



## ASSESSMENT OF PREVALENCE OF RESTLESS LEG SYNDROME IN CHRONIC KIDNEY DISEASE PATIENTS ON MAINTENANCE HEMODIALYSIS AND THEIR CORRELATION WITH OUTCOME

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**ABSTRACT** Restless legs syndrome (RLS) is a neurological disorder characterized by sensory motor symptoms such as paresthesias and restlessness that mainly affect the lower limbs, occurring during rest in the evenings or overnight. To assess the prevalence of restless leg syndrome in patients on maintenance hemodialysis, assess their outcomes in the form of recurrent hospitalisations and correlation the outcome with mortality. 200 Patients of age group between 18 -60 years undergoing Maintenance Hemodialysis at Tertiary Care Hospital. The prevalence of RLS in maintenance hemodialysis patients was found to be 14.5% and factors associated with RLS in dialysis patients are increasing age, increasing duration of dialysis and serum iron.

**KEYWORDS** :Restless Legs Syndrome, Chronic Kidney Disease, Hemodialysis

### INTRODUCTION

Restless legs syndrome (RLS) is a neurological disorder characterized by sensory motor symptoms such as paresthesias and restlessness that mainly affect the lower limbs, occurring during rest in the evenings or overnight and are at least partially relieved by movement<sup>1</sup>. RLS can be primary or due to iron deficiency or other neurological disorders, or with physiological situations such as pregnancy, that may precipitate symptoms from epidemiological studies carried out in Northern Europe. The prevalence of RLS is 5% to 10% in adults with a high occurrence of familial patterns. Studies in patients with end stage renal disease (ESRD) showed a prevalence of RLS ranging from 12 to 62%, which is significantly higher compared to the general population.

The etiology of RLS in uremia is still not well defined, but the role of renal in sufficiency is confirmed by the resolution or improvement of RLS symptoms after kidney transplantation and by their recurrence after graft failure. Additional evidence of the occurrence of RLS with declining renal function in transplanted patients further suggests the association between kidney function and RLS<sup>2</sup>.

The biochemical factors and medical comorbidities that predispose to the development of WED/RLS among dialysis patients are yet to be confirmed. Some factors thought to be associated with WED/RLS are diabetes mellitus, use of coffee, afternoon shift of dialysis, female gender, lower hemoglobin (Hb), and homocysteine. However, a recent meta analysis reported that WED/RLS in dialysis patients was associated with diabetes mellitus among Asians while in Caucasians, the association was strong with low Hb and low iron.

The difference in the methodology used to diagnose WED/RLS appears to be the cause of the contradictory findings reported in the earlier studies. Few studies have used the International RLS Study Group (IRLSSG) criteria through questionnaire, while others have used the standardized questionnaire, others have relied on the clinical. Considering the inconsistent literature in this area, the present study planned to study to find out the prevalence of WED/RLS among subjects undergoing maintenance HD.

### AIM OF THE STUDY

To assess the prevalence of restless leg syndrome in patients on maintenance hemodialysis and correlation the outcome with mortality. To assess their outcomes in the form of recurrent hospitalisations and mortality.

### MATERIAL AND METHODS

200 Patients of age group between 18-60 years undergoing Maintenance Hemodialysis at Tertiary Care Hospital from January 2016 to January 2018.

### Inclusion criteria:

- 1) Those patients on MHD between 18 -60 years
- 2.) Those patients who have given consent.

### Exclusion criteria:

- 1) Patients who are 60 years
- 2) Those patients who are having History of RLS prior to the Development of CKD
- 3) Patients with diabetic Neuropathy.

### RESULTS

A total 200 number of patients undergoing maintenance are included in this study 133 (66.5%) were males and 65 (33.5%) females. Mean age of study group is 43.3±12.23 years. Mean vintage of dialysis is 33.7±24.7 months. Most common cause of ESRD in the present study is presumed chronic interstitial nephritis in contrast to other studies where DM is the leading cause of ESRD. In present study most of patients with DM suspected of having diabetic neuropathy are excluded. Out of 200 patients 29 are satisfied IRLSSG criteria. Patients are divided in to RLS positive and RLS negative groups and baseline characteristics of two groups are compared. P value was calculated using chi-square test and t test. Significant P value taken as <0.05. All the demographic data collected through face to face Questionnaire and most recent lab reports available with patients are collected and weight of the patients collected just before starting of dialysis.

### Baseline characteristics of study group

Males	133
Females	65
DM	28
HTN	163
CIN	99
CGN	69
ADPKD	13
DN	19
HbsAg	19
HCV	26
Mean Age	43.3 ± 12.23 years
Mean vintage of dialysis	33.7 ± 24.7 months
Mean weight	55.6±7.7 kg
Mean Hb	8.63 ± 1.63
Mean serum Iron	60.8 ± 12.9

### Comparison between RLS positive and Negative Groups

		RLS Positive (29)	RLS Negative (17)	P Value
Gender	Male	23	110	0.11
	Female	6	61	
DM	Present	7	21	0.08
	Absent	22	150	
HTN	Present	23	140	0.74
	Absent	6	31	
HbsAg	Positive	5	14	0.12
	Negative	24	157	
HCV	Positive	6	20	0.183
	Negative	23	151	

H/o CVA	Present	3	18	0.97
	Absent	26	153	
Native Kidney Disease	ADPKD	2	12	0.36
	CGN	11	55	
	CIN	11	88	
	DN	5	14	
Frequency of dialysis	Twice	12	67	0.82
	Thrice	17	104	
H/o blood transfusions	Present	8	36	0.45
	Absent	21	133	
H/o Tuberculous	Present	1	4	0.724
	Absent	28	167	
H/o Hospitalization	Present	5	13	0.09
	Absent	24	158	
Mortality 2 yr follow up		2	5	0.09
Age		48.75+ 8.92	42.46 + 12.50	0.01
Vintage of Dialysis		44.65 + 23.65	31.72 + 24.58	0.009
K t/v		1.24 + 0.62	1.27 + 0.17	0.45
IDWG		3.49 + 0.77	3.56 + 0.96	0.69
Weight		54.50 + 7.18	55.90 + 7.79	0.367
Hemoglobin		8.6 + 1.69	8.3 + 1.62	0.302
Serum Iron		65.59 + 14.7	59.26 + 13.9	0.026

**Comparison of variables between mild, moderate and severe RLS**

		Type of severity			P Value
		Mild RLS	Moderate	Severe RLS	
Gender	Male	13	7	3	0.09
	Female	1	2	3	
DM	Present	1	3	3	0.09
	Absent	13	6	3	
HTN	Present	11	8	4	0.57
	Absent	3	1	2	
HbsAg	Positive	2	2	1	0.8
	Negative	12	7	5	
HCV	Positive	4	2	0	0.34
	Negative	10	7	6	
H/o CVA	Present	3	0	0	0.167
	Absent	11	9	6	
H/o TB	Present	0	1	0	0.316
	Absent	14	8	6	
H/o blood transfusions	Present	5	2	1	0.62
	Absent	9	7	5	
Frequency of dialysis / wk	Twice	6	3	2	0.8
	Thrice	8	6	3	
Native Kidney Disease	ADPKD	1	1	0	0.16
	CGN	4	5	2	
	CIN	8	2	1	
	DN	1	1	3	
H/o Hospitalization	Present	2	2	2	0.88
	Absent	12	7	7	
Mortality 2 yr follow up	Present	1	0	0	0.45
	Absent	13	9	9	
Age		47.92 + 10.62	51.77 + 5.60	46.16+ 8.65	0.45
Vintage of Dialysis		42.21 + 25.58	47.55 + 18.78	46.00 + 28.81	0.86
K t/v		1.23 + 0.04	1.24 + 0.05	1.28 + 0.09	0.26
IDWG		3.53 + 0.75	3.47 + 0.82	3.41 + 0.86	0.95
Weight		56.8 + 6.7	52.33 + 8.12	52.5 + 6.08	0.24
Hemoglobin		8.7 + 1.82	8.3 + 1.76	8.9 + 1.40	0.75
Serum Iron		60.17 + 11.09	62.7 + 12.18	82.66 + 14.3	0.002

**DISCUSSION**

In present study the prevalence of RLS is 14.5%. This is in concordance with other studies conducted in dialysis population all over the world. Ohayon et al showed 3.9 to 15% prevalence of RLS among general population<sup>3</sup>.

Global prevalence of RLS was reported to be vary between 6 – 62 % and compared to general population prevalence is high in almost all studies. The prevalence of RLS is 62% in the Chinese population 12-23% in Japanese and 20-45% in Caucasians. Winkelman et al found 20% prevalence in American population. This suggests that there may be racial difference in the prevalence of RLS In India Bhowmik et al reported 6.6% prevalence in 121 patients. In present study the prevalence is found to be higher compared to Bhowmik et al study<sup>4,5,6,7</sup>.

**Comparison of our study to other studies**

Study (year) (Ref)	Country	No. of patients	Prevalence of RLS %
Winkelman et al (1996)	USA	204	20
Collado – Seidel et al (1998)	Germany	136	23
Huiqui et al (2000)	Switzerland	38	34
Hui DS et al (2000)	China	201	62
Thorp et al (2001)	USA	38	42
Kutner et al (2002)	USA	308	48
Takaki et al (2003)	Japan	490	12
Bhowmik et al (2003)	India	121	6.6
Goffredo Filho et al (2003)	Brazil	176	14.8
Gian Luigi Gigli et al (2004)	Italy	601	21
Mucsi et al (2005)	Hungary	-	14
Siddiqui S, et al	UK	277	45.8
Kawauchi (2006) 20 (2005)	Japan	228	23
Present Study	India	200	14.5

Present study showed the correlation of age with RLS mean age of the RLS positive group is more than the RLS negative group. INSTANT study was done in France in general population showed increase in prevalence of RLS until age 64 yrs in both sexes. Most of the studies conducted in dialysis population showed no significance with age<sup>8</sup>.

Present study showed significant association of RLS with vintage of dialysis Beladi Mousavi et al from Iran, Siddiqui et al study from UK in their study showed significant relation with the duration dialysis and presence of RLS. Three other studies have found an association between RLS and increasing duration of dialysis but some other studies have not showed this finding<sup>9</sup>.

Present study showed RLS had significant association of with serum iron. In this study mean serum iron of RLS positive group is 65.59±14.7 and RLS negative group is 59.26±13.9. Serum iron is more in RLS positive patients which is in contrast to other studies. Winkelman et al found correlation between RLS symptoms and transferrin saturation Nikic et al Iron deficiency in end-stage renal disease patients may lead to anemia and affect the dopamine metabolism, contributing to RLS. Wali and Alkhouli et al, in a recent report found iron deficiency, anemia, and calcium were not found to be statistically related to RLS in hemodialysis patients<sup>10</sup>.

In contrast to previous studies in present study there is negative correlation with serum iron and presence of RLS and RLS severity. But mean iron in both groups is below the lower limit of normal.

Present study showed RLS had no significant association with gender. In contrast to present study Siddiqui et al study from UK and Hamdan H. Al-Jahdali et al in Saudi Arabia in their study showed significant association of RLS with female gender. They explained high prevalence in female population may be due to sex hormones. Manna et al. reported that RLS is significantly associated with the female gender. Berger et al also reported that the incidence of RLS is approximately 10 times greater among women in the general population. However, similar to present study, some studies have not found gender differences between patients with and without RLS. Bhowmik et al Indian study showed no significant association between RLS and gender.

In present study there is no significant association between RLS and diabetes mellitus. In contrast to present study Siddiqui et al and Hamdan H. Al-Jahdali et al showed significant association between RLS and diabetes mellitus. Merlino G et al in their study showed association of RLS with DM. Similar to present study Winkelman et al in US and Bhowmik et al in India showed no significant association between RLS and diabetes mellitus.

Present study also showed no significant correlation between RLS and weight of patients. Siddiqui et al in their study found that there is correlation between RLS weight of the patients which is significant. Gao et al in their study with a large cohort found that the prevalence of RLS in end-stage renal disease patients was positively related to their BMI for patients with highest BMI compared with patients with lowest BMI.

Like previous studies the present study showed no significant association of RLS with comorbidities like CVA, tuberculosis, positivity of viral markers like HbsAg and Hcv adequacy of dialysis (k t/v), history of blood transfusions and anemia.

Present study showed RLS had no significant association with Mortality and hospitalisations. Both RLS positive and Negative groups patients are followed up for 2 years to observe for hospitalisations and mortality, there is no significant difference between two groups. In contrast to present study Winkelmann et al study conducted in American population showed significant morbidity and increased mortality in 2.5 years follow up. In concordance with present study De Ferio et al study showed RLS diagnosis was not associated with mortality in hemodialysis patients.

According to RLS severity rating scale in present study more number of patients are in mild (48.2%) and less number in the moderate (31.03%) and severe (20.6%) groups and no patients are in very severe group. In most previous studies conducted in dialysis population there were more patients in the severe and very severe groups. There is no significant correlation of severity of RLS with age and vintage of dialysis which are significant between RLS positive and RLS negative.

In present study serum iron is negatively correlated with the severity of RLS which is opposed to other studies. Some studies showed no correlation between RLS and serum iron. Bhowmik et al in their study in India showed no correlation between RLS and serum iron in their study most of the patients had severe RLS. In present study severe cases are less in number compared to other studies. Most studies not compared the severity in RLS positive patients<sup>11</sup>.

## CONCLUSION

- 1) The prevalence of RLS in maintenance hemodialysis patients was found to be 14.5%
- 2) Factors associated with RLS in dialysis patients are increasing age, increasing duration of dialysis and serum iron.
- 3) There is no significant association of RLS with other factors like DM, HTN, HbsAg & HCV positivity, anemia, IDWG
- 4) There is no significant association of RLS with hospitalizations and Mortality.

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