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Original Article

Restless Legs Syndrome in Patients with Hypertension and Diabetes Mellitus

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ABSTRACT

Objective: To analyze frequency of restless legs syndrome (RLS) in patients with hypertension and diabetes mellitus.
Study Design: Cross-sectional study.
Place and Duration of study: Department of Medicine at PNS Rahat Hospital Karachi, Pakistan from Oct 2023 to Mar 2024.
Methodology: A total of 240 patients who visited OPD were included in the study and evaluated. Sixty patients were placed in each in each category: Hypertension (Group-A), Diabetes Mellitus (Group-B), Hypertension plus Diabetes Mellitus (Group-C), and controls Group (Group-D). RLS was ascertained by question proforma as per International RLS Study Group Criteria.
Results: RLS was identified in 34 (56.6%) patients in Group-A, 35 (58.3%) patients in Group-B and 46 (76.6%) patients in Group-C. RLS was verified in 32 (53.3%) patients in Group-D. Female gender was found to have been slightly more affected by RLS in comparison to males. Moreover, it was also notably observed that in Groups C and D, patients aged fifty years and above were the most frequently observed age group.
Conclusion: Frequency of RLS is significantly more noteworthy in individuals with both diabetes and hypertension, and diabetes alone, followed by those with hypertension. It is necessary to raise physician perception of RLS because it is a common disorder in community. Since it can significantly lower quality of life, patients need to be diagnosed and provided the option of therapy.

Keywords: Diabetes Mellitus, Hypertension, Restless Legs Syndrome.

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INTRODUCTION

Restless legs syndrome (RLS) is a persistent neurosensorimotor illness marked by a need to move the legs that is frequently accompanied by uncomfortable or unpleasant sensations.[1] Symptoms include a crawling, creeping or soda bubbling sensation, which disappears when one moves their legs. Upper limbs can occasionally also be impacted.[2] These symptoms typically manifest during rest, making it difficult to fall asleep. Patients with RLS typically have a worse quality of life, are drowsy during the day, have less energy, are irritable, tired, and depressed, since the condition disrupts their sleep at night.[3] RLS may subside if the underlying reason is identified and addressed. The international RLS study Group established the diagnostic criteria for RLS in 1995.[3] However, there is no specific laboratory test for a biological marker, and the diagnosis of RLS is primarily based on clinical grounds.

RLS prevalence estimates range from 4% to 29% according to extensive community surveys conducted in Europe and North America. The prevalence is higher in women and rises with age and the presence of concomitant morbidities.[4] Even with the high reported prevalence, it is still thought that the incidence of RLS is understated. General practitioners usually misdiagnose RLS as anxiety, depression, and varicose veins that leads to concealing this disorder within general population.[5,6]

RLS was once identified as a peripheral neurological condition, but it has been found that RLS originates in the central nervous system.[7] Structural alterations in the peripheral and central neural systems are important factors in the onset of symptoms, and can be affected in certain chronic illnesses that target nerves.[8]

RLS can significantly lower quality of life, especially in patients of chronic diseases such as diabetes, hypertension, or both.[9,10] The aim of our study was to analyze frequency of restless legs syndrome (RLS) in patients with hypertension and diabetes mellitus.

METHODOLOGY

This cross-sectional study was conducted in the Department of Medicine at PNS Rahat Hospital Karachi from October 2023 to March 2024. Hospital Ethical Review Committee permission was taken prior

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to data collection (IERC No. MED-02/23 dated 27-09-2023).

Inclusion Criteria: Patients of either gender, aged above 18 years, diagnosed cases of diabetes mellitus, hypertension and diabetes plus hypertension with minimum of 5 years of disease duration were included.

Exclusion Criteria: Patients with other disorders like anemia, chronic kidney disease (CKD), peripheral neuropathy and patients with psychiatric illness were excluded.

Sample size was calculated using the WHO calculator, with 29% reported prevalence of restless legs syndrome (RLS).[11] This came to 240. Sixty patients were placed in each in each category: Hypertension (Group-A), Diabetes Mellitus (Group-B), Hypertension + Diabetes Mellitus (Group-C), and controls Group (Group-D).

Enrollment of subjects was carried out after taking consent from individuals according to set eligibility criteria, using non-probability consecutive sampling. The clinical history, physical examination, demographic information, and pertinent baseline investigations were done. All patients were clinically evaluated by Neurologist. RLS was ascertained by set question proforma in accordance with International RLS Study Group Criteria. The four fundamental minimally required criteria were as follows: a) the need to move one's legs, which is typically brought on by or accompanied by uncomfortable leg sensations; b) momentary relief from discomfort through movement, such as walking or stretching; c) the beginning or worsening of symptoms during rest or inactivity, such as when sitting or lying down; and d) an aggravation or onset of symptoms during the evening or night.[4] A proven tool for assessing the severity of restless legs syndrome (RLS) is the International Restless Legs Syndrome Study Group rating scale (IRLS).[12]

Statistical Package for Social Sciences (SPSS) version 25 was used for data analysis. Qualitative variables were expressed as frequency and percentages.

RESULTS

Our cohort included 60 individuals with hypertension (Group-A) which had 28 males and 32 females), 60 individuals with type I or II diabetes mellitus (Group-B), which had 37 males and 23 females, 60 patients with both hypertension and diabetes (Group-C), which had 29 males and 31 females, and 60 patients in the control group (Group-D0, which had 24 males and 36 females. In terms of occurrence of frequency, RLS was identified as more frequent in patients of Group-C (n=46, 76.6%), followed by Group-B (n=35, 58.3%) and Group-A (n=34, 56.6%). RLS was also verified in 32 (53.3%) of patients in Group-D. Moreover, gender-wise prevalence of RLS has been found slightly more in female gender as compared to male (Table-I).

Table–I: Gender-wise Prevalence of Restless legs Syndrome (RLS) across Groups (n=240)

Variable	Gender n	RLS n
Group-A	M 28	16
	F 32	18
Group-B	M 37	22
	F 23	13
Group-C	M 29	21
	F 31	25
Group-D	M 24	11
	F 36	21

M=Male, F = Female

The patients' average age was 56.1±10.9 years in Group-A, 56.8±19.2 years in Group-B, and 58.65±9.91 years in Group-C. The average age of Group-D was 51.8±10.3 years. An age of fifty years and above was the most frequently observed age group in the Groups C and D (Figure-1).

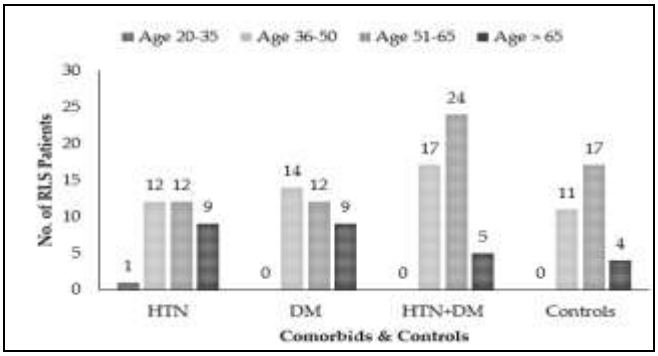

Figure: Age Distribution of Restless Legs Syndrome (RLS) among Patients and Controls

It is also pertinent to highlight here that most of the patients with RLS had disturbance in sleep and few had found it difficult to perform their daytime routine activities. RLS was found more frequently in patients who had both diseases together.

DISCUSSION

Our study has revealed that restless legs syndrome (RLS) occurs more often in patients with diabetes mellitus plus hypertension, followed by those

with diabetes mellitus alone, and hypertension alone as compared to healthy individuals. It is evident that the frequency of RLS is higher in patients with diabetes mellitus plus hypertension, signifying more impact of two disorders together in the same patient. A systematic review and modelling analysis on prevalence of RLS was carried out by Song *et al*., that revealed marked association of RLS with advanced age, diabetes mellitus, smoking and depression.[13] Manan *et al*., in study observed strong relationship between diabetes and RLS which they found to be less frequent in the control group, while in our study RLS was almost as frequent in the control as well as diabetes groups.[14] RLS in individuals with type II diabetes was evaluated using artificial intelligence (AI) models by Iftikhar *et al*., and discovered that about 28% of individuals had restless leg syndrome (there were 300 patients in total). Among the patients, 63.3% had hypertension, 68% had peripheral neuropathy, 2.7% had chronic renal failure (CRF), and 11% were smokers. Females had more preponderance in comparison to males.[15] In a study on the prevalence of RLS in patients with type II diabetes mellitus in Pakistan, Nawaz *et al*., assessed severity of RLS and found very severe RLS followed by severe, moderate and mild forms in 3.1%, 23.5%, 34% and 21.1% of the patients respectively, while 18.3% were found to have no RLS. All subjects were found to have hyperglycemic ranges.[16]

Tutan et al. studied the association of RLS with glycemic control and psychological status in adults with type 2 diabetes and found that there were no discernible differences between the RLS positive and RLS negative groups when the HbA1c levels were pooled.[17]

Guo *et al*., analyzed the relationship between RLS and hypertension in 4080 men and women, revealing that 3869 participants did not have RLS while 211 did. In this study, 6.8% women had more occurrence as compared to 3.2% in men with overall prevalence of 5.2%.[18] Khan *et al*., also found it's higher rate in diabetic population in their study.[19] Pinheiro *et al*., evaluated prevalence of RLS and quality of sleep in type 2 diabetes patients and an observable findings were RLS was diagnosed in 17(8%) subjects and mean sleep onset in subjects with RLS was 56 min versus 29 min in diabetics without RLS.[20] Senanayake *et al*. carried out a large-scale observational study with respect to comorbidities of patients with RLS. Their study highlighted female predominance being common in patients with younger than 65 years of age. Comorbid conditions revealed were hypertension, insomnia, diabetes and migraine. Other associated conditions observed were depressive disorders, anxiety disorders, tobacco use disorders, alcohol abuse, opioid dependence and cannabis use.[21]

After analyzing 31 studies with 8020 participants, Ning *et al*., came to the conclusion that GROUP-B patients had a combined RLS occurrence of 25% (based on IRLSSG diagnostic criteria), which was significantly greater than the 5–10% reported in the general population. Countries in Asia have greater prevalence (26%) compared to non-Asian countries (23%). Furthermore, compared to female patients, male patients had a higher prevalence of RLS (49% vs. 29%). It was also found that individuals having diabetes had an almost twice increased chance of developing RLS compared to those without the disease.[22] Gupta *et al*., in a research work on prevalence of RLS in patients with resistant hypertension and stroke patients and found that it was more prevalent in patients with resistant hypertension.[23] It was noted in the 1940s and 1950s that chilly foot complaints frequently accompanied RLS symptoms, and based on his observation that vasodilatory drugs provided relief, he surmised that both complaints mentioned a same etiology in vasoconstriction.[8] Similarly, Walters *et al*., found that those with RLS had a high incidence of cardiovascular illness and hypertension in the Wisconsin Sleep Cohort, a prospective community-based epidemiology study.[9]

Masood *et al*., recently conducted study in Pakistan to ascertain frequency of RLS in patients of diabetes mellitus and hypertension, and found almost similar results with slight differences compared with the results of our current study. According to their findings, RLS was found in 48(64.0%) persons with diabetes mellitus, 37(49.3%) with hypertension, and 58(77.3%) in patients with diabetes mellitus and hypertension.[24]

Additionally, it was suggested that sleep disorders linked to RLS and disruptions in daily activities during the day could be serious health problems. Cubo *et al*., in a community-based population study with 11 years of surveillance of patients with RLS, found that the disorder does not have higher mortality, but has an adverse effect on quality of life.[25] Since RLS is a prevalent problem in the general population, efforts need to be made to

raise physician awareness of the condition. Patients must be diagnosed and given the option of therapy because it can seriously impair quality of life. Nonetheless, additional epidemiological research is necessary to determine the prevalence rate, systematic correlations, and severity of RLS in order to reduce the number of instances. In the current era of Artificial Intelligence (AI) which is being used worldwide for identification of various health related issues in order to prevent patients from developing comorbidities, it is necessary to determine the incidence of RLS in distinct patient groups with illnesses using more sophisticated artificial intelligence-based models.

LIMITATIONS OF STUDY

Our main limitations were a small sample size, and that this was a single-centre study from a hospital catering to a specific faction, which may result in reduced generalizability of our findings.

CONCLUSION

Our study revealed that patients with hypertension and diabetes mellitus (76.6%), patients with diabetes mellitus (58.3%), and patients with hypertension (56.6%) are more likely to experience restless legs syndrome, and the frequency of RLS is greater in diseased individuals than in controls (53.3%). We also discovered that women have a somewhat higher frequency of RLS than men.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MR & ST: Data acquisition, data analysis, critical review, approval of the final version to be published.

SOA & RSH: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

KS & SO: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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