Original Article

Frequency of Restless Legs Syndrome among End-Stage Renal Disease Patients on Maintenance Hemodialysis

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ABSTRACT

Objective: To determine the frequency of restless leg syndrome among patients of end-stage renal disease undergoing hemodialysis.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Nephrology Department, Ganga Ram Hospital, Lahore from 20th October 2019 to 20th April 2020.

Materials and Methods: One hundred and sixty patients on hemodialysis were enrolled. Patients were assessed for age, gender, body mass index, presence of hypertension, diabetes, anemia, and RLS as per operational definition.

Results: 98 (60.5%) were male patients and 64 (39.5%) were female patients, 37% were from the age group of 18-40 years, 35 patients (21.6%) were having an iron deficiency, 151(93.2%) were hypertensive, 59(36.4%) were diabetic, 45(27.8%) were on antipsychotic/antidepressant drugs and 21(13%) were using antihistamines. 85 patients (52.5%) were having RLS. Among 45 patients who were on antipsychotics/antidepressants, 31 (68.9%) were having RLS with statistical significance (p-value 0.009). Among 21 patients who were on antihistamines, 19(90.5%) were having RLS with a statistically significant p-value of 0.00018. Among iron deficient patients 35(21.6%), 16(45.7%) were having RLS and 19(54.3%) were not exhibiting RLS symptoms, showed no statistically significant difference (p-value 0.366).

Conclusion: The frequency of Restless Legs Syndrome is 52.5% among end-stage renal disease patients on maintenance hemodialysis.

Key Words: Restless leg syndrome, End-stage renal disease, Hemodialsis

INTRODUCTION

Unpleasant sensation in lower limbs that compels the individual to sways his legs, is a neurological pathology often termed as Restless legs syndrome (RLS)[1]. These feelings are often explained by patients as creepy, pin pricking, stretching, or distressing sensation in lower limb muscles. These feelings tend to worsen at night time especially during sleep and movements of legs help in overcoming these symptoms.

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RLS follows a specific day and night cycle, the appearance of symptoms occurs in the evening and becomes severe during nighttime sleep, whereas little or no symptoms occur during daytime.[2]

Fluctuation in the severity of these symptoms persists lifelong and complete resolution is rarely seen.[3]In many cases no cause has been identified hence called idiopathic RLS, whereas it could be secondary to some systemic diseases like anemia, peripheral sensory neuropathy, Diabetes, and thyroid disorders. It has been observed in alcoholic individuals and pregnant females as well.[4] A significant proportion of chronic kidney disease (CKD) patients experience these symptoms. RLS is one of the chief problems of hemodialysis (HD) patients reported to nephrologists. Maintenance HD is a lifelong therapeutic option for end-stage renal disease (ESRD) patients, which not only brings financial constraints, reduction in physical and mental wellbeing, altered sleep patterns, and severe depression. RLS is frequently observed in patients with the HD-induced ailments.[5]

RLS is also considered a part of sleep disorder as it augments insomnia, poor sleep quality, interrupted sleep, and reduced sleep duration. Lack of normal sleep, in turn, augments anxiety, depression, and

deterioration in overall quality of life.[6] It has been observed that an increase in cardiovascular accidents and nocturnal hypertension is strongly associated with RLS-induced sleep disorders.[7]

RLS incidence of 5–15% is documented in the normal population.[7]Hallmark REST trial (RLS epidemiology symptoms and treatment) conducted in 2014 among 23 thousand normal individuals showed an 11.9% prevalence of RLS.[8] In Pakistani study conducted by Khalid M, et al reported 23.6% prevalence in the general population.[9] As compared tothe normal population, the prevalence in CKD patients is around 24.2% and, the prevalence in HD patients is 35.5-40.7%. RLS prevalence varies from country to country, the lowest reported incidence is 17% whereas the highest is 62%.[10] In Pakistani HD patients prevalence is 24%.[11]

The pathophysiology of RLS is complex and multiple abnormalities play a crucial role in the development and severity of RLS. Endothelial cells at the blood-brain barrier act at storage sites of iron for the brain, in iron-deficient states uptake of iron by neurons is reduced resulting in altered neuronal dopaminergic function. This signifies the role of iron deficiency anemia in the development of RLS.[12] Apart from iron deficiency, structural and functional abnormalities in central or peripheral dopamine-producing neurons have been observed in the uremic milieu among CKD and HD patients.[13] The presence of RLS in other family members signifies the role of genetic defects. Females and longer duration on HD were linked to the severity of RLS documented by different studies.[10]

Although multiple studies have been conducted to explore RLS in HD patients worldwide, there is a lot of variation in results especially in its burden and confounding factors. The results of this study will help us to understand the frequency of RLS in our population and it will help in the early recognition and treatment of the patients suffering from RLS.

MATERIALS AND METHODS

This cross-sectional study was conducted in Nephrology Department, Ganga Ram Hospital, Lahore, from October 20, 2019, to April 20, 2020. The sample size of 162 was estimated by using a 95% confidence level with a 5% margin of error and taking an expected percentage of RLS as 12.4% in ESRD patients undergoing hemodialysis.[9] Patients of both gender, ages between 18-70 years who were on HD for at least 3 months were included. Patients having acute kidney injury, musculoskeletal disorders, recent myocardial infarction or unstable angina, any catabolic process were excluded from the study. After approval of the Hospital Ethical Committee, written informed consent, demographic information was recorded. Patients were assessed for age, gender, body mass index, presence of hypertension, diabetes, smoking, and anemia. RLS was assessed using the International Restless Leg Syndrome Study Group rating scale.[14]

Data were entered and analyzed using SPSS-25.0. For post-stratification, a Chi-square test was applied to see the significance. A p-value ≤0.05 was considered significant.

RESULTS

There were 98 (60.5%) male patients and 64 (39.5%) female patients. Among these patients 37% were from the age group of 18-40 years, 63% were from the age group 41-70 years. Among these patients, 43.8% had BMI>25 and 56.2% had BMI between 18-25.

Table No.1: Stratification of gender, age, diabetes, hypertension, iron deficiency, BMI, HD duration, antidepressants and antihistamines according to RLS (n=162)

Variable	RLS		P value
	Yes	No	
Gender			
Male	45 (45.9%)	53 (54.1%)	0.039
Female	40 (62.5%)	24 (37.5%)	
Age (years)			
18-40	28 (46.7%)	32 (53.3%)	0.257
41-70	57 (55.9%)	45 (44.1%)	
Diabetes			
Yes	32 (54.2%)	27 (45.8%)	0.733
No	53 (51.5%)	50 (48.5%)	
Hypertension			
Yes	78 (51.7%)	73 (48.3%)	0.442
No	7 (63.6%)	4 (36.4%)	
Iron Deficiency			
Yes	16 (45.7%)	19 (54.3%)	0.366
No	69 (54.3%)	58 (45.7%)	
BMI			
Low or normal	44 (48.4%)	47 (51.8%)	0.235
Overweight	41 (57.75)	30 (42.35)	
HD Duration			
6-12 Months	2 (25%)	6 (75%)	0.051
1-3 Years	26 (66.7%)	13 (33.3%)	
>3 Years	57 (49.6%)	58 (50.4%)	
Antidepressants			
Yes	31 (68.9%)	14 (31.1%)	0.009
No	54 (46.2%)	63 (53.8%)	
Antihistamines			
Yes	19 (90.5%)	2 (9.5%)	0.00018
No	66 (46.8%)	75 (53.2%)	

Among them, 4.9% were on MHD for 6-12 months, 24.1% for 1-3 years, and 71.0% for >3 years.35 patients (21.6%) were having an iron deficiency, 151(93.2%) were hypertensive, 59(36.4%) were diabetic, 45(27.8%) were on antipsychotic/antidepressant drugs and 21(13%) were using antihistamines. Our study showed

that 85 patients (52.5%) were having RLS Eighty five patients (52.5%) were having RLS. On stratification of RLS with age, 46.7% were having RLS in 18-40 years age group, and 55.9% in 41-70 years age group, with no statistical significance (p-value 0.257). In our study group, among 98 male patients, 45.9% (45) were having RLS & among 64 female patients, 62.5% (40) were having RLS, with statistical significance (p-value 0.039). Among 59 diabetics, 32(54.2%) were having RLS and among 151 hypertensives 51.7% were having RLS without any statistical significance (p-value0.733, 0.442 respectively).Among 91 patients who have (BMI 18-25) 44 patients (48.41%) were having RLS and 71 patients (BMI >25), 41 (57.7%) were having RLS without any statistical significance (p-value 0.235). Among these 8 patients who were on HD for 6-12 months, 2(25%) were having RLS, and among 39 pts who were on HD for 1-3 years,26(66.7%) was having RLS and among 115 pts who were on HD for >3 years, 57 (49.6%) were having RLS without any statistical significance (p-value 0.051).Among 45 patients who were on antipsychotics/antidepressants, 31 (68.9%) were having RLS with statistical significance (p-value 0.009). Among 21 patients who were on antihistamines, 19(90.5%) were having RLS with a statistically significant p-value of 0.00018. Among Iron deficient patients 35(21.6%), 16(45.7%) were having RLS and 19(54.3%) were not exhibiting RLS symptoms, showed no statistically significant difference (p-value 0.366) (Table 1).

DISCUSSION

Diagnosis of RLS depends upon the presence of four symptoms as proposed by the International RLS Study Group, that includes: (1) unpleasant sensation in legs that produces a desire to move legs, (2) occurring in resting state, (3) resolved by legs movements, and (4) exhibiting circadian rhythm with maximum symptoms appearance at night. But these symptoms must be differentiated from other closely related clinical conditions that can mimic RLS. These disorders are leg cramps, peripheral sensory neuropathy, arthritis, habitual leg movements, and sleeping position discomfort. It has been seen that these 4 criteria demonstrate a positive predictive value of <50% in the general population whereas the specificity of 84% is present in RLS patients.[15]

In different studies done all over the world the frequency of RLS in the general population is reported to be between 20 to 25%,[16] and in patients of ESRD on HD is 23.3 to 38%.[17,18] Our study showed 52.5% of patients have RLS. There could be three major reasons for this variable reports of RLS frequency, first the genetic heterogeneity of the different study groups population, second the difference in diagnostic criteria and tools used for RLS, third and the most important, the presence or absence of confounding factors that can

precipitate RLS. Studies have proved that genetic factors play an important role in the pathogenesis of RLS and autosomal dominant pattern in familial RLS has been observed in Canada, Italy, and France.[19]The frequency of RLS was 52.5% in our study as compared to 26% in the Indian population,[20] 33% in the Japanese population,[21] 20-50% in the Saudi population,[22] and 14-21% in Caucasians.[23] Different scoring scales for RLS are IRLSSG diagnostic criteria (International Restless Legs Syndrome Study Group)[24], RLS-6 scale, JHRLSSS (John Hopkins RLS Severity Scale), and the investigator-based CGI (Clinical Global Impressions).[7] Diversity in these diagnostic tools can be a contributing factor for diverse RLS prevalence studies results.

In our study females are affected more as compared to male patients, possibly due to hormonal differences in both genders.[25]Advanced age is also considered as a risk factor for an idiopathic class of RLS. However, some researchers proved that this link between old HD patients and RLS is not always present.[25] In our study advancing age does not affect RLS frequency. Several studies have proved increased RLS occurrence in iron deficiency anemia[10] but in our study, no statistically significant correlation is found. The presence of depression and use of antidepressants has been linked to increased severity of RLS,[26] likewise in our patient's use of antidepressants showed more prevalent RLS. Links have been proved between antihistamine use and RLS as shown in our study as well.[27]

CONCLUSION

The frequency of Restless Legs Syndrome is 52.5% among end-stage renal disease patients on maintenance hemodialysis.

Author's Contribution:

Concept & Design of Study:	Sumaira Ishaq
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