

RESTLESS LEGS SYNDROME IN END STAGE RENAL DISEASE PATIENTS UNDERGOING MAINTENANCE HEMODIALYSIS

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ABSTRACT

Objective: To study the frequency of restless legs syndrome in patients of end stage renal disease undergoing maintenance hemodialysis.

Design: Cross sectional descriptive study.

Place and Duration of Study: Department of medicine, CMH Multan from Nov 2010 to April 2011.

Patients and Methods: One hundred and ninety four (n=194) patients of End stage renal disease who had been on maintenance hemodialysis for at least 3 months, were included in the study after full informed consent and using consecutive sampling. Patients having dementia, psychiatric illness, pregnancy, hypothyroidism, Parkinson's disease and alcoholics were excluded from the study. Patients who fulfilled all four diagnostic criteria for restless legs syndrome as proposed by International restless legs syndrome study group (IRLSSG), by direct questioning were diagnosed as having restless legs syndrome.

Results: The frequency of restless legs syndrome was found to be 12.4% in patients undergoing hemodialysis (10.5% in males versus 16% in females). The mean duration of hemodialysis was higher among RLS positive patients (12.88 ± 5.543 months) as compared to RLS negative patients (6.94 ± 4.610 months).

Conclusion: RLS is a frequent, under-diagnosed co-morbidity in patients undergoing maintenance hemodialysis.

Keywords: RLS (Restless legs syndrome), Maintenance hemodialysis, ESRD (End stage renal disease).

INTRODUCTION

Patients on maintenance hemodialysis have a significantly impaired quality of life compared to general population and renal transplant patients¹.

Restless leg syndrome is an extremely distressing neurological disorder that is frequently present in patients undergoing dialysis and contributes to the poor quality of life².

The diagnosis of RLS is a clinical one. In 1995, clinical diagnostic criteria for the restless legs syndrome were established by the International Restless Legs Syndrome Study Group (IRLSSG)³ which were further reviewed by the IRLSSG and published in 2003⁴.

There are four essential criteria to make a definite diagnosis of RLS according to IRLSSG.

(1) An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs.

(2) The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting.

(3) The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching.

(4) The urge to move or unpleasant sensations are worse in the evening or night than during the day.

All the four criteria must be met to make a positive diagnosis of RLS.

Supportive criteria not essential but helpful in diagnosis include:

1. Positive family history of RLS.
2. Response to dopaminergic therapy.
3. Periodic limb movements during wakefulness or sleep (PLMs).

The prevalence of restless leg syndrome is higher among patients undergoing hemodialysis with wide variations among different

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populations, ranging from 6.6% to 50% in various studies⁵⁻⁹.

The symptoms of restless leg syndrome are associated with poor sleep, diminished quality of life and increased morbidity and mortality^{2,10}. RLS has also been associated with increased risk of cardiovascular events and premature discontinuation of hemodialysis sessions^{11,12}. Therapy with levodopa, dopaminergic agonists, anticonvulsants, and clonidine are reported to be effective in managing symptoms of RLS in uremic patients¹³.

Restless legs syndrome as a disorder can easily go unrecognized due to the nature of symptoms and has been shown to be greatly under-diagnosed and undertreated^{14,15}. Indeed the syndrome has been described as "the most common disorder you have never heard of."^{16,17}.

Studies reporting the prevalence of restless leg syndrome in hemodialysis patients are lacking in Pakistan. The aim of the study is to find out the frequency of this frequent and neglected problem in patients undergoing hemodialysis in our population, the recognition and treatment of which plays a role in improving sleep as well as the quality of life of these patients.

PATIENTS AND METHODS

This cross sectional study was carried out in the department of Medicine, Combined Military Hospital, Multan from November 2010 to April 2011 on patients of End stage renal disease presenting to this hospital. Inclusion criteria were age of at least 18 years and current history of hemodialysis of at least 3 months. Patients having hypothyroidism, Parkinson's disease, psychiatric illness, dementia, those with history of alcohol intake, and pregnant ladies were excluded from the study. Sample size was calculated as 194 cases using WHO sample size calculator with regards to an estimated population proportion of 6.6%⁵. A total of one hundred and ninety four (n=194) patients presenting to the nephrology OPD and Dialysis centre of CMH Multan were interviewed during the duration of study after approval of

hospital ethical committee and full informed consent of the patients. Data collected included age, gender, duration of hemodialysis, BMI (body mass index), and presence or absence of Diabetes mellitus. The information was obtained from the patients by direct questioning.

The patient's history and medical documents were used to note the demographic data, drug history and confirm the diagnosis. Detailed medical examination prior to inclusion was done to exclude other diseases or conditions mimicking RLS.

Patients were asked 4 questions based on the IRLSSG criteria.

1. Do you have desire to move your limbs due to abnormal sensations i.e. pins or needles, ants crawling?

2. Does moving your limbs relieve/reduce these sensations?

3. Are these symptoms worse when you rest/sit still or lie?

4. Are these symptoms worse at bedtime or in the evening?

Patients who fulfilled all 4 criteria were diagnosed as having RLS. Patients were categorized as those having RLS and those without RLS. Variables included in the study included age, sex, diabetes mellitus, duration of hemodialysis and BMI. The data was entered in SPSS (version 17) and analyzed. Data was summarized as means \pm standard deviation, number or percentage as appropriate. Fisher's exact test and unpaired t-test were used for the comparison of variables and data as applicable. A p-value of less than 0.05 was considered significant.

RESULTS

A total number of 194 patients, 133 males (68.6%) and 61 females (31.4%), were evaluated during the duration of study after informed consent.

The mean age of the patients was 50.31 ± 12.692 years. The mean duration of hemodialysis was 7.68 ± 5.109 months, while the mean BMI of the patients was 21.4 ± 1.94 kg/m². 40 patients

(20.6%) were suffering from diabetes mellitus. Clinical and demographic data of the patients are presented in table-1.

Twenty four patients fulfilled the diagnostic criteria of RLS. The overall frequency of RLS was found to be 12.4%. None of the patients had received a diagnosis of RLS before and none of

DISCUSSION

Restless legs syndrome as a common neurological disorder has not been well characterized in Pakistan and studies determining its prevalence in general population as well as in patients undergoing hemodialysis are lacking in Pakistan.

Table-1: Demographic characteristics of the patients.

Age	50.31 ± 12.692 years
Gender	
Males	133 (68.6%)
Females	61 (31.4%)
BMI (Kg/m ²)	21.4 ± 1.94
Duration of HD (Months)	7.68 ± 5.109
Diabetes Mellitus	40 (20.6%)
RLS Positive according to IRLSSG Criteria	24 (12.4%)

Data are shown as mean ±SD or number (%)

BMI: Body mass index, RLS: Restless legs syndrome, HD: Hemodialysis, IRLSSG: International Restless legs syndrome study group

Table-2: Characteristics of the patients with or without resting leg syndrome (RLS).

Variable	RLS Positive	RLS negative	p-value
Gender			0.25**
Male	14 (10.5%)	119 (89.5%)	
Female	10 (16%)	51 (84%)	
Diabetes			0.11**
Diabetics	8 (20%)	32 (80%)	
Non-Diabetics	16 (10.4%)	132 (89.19%)	
Age in years	54.29 ± 8.431	49.75 ± 13.104	0.101*
Dialysis duration(Months)	12.88 ± 5.543	6.94 ± 4.610	0.0001*
BMI as kg/m ²	20.67 ± 2.099	21.51 ± 1.901	0.0469*

the patients was on dopaminergic therapy. Comparison of the clinical characteristics of the patients with or without RLS is presented in table-2. RLS was present in 10.5% (14/133) of males and 16.4% (10/61) of females.

Among diabetics 8 patients had RLS (20%) while 16 of the non-diabetic patients had RLS (10.4%). The mean duration of hemodialysis was higher among patients with RLS (12.88 ± 5.543 months) as compared to patients with no-RLS (6.94 ± 4.610 months). The difference between RLS and non RLS patients regarding mean BMI and age was not statistically significant.

A number of studies in different populations have been done utilizing the IRLSSG diagnostic criteria to find the prevalence of RLS. Patients fulfilling all the four criteria proposed by IRLSSG have been diagnosed as definitive RLS while in some studies patients fulfilling at least 3 of the four criteria have been labeled as having "questionable RLS"¹⁸. A single screening question, "When you try to relax in the evening or sleep at night, do you ever have unpleasant, restless feelings in your legs that can be relieved by walking or movement?", has been found to have a sensitivity of 100% and specificity of 96.8% in diagnosing RLS¹⁹. However in our study strict IRLSSG criteria were used and patients who

fulfilled all the four criteria were diagnosed as having RLS.

This study showed that the RLS is common in patients undergoing hemodialysis and remains under-diagnosed and under-treated. None of the patients full-filling the diagnostic criteria of RLS in this study had received this diagnosis or specific therapy for RLS including dopamine agonists before.

The prevalence of RLS in patients undergoing hemodialysis has a considerably wide variation ranging from 6.6% to 50% in different populations. Bhowmick et al⁵, reported the prevalence of RLS in Indian hemodialysis population to be approximately 6.6%. In Japan and Korea the prevalence has been estimated to be 23%⁷ and 28%⁸ respectively. A higher prevalence of RLS (45.8%) was reported in a large dialysis population in UK by Siddiqui et al⁶, and by Al-jahdali⁹ in Saudi Arabia (50%). This wide variation has been attributed to the lack of standardized criteria before 1995⁶. However even after applying the strict IRLSSG criteria, studies in different populations groups have yielded widely different results. Genetic differences, different dialysis strategies and environmental factors have been suggested to cause these variations⁹.

The frequency of RLS in our study was higher than that of India and much less than that reported in UK, Saudi Arabia. An important consideration is that the mean age in our study was much higher (50.31 ± 12.692 years) as compared to the Indian study which had the mean age of patients of 34.5 ± 11.1 years.

Several studies have reported RLS to be independently associated with the female gender^{6,9}. Berger et al²⁰, reported the prevalence of RLS among females to be twice as that of males. Excretion of sex hormones following circadian rhythms has been suggested to be related to this association.

The mean duration of hemodialysis in our study was higher among patients with RLS than those without RLS. Siddiqui et al⁶ and Gigli et

al²¹, have reported an association between RLS and increased duration of hemodialysis however this remains controversial as several other studies did not find any association between the two¹⁸.

In our study, no association was found between RLS and increased body mass index. This result was dissimilar to that of Siddiqui et al.⁶ who reported a higher prevalence with increased weight. Kim et al⁸, however reported no association between RLS and increased BMI.

Numerous studies have shown increased prevalence of RLS among diabetics. Although polyneuropathy is a risk factor for RLS in diabetics, it only partially explains the prevalence of RLS in diabetics²².

The study had some limitations. As the scope of study was limited to evaluating frequency of RLS based on IRLSSG criteria, nerve-conduction studies and biochemical profiles were not done in the patients under study. However attempt was made to exclude diseases and conditions that could mimic, cause or exacerbate RLS by means of careful history, clinical and neurological examination. Furthermore the severity as well as the impact of RLS was not assessed in this study.

CONCLUSION

This study suggests that RLS is frequent in patients undergoing hemodialysis and remains un-diagnosed and under-treated. Detailed history of the patients is essential for diagnosing this very common and distressing disorder. Physicians managing these patients must be aware of this important condition and diagnosis should be suspected in patients presenting with insomnia, paraesthesiae or other abnormal sensations in the limbs.

REFERENCES

1. Sathvik BS, Parthasarathi G, Narahari MG, Gurudev KC. An assessment of the quality of life in hemodialysis patients using the WHOQOL-BREF questionnaire. *Indian J Nephrol.* 2008; 18(4): 141-149.
2. Mucsi I, Molnar MZ, Ambrus C, Szeifert L, Kovacs AZ, Zoller R, et al. Restless legs syndrome, insomnia and quality of life in patients on maintenance dialysis. *Nephrol Dial Transplant.* 2005; 20(3): 571-7.
3. Walters AS. Toward a better definition of the restless legs syndrome. The International Restless Legs Syndrome Study Group *Mov Disord.* 1995; 10(5): 634-42.
4. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs

- syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med.* 2003; 4(2): 101-19.
5. Bhowmik D, Bhatia M, Gupta S, Agarwal SK, Tiwari SC, Dash SC. Restless legs syndrome in haemodialysis patients in India: a case controlled study. *Sleep Med.* 2003; 4(2): 143-6.
 6. Siddiqui S, Kavanagh D, Traynor J, Mak M, Deighan C, Geddes C. Risk factors for restless legs syndrome in dialysis patients. *Nephron Clin Pract.* 2005; 101(3): c155-60.
 7. Kawauchi A, Inoue Y, Hashimoto T, Tachibana N, Shirakawa S, Mizutani Y, et al. Restless legs syndrome in hemodialysis patients: health-related quality of life and laboratory data analysis. *Clin Nephrol.* 2006; 66(6): 440-6.
 8. Kim JM, Kwon HM, Lim CS, Kim YS, Lee SJ, Nam H. Restless legs syndrome in patients on hemodialysis: symptom severity and risk factors. *J Clin Neurol.* 2008; 4(4): 153-7.
 9. Al-Jahdali HH, Al-Qadhi WA, Khogeer HA, Al-Hejaili FF, Al-Ghamdi SM, Al Sayyari AA. Restless legs syndrome in patients on dialysis. *Saudi J Kidney Dis Transpl.* 2009; 20(3): 378-85.
 10. Unruh ML, Levey AS, D'Ambrosio C, Fink NE, Powe NR, Meyer KB, et al. Restless legs symptoms among incident dialysis patients: association with lower quality of life and shorter survival. *Am J Kidney Dis.* 2004; 43(5): 900-9.
 11. La Manna G, Pizzi F, Persici E, Baraldi O, Comai G, Cappuccilli ML, et al. Restless legs syndrome enhances cardiovascular risk and mortality in patients with end-stage kidney disease undergoing long-term haemodialysis treatment. *Nephrol Dial Transplant.* 2011; 26(6): 1976-83.
 12. Winkelman JW, Chertow GM, Lazarus JM. Restless legs syndrome in end-stage renal disease. *Am J Kidney Dis.* 1996; 28(3): 372-8.
 13. de Oliveira MM, Conti CF, Valbuza JS, de Carvalho LB, do Prado GF. The pharmacological treatment for uremic restless legs syndrome: evidence-based review. *Mov Disord.* 2010 30; 25(10): 1335-42.
 14. Allen RP, Walters AS, Montplaisir JY, Hening W, Myers A, Bell TJ, et al. Restless legs syndrome prevalence and impact: REST general population study. *Arch Intern Med.* 2005 13; 165(11): 1286-92.
 15. Allen RP, Stillman P, Myers AJ. Physician-diagnosed restless legs syndrome in a large sample of primary medical care patients in western Europe: Prevalence and characteristics. *Sleep Med.* 2010; 11(1): 31-7.
 16. Yoakum R. Night walkers: do your legs seem to have a life of their own? Your torment has a name. *Modern Maturity.* 1994; 55: 82-4.
 17. Byrne R, Smita S, Chaudhuri KR. Restless legs syndrome: diagnosis and review of management options. *Neuropsychiatr Dis Treat.* 2006; 2(2): 155-64.
 18. Salman SY. Restless legs syndrome in patients on hemodialysis. *Saudi J Kidney Dis Transpl.* 2011; 22(2): 368-72.
 19. Ferri R, Lanuzza B, Cosentino FI, A single question for the rapid screening of restless legs syndrome in the neurological clinical practice. *Eur J Neurol.* 2007; 14(9): 1016-21.
 20. Berger K, Luedemann J, Trenkwalder C, John U, Kessler C. Sex and the risk of restless legs syndrome in the general population. *Arch Intern Med.* 2004 26; 164(2): 196-202.
 21. Gigli GL, Adorati M, Dolso P, Piani A, Valente M, Brotini S, Budai R. Restless legs syndrome in end-stage renal disease. *Sleep Med.* 2004; 5(3): 309-15.
 22. Merlino G, Fratticci L, Valente M, Association of restless legs syndrome in type 2 diabetes: a case-control study. *Sleep.* 2007; 30(7): 866-71.
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