

Restless leg syndrome (RLS) in end stage renal disease

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A B S T R A C T

Introduction: End stage Renal Disease refers to permanent, irreversible loss of renal functions due to variety of underlying disorders. The condition is quite prevalent in our part of the world. The occurrence of Restless legs syndrome (RLS) in such patients, especially those on hemodialysis, surpasses that in the general population. RLS significantly blemishes their quality of life. The syndrome has subtle and nonspecific symptoms which are commonly neglected in dialysis centers. The study aims to determine the frequency of restless leg syndrome in patients of advanced renal disease.

Methodology: A Cross Sectional Study conducted at Department of Medicine, Mayo Hospital Lahore from Dec 2018 to June 2019 (6 months). Patients of 20-80 years of age and of both genders, diagnosed as ESRD for ≥ 3 months were enrolled and evaluated for RLS. The condition was diagnosed as per International RLS Study Group (IRLSSG) criteria. The demographic data (age, gender, BMI and duration of symptoms) was recorded. History of smoking, alcohol use and chronicity of disease was also noted. Data was analyzed with SPSS v25.0. Mean and percentages were calculated. Chi-Square test was applied. p-value of ≤ 0.05 was taken as significant.

Results: Total of 75 patients were enrolled. Males were 54 (72.0%) while 21 (28.0%) were females. Mean age was 47.3 ± 13.1 (22-73) years. RLS was observed in 29 (38.7%) cases. Age, gender, duration of illness, smoking and alcohol consumption had no significant association with RLS (p values 0.642, 0.669, 0.208, 0.245, 0.565, 0.745) respectively.

Conclusion: Restless legs syndrome is frequently encountered condition in ESRD patients.

Keywords: End Stage Renal Disease, Restless Legs Syndrome

Introduction

End-stage renal disease (ESRD) refers to advanced stage of chronic renal failure (CRF), where kidneys can no longer function on their own. Such patients must receive dialysis or kidney transplantation for survival. Majority of patients remain on hemodialysis for next many years as transplantation is not affordable or possible for most of the cases. Although CRF is more commonly encountered in elderly patients but younger population is also frequently diagnosed as CRF due to various underlying conditions. Global estimate of ESRD patients needing renal

replacement therapy is between 4.902 and 7.083 million.¹ Almost 21.2% of Pakistani adult population suffers from CKD.² At advanced age of ≥ 50 years' incidence is 43.6% whereas younger than 30 years have almost 10.5% incidence.³ Variety of underlying diseases are responsible for ESRD. Diabetes, hypertension, glomerulonephritis and renal stones are identified as prevalent predisposing conditions.^{2, 3} Anemia, metabolic bone disease, heart failure, fluid and electrolyte imbalance and neurological disorders are potential implications of ESRD.^{4, 5} Restless

leg syndrome (RLS) / Willis Ekbohm disease, is quite commonly encountered in ESRD patients undergoing hemodialysis.⁶ It is a condition that causes an uncontrollable urge to move the legs, usually because of an uncomfortable sensation. Diagnosis is made, following revised International Restless Leg Syndrome Study Group (IRLSSG) diagnostic criteria (2012).⁷ It can present as a primary, isolated neurological disorder or can be seen, secondary to certain diseases or conditions i.e., pregnancy, iron deficiency, kidney failure, some types of medication, sleep deprivation, Parkinson's Disease, peripheral neuropathy and varicose veins.^{7, 8} Due to its subtle presentation, RLS goes unnoticed in many cases. Zhenchuan with coworkers reported that ESRD patients undergoing hemodialysis can have RLS up to 25-50%.⁸

The prevalence of RLS in ESRD varies over the globe. Literature reports 19.4% in Saudi Arabia⁹, 25.3% in Taiwan¹⁰ and 38.6- 64.8% in Pakistan.^{11, 12} The sensations of RLS usually are worse during inactivity and often disturb sleep, leading to chronic sleep deprivation and stress. Approximately 85% of patients with RLS have periodic movements of sleep.¹² Treatment of the condition is most effective in secondary cases. The drug therapy includes dopaminergic agents, benzodiazepines, opioids, anticonvulsants and iron supplements.^{7, 12} Renal transplantation cures the condition in ESRD patients.¹¹

Mortality of ESRD patients with or without RLS remains the same.¹² Untreated RLS increases risk for development and aggravation of hypertension, learning and memory difficulties.¹¹ Aim of our study was to determine the frequency of restless leg syndrome in patients of end-stage renal disease.

Methodology

This cross sectional study was conducted in Department of Medicine, Mayo Hospital Lahore over a period of 6 months i.e. (Dec 2018 – June 2019). Total of 75 cases were enrolled in the study (95% confidence level with 9% margin of error and taking expected percentage of restless leg syndrome in patients with ESRD as 19.4%.⁸ Patients of age 20-80 years who were suffering from ESRD for at least ≥ 3 months (as per operational definition) were included in the study.¹³ Patients having Pregnancy, Parkinson's disease, Peripheral neuropathy, Periodic leg movement of sleep and seizure disorder were excluded.

After taking informed consent, demographic data (age, gender, BMI and duration of symptoms), History of smoking and alcohol use was recorded on a self-designed proforma. Patients were evaluated clinically for restless leg syndrome. If patient complained of irresistible urge to move the legs and/or arms, often associated with a sensation of pain, burning, pricking, tingling, numbness, or other unpleasant or unusual sensations, then restless leg syndrome was labeled (as per operational definition).⁸ Data were entered and analyzed through SPSS v25.0. Mean and SD were calculated for quantitative variables like age, BMI and duration of ESRD. Frequency and percentage were calculated for qualitative variables i.e. gender and restless leg syndrome. Data were stratified for effect modifiers like age, gender, BMI smoking, alcohol use and duration of ESRD. Chi-Square test was applied to compare restless leg syndrome in stratified groups taking p-value ≤ 0.05 as significant.

Results

Total of 75 patients were enrolled. Males were 54 (72.0%) while 21 (28.0%) were females. Mean age (in years) at diagnosis was 47.3 ± 13.1 (22 and 73). Patients between 20-40 years' age group were 28 (37.3%), while 33 (44.0%) and 14 (18.7%) were between 41-60 years and >60 age groups respectively. The 35 (46.7%) patients had normal weight while 15 (20.0%) cases were underweight. Overweight and obesity was seen in 19 (25.3%) and 6 (8.0%) cases respectively. The ESRD with <1-year duration was found in 25 (33.3%) cases while 24 (32.0%) and 26 (34.7%) had duration of disease 1-3 years and >3 years respectively. Among ESRD patients, 7 (9.3%) had alcohol consumption and 45 (60.0%) were smoker. RLS was observed in 29 (38.7%) patients of ESRD (Figure 1). The 10 (34.4%) males while 19 (65.5%) females had RLS.

No significant difference among gender, age groups, smoking, BMI, usage of alcohol and duration of disease and RLS ($p=0.642, 0.669, 0.208, 0.245, 0.565, 0.745$ respectively) could be seen.

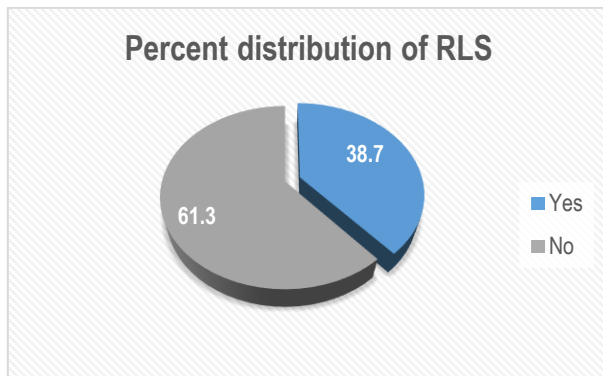


Figure 1: Percent distribution of restless legs syndrome (RLS)

Table 1: Association of RLS with various factors

Characteristics	RLS (f)	RLS(%)	P -value
Smoking	20/45	44.4	0.208
Alcohol consumption	2/7	28.7	0.565
Duration of Disease			
< 1 year	11/25	44	0.745
1-3 years	8/24	33.3	
>3 years	10/26	38.5	
Age group in years			
20-40	9/28	32.1	0.669
41-60	14/33	42.4	
>60	6/14	42.9	
Gender			
Male	20/54	37	0.642
Female	9/21	42.9	
Body mass index			
Underweight	4/15	26.7	0.598
Normal	13/35	37.14	
Overweight	9/19	47.36	
Obese	3/6	50	

Discussion

RLS is now recognized as a neurologic movement disorder which typically appears during inactivity, relieved with movement and worsens in sleep hours.^{7, 13} RLS sufferers represent 2 to 3% of the general population.¹⁴ Seyed Mohammad et al positively screened 1580 individuals for RLS with a reported prevalence rate of 60/1000.¹⁴ Our cohort consisted of targeted (ESRD) population only. We found 38.7% of RLS in ESRD patients, all of them were on hemodialysis. Literature reports

incidence of 13.3-36.7%¹⁴⁻¹⁷ in various populations. Researches who used IRLSSG criteria for diagnosis of RLS also report wide range of positivity in results. Xiao and coworkers reported prevalence of RLS in ESRD as 20.44%.²¹ Higher value in our population may be due to heterogeneity of the study populations and difference in diagnostic criteria. Simultaneous occurrence of iron deficiency anemia and inadequate hemodialysis might increase RLS in patients.¹⁸⁻²⁰ Increase in prevalence of RLS is reported with advancing age.¹⁴ We found most cases around age of 60 years (42.9%). Mean age at presentation was 47.3% in our population, while Priya with coworkers found 50.7 years which is comparable.²³ Females are more commonly affected with RLS as compared to males (42.9 Vs 37%). Similar findings were observed by Xiao and coworkers.²¹ Whereas Seyed and colleagues did not find any gender difference in their cohort.¹⁴

Multiple studies have been done to find out the associated risk factors which may have a role in development of RLS. It revealed in literature that smoking is associated with RLS whereas consumption of coffee and tea could not be related to development of RLS.²⁴ We did not find statistically significant association of alcohol consumption (p value 0.565) and smoking to RLS (p value 0.208) whereas literature reports significant association of RLS with alcohol consumption.²¹

Though 50% of our obese patients had RLS yet it was not statistically significant (p value 0.598). Niloufar with coworkers found BMI to be significantly associated with RLS.²⁴ The iron deficiency and other types of anemias as well as serum calcium level have all been linked to RLS but we were unable to get enough data on this.^{22, 23}

Certain studies report that incidence of RLS increases with chronicity of the disease and HD but our results for <1 year and >3 years' disease duration were comparable without any statistical significance (p value 0.745).^{8, 9, 24} Our study had few limitations like relatively small sample size. We could not gather information of anxiety depression, laboratory data like anemia and data on treatment of RLS. Further studies with large sample size are required to establish effective treatment of the condition which will improve suffering of these patients.

Conclusion

It is concluded that RLS is prevalent in patients with ESRD. Females are predisposed to develop RLS as compared to males.

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