰ However, Hamed et al. reported 65.5% RLS prevalence in males.⁶ A German study also reported no significant difference between RLS in men and nulliparous women hence indicating high estrogen as a trigger for RLS.²¹

In this study RLS was less prevalent in obese patients (13.5%) as compared to patients who were just overweight (16.9%). This finding is partly similar to the meta-analysis conducted by Lin S et al.²² Our analysis demonstrated a positive association between obesity or being over-weight and RLS (ORs: 1.44 and 1.29, respectively), and interestingly this relationship held true more strongly for females.¹³ The meta-analysis does not comment upon the kidney status of the participants and we surmise that such patients were excluded, thus making it impossible to apply the findings to our patient population. Vascular mechanisms proposed to be the pathophysiological basis of RLS (hypertension, high serum cholesterol) are even more pronounced in patients with CKD and the findings by Han et al actually apply to the patients with CKD more aptly.²³ However, a study by Ramachandran found no association between RLS in CKD patients and BMI.²⁴ Another study contradicting our results showed an increasing prevalence of RLS with increasing with BMI while our study reported less incident in patients with more than 30 BMI.²⁵

The importance of the present study is the presence of undiagnosed RLS in CKD pre-Dialysis population since all of the RLS cases in our study were not diagnosed to be having RLS previously. These symptoms if left untreated may worsen quality of life. This becomes even more important in the light of the findings that RLS patients may be at a higher risk of cardiovascular events. We suggest that, since The IRLSSG questionnaire is easy to administer and can even be done by a trained staff nurse or coordinator, it should be a part of routine evaluation of CKD patients for early diagnosis and intervention.

The study has some limitations. Very few cases from stage V CKD were reported. It may be due to the fact that patients with CKD V present late and are usually symptomatic requiring urgent initiation of Renal Replacement Therapy (RRT) and thus were excluded from our study. The study was single centered with a short study period. Large multicentered studies with distinct study groups can yield better results.

Conclusion

We concluded that restless leg syndrome is more common in chronic kidney disease stage V as compared to lower chronic kidney disease stages (III & IV). If untreated, it can affect patients' quality of life and increase the risk of cardiovascular activities. Hence kidney disease patient should be examined regularly for timely diagnosis and treatment of restless leg syndrome.

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Authors Contribution

MBB: Study designing, data analysis, results and interpretation

OS: Idea conception, manuscript writing and proof reading

AHS: Study designing, data analysis, results and interpretation

AK: Data collection

GAQ: Idea conception, data collection

NR: Study designing, Manuscript writing and proof reading

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