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Association of Restless Legs Syndrome with Hypertension and its Complications: A Cross-Sectional Study

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ABSTRACT

Background: Hypertension-associated complications and comorbidities continue to be widespread, although hypertension management has improved. Given the wide variability in the global frequency of Restless Legs Syndrome (RLS) in hypertensive patients and lack of data specific to Pakistan, where ethnic, healthcare and awareness differences limit the applicability of international findings, this study aims to determine the frequency of RLS in hypertensive individuals within the Pakistani population.

Methodology: This cross-sectional study was carried out from April to July 2025 at Departments of Medicine, Cardiology and Nephrology at Chaudhary Muhammad Akram Teaching and Research Hospital Lahore Pakistan. Using non-probability convenience sampling, 406 hypertensive patients aged ≥18 years were included. Patients were excluded if they had hypertensive emergencies, seizures, ongoing stroke or myocardial infarction, iron deficiency anemia, malignancies, a history of leg surgery or amputation, alcohol use disorder, acute kidney injury, were on hemodialysis or were pregnant. RLS was diagnosed according to the National Institutes of Health (NIH) criteria. Hypertension was defined as having blood pressure readings greater than 140/90 mm Hg on two separate occasions 2 weeks apart, ambulatory measurements exceeding 140/90 mm Hg at least 15 days apart, a prior diagnosis or antihypertensive medication use. Demographic information was collected and each participant underwent clinical evaluation to assess blood pressure control, antihypertensive treatment, comorbid conditions and the presence of RLS.

Results: Among the 406 patients, RLS was present in 64 (15.8%) patients. Post-stratification chi-square analysis showed that CKD ($p<0.001$) and IHD ($p=0.010$) had statistically significant associations. In multivariate logistic regression analysis, CKD emerged as a significant independent predictor of RLS ($p<0.001$, OR=12.649, 95% CI: 3.150–49.362). No other variables including gender, age, employment, marital status, hypertension duration or control, treatment regime, hypertensive retinopathy, diabetes, hypothyroidism or family history of hypertension had statistical significance.

Conclusion: Not an uncommon finding, RLS was more common with presence of co-morbid conditions in hypertensive patients. Routine screening for RLS, especially in hypertensive patients with CKD, may help improve patient outcomes.

Keywords: Restless Legs Syndrome, Hypertension, Chronic Kidney Disease, Hypertensive Retinopathy, Pakistan.

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INTRODUCTION

Restless Legs Syndrome (RLS) is clinically defined by a strong, often irresistible urge to move the limbs, typically accompanied by unpleasant sensations that are relieved through movement.[1] Symptoms typically worsen in the evening and at night, frequently disturbing patients' sleep.[1] The condition is linked to dysfunction in dopamine neurons located in the substantia nigra, with iron deficiency in these neurons playing a key role in its pathophysiology.[2,3] Notably, systemic iron levels are often normal despite this neuronal iron deficiency. RLS prevalence in adults ranges from 2% to 12% in Western populations, while studies in Asian countries such as China have reported much lower rates, as low as 0.1%.[1,2,4] RLS may be a primary disorder or secondary due to conditions including iron deficiency anemia, chronic renal disease, pregnancy, autoimmune rheumatic diseases, Parkinson's disease, and multiple sclerosis.[5] Diagnosis relies mainly on clinical criteria established by the National Institute of Health (NIH), or the International Restless Legs Syndrome Study Group (IRLSSG) as no definitive laboratory tests are available.[6]

Data on RLS in Pakistani hypertensive patients is scarce; nevertheless, a study by Masood et al. found a 49.3% prevalence of RLS among those with hypertension, which points to a major burden of this disease.[7] Moreover, the same study revealed that people with diabetes with co-existing hypertension had an even greater prevalence of RLS at 77.3% than 64.0% in those with only diabetes, implying that hypertension may boost the risk of developing RLS.[7] Studies on RLS have also investigated its relationships with obesity, pregnancy and renal failure in Pakistan. Malik et al. discovered RLS in 43.2% of obese people highlighting link to advanced age, sedentary lifestyle and insomnia.[8] In Lahore, Siddiqi et al. found RLS in 38.7% of end-stage renal disease patients having no association with demographic or lifestyle variables.[9] RLS was discovered in 25.4% of pregnant females of Lahore.[10]

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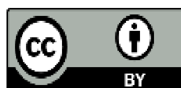

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However, data regarding prevalence of RLS in patients with hypertension in the general population remains limited.

Significant improvements have been made in management of hypertension including earlier diagnosis and treatment initiation, stringent targets of blood pressure control, comprehensive risk assessment, increased use of single-pill combination therapy, integration of digital health technologies and the development of novel therapies such as renal denervation and RNA-based agents. Despite this, its complications and comorbidities remain widespread and continue to contribute notably to patient morbidity, with cardiovascular disease being the commonest mortality cause.[11,12] It has been postulated that RLS shares common pathological pathways with hypertension including renal dysfunction, endothelial damage and dysautonomia.[2,5] The reported global prevalence of RLS among individuals with hypertension shows considerable variation, and data specific to the Pakistani population are notably limited. Variations in ethnicity, healthcare systems, and levels of disease awareness suggest that international findings may not be entirely applicable to the local context. This lack of region-specific data highlights the importance of conducting localized studies, prompting the present research to assess the frequency of RLS in hypertensive patients.

METHODOLOGY

This cross-sectional study was conducted from April to July 2025 at Departments of Medicine, Cardiology and Nephrology at Chaudhary Muhammad Akram Teaching and Research Hospital Lahore Pakistan with the primary aim was to assess the prevalence of RLS among individuals diagnosed with hypertension. Hypertension was defined as blood pressure consistently above 140/90 mm Hg, confirmed by at least two separate measurements taken at least 2 weeks apart, or by ambulatory (24-hour) blood pressure readings exceeding this threshold at least 15 days apart, or by a known diagnosis or documented use of antihypertensive medication**.** RLS was identified according to the National Institutes of Health (NIH) criteria, which include a strong urge to move the legs typically accompanied by uncomfortable sensations which begins or worsens during rest, improves with physical activity such as walking or stretching, and is more noticeable in the evening or at night.[6] Hypertensive retinopathy was determined through ophthalmologic examination and characterized by findings such as generalized or focal arteriolar narrowing, retinal hemorrhages, arteriovenous (AV) nicking, hard exudates, cotton-wool spots or swelling of the optic disc. Chronic kidney disease (CKD) was labeled as a sustained decrease in eGFR <60 mL/min/1.73 m² for more than three months, along with ultrasound features like reduced kidney size, cortical thinning or increased cortical echogenicity. Ischemic heart disease (IHD) was diagnosed as a history of unstable angina or acute myocardial infarction. Diabetes Mellitus was identified in individuals with an HbA1c level above 7.0%, at least two random blood glucose readings ≥200 mg/dL, a known diagnosis or use of antidiabetic therapy. Hypothyroidism was confirmed through elevated thyroid-stimulating hormone (TSH) levels in conjunction with low free thyroxine (T4) or in patients receiving thyroid hormone replacement therapy.

Using confidence level of 95% and margin of error 5%, sample size was calculated to be 384, based on an expected prevalence of RLS of 49.3% among individuals with hypertension. [7] Ultimately, 406 hypertensive patients aged 18 years and older, representing both genders, were included to ensure sufficient statistical power and increase the strength of study. Exclusion criteria were the presence of hypertensive emergencies including hypertensive crisis and urgency, seizures, acute stroke or acute myocardial infarction, iron deficiency anemia, malignancies, a history of leg surgery or amputation, alcohol dependence, acute kidney injury, current hemodialysis, or pregnancy.

After institutional ethical approval and obtaining informed consent, 406 hypertensive patients meeting the study criteria were recruited using non-probability convenience sampling. Information including patient gender, age, marital and employment status, and hypertension duration were collected. Each participant underwent a clinical assessment to evaluate blood pressure control, current antihypertensive treatment, and the presence of hypertensive retinopathy, diabetes mellitus and hypothyroidism. Relevant medical records were reviewed to gather data on blood pressure measurements, HbA1c, TSH, serum creatinine and urine analysis for confirmation of associated comorbidities. These variables were studied because they may influence development and severity of RLS by various mechanisms such as peripheral neuropathy, renal dysfunction, vascular damage or dopaminergic malfunction, allowing for control of confounding factors and independent associations with RLS. Patients were then assessed for the presence of RLS according to the NIH criteria. Only the participants fulfilling the entire NIH criteria were labeled as having RLS.

SPSS version 23 was used for data entry and analysis. Means with standard deviations and frequencies with percentages were generated for continuous and categorical variables, respectively. For associations of variables following stratification, Chi-square tests with significant $p \leq 0.05$ was conducted. Furthermore, to identify potential predictors of RLS among the hypertensive participants logistic regression analysis was done.

RESULTS

Out of the 406 hypertensive patients enrolled, 204 (50.2%) patients were aged ≥45 years, having mean age 46.5±9.6 years. Majority were female (304, 74.9%), unemployed (238, 58.6%) and married (358, 88.2%) as depicted in Table 1. Mean duration of hypertension was 5.8±3.7 years with 228 (56.2%) being hypertensive for ≥5 years. Blood pressure was controlled in 282 (69.5%) patients. A combination of two antihypertensive drugs was the most common treatment regimen, used by 210 (51.7%) individuals, followed by three-drug combinations in 98 (24.1%), as shown in Table 1. Hypertensive retinopathy was seen in 38 (9.4%) patients, CKD in 44 (10.8%), IHD in 104 (25.6%), diabetes mellitus in 204 (50.2%) and hypothyroidism in 16 (3.9%). A family history of hypertension was reported in 336 (82.8%) patients.

Table 1: Patient Variables

Patient variables		Frequency (n)
Gender	Female	304
	Male	102
Age	≤44 years	202
	≥45 years	204
Employment Status	Employed	168
	Unemployed	238
Marital Status	Married	358
	Unmarried	48
HTN Duration	≤4 years	178
	≥5 years	228
HTN Control	Good / Controlled	282
	Poor / Uncontrolled	124
Current HTN treatment regime	One drug	92
	Two drugs combination	210
	Three drugs combination	98
	Four drugs or more	06
Hypertensive Retinopathy	Present	38
	Absent	368
CKD	Present	44
	Absent	362
IHD	Present	104
	Absent	302
DM	Present	204
	Absent	202
Hypothyroidism	Present	16
	Absent	390
Family history of HTN	Present	336
	Absent	70
RLS	Present	64
	Absent	342

RLS was present in 64 (15.8%) patients. Post-stratification chi-square analysis showed that CKD ($p<0.001$) and IHD ($p=0.010$) had statistically significant associations with RLS as demonstrated in Table 2. Other variables such as gender, age, employment, marital status, duration of hypertension, treatment regimen, hypertension control, hypertensive retinopathy, diabetes, hypothyroidism and family history did not show significant associations with RLS as presented in Table 2.

Table 2: Chi-Square Test for stratification with regards to Restless Legs Syndrome

Demographic and Clinical Variables		RLS Absent	RLS Present	Pearson Chi-Square Value	p-value
Gender	Female	256 (84.2%)	48 (15.8%)	0	0.986
	Male	86 (84.3%)	16 (15.7%)		
Age	≤44 years	168 (83.2%)	34 (16.8%)	0.173	0.678
	≥45 years	174 (85.3%)	30 (14.7%)		
Employment Status	Employed	134 (79.8%)	34 (20.2%)	2.161	0.142
	Unemployed	208 (87.4%)	30 (12.6%)		
Marital Status	Married	308 (86.0%)	50 (14.0%)	3.682	0.055
	Unmarried	34 (70.8%)	14 (29.2%)		
HTN Duration	≤4 years	152 (85.4%)	26 (14.6%)	0.16	0.689
	≥5 years	190 (83.3%)	38 (16.7%)		
HTN Control	Good / Controlled	246 (87.2%)	36 (12.8%)	3.124	0.077
	Poor / Uncontrolled	96 (77.4%)	28 (22.6%)		
Treatment regime	One drug	78 (84.8%)	14 (15.2%)	3.262	0.353
	Two drugs combination	184 (87.6%)	26 (12.4%)		
	Three drugs combination	76 (77.6%)	22 (22.4%)		
	Four drugs or more	04 (66.7%)	02 (33.3%)		
Hypertensive Retinopathy	Present	28 (73.7%)	10 (26.3%)	1.758	0.185
	Absent	314 (85.3%)	54 (14.7%)		
CKD	Present	22 (50.0%)	22 (50.0%)	21.78	<0.001
	Absent	320 (88.4%)	42 (11.6%)		
IHD	Present	76 (73.1%)	28 (26.9%)	6.556	0.01
	Absent	266 (88.1%)	36 (11.9%)		
DM	Present	174 (85.3%)	30 (14.7%)	0.173	0.678
	Absent	168 (83.2%)	34 (16.8%)		
Hypothyroidism	Present	16 (100.0%)	0 (0.0%)	1.558	0.212
	Absent	326 (83.6%)	64 (16.4%)		
Family history of HTN	Present	280 (83.3%)	56 (16.7%)	0.599	0.439
	Absent	62 (88.6%)	08 (11.4%)		

In multivariate logistic regression analysis, CKD emerged as a significant independent predictor of RLS ($p< 0.001$, OR=12.649, 95% CI: 3.150–49.362) as shown in Table 3. Other variables including gender, age, employment, marital status, duration of hypertension, hypertension control, hypertensive retinopathy, diabetes, IHD, hypothyroidism or family history did not influence RLS prediction as depicted in Table 3.

Table 3: Results of logistic regression analysis

Demographic and clinical variables	Beta Coefficient (B)	S.E.	Wald	df	p-value	Odds Ratio (OR)	95% C.I. for OR Lower	95% C.I. for OR Upper
Gender	-0.04	0.507	0.006	1	0.937	0.961	0.356	2.596
Age	-0.734	0.57	1.659	1	0.198	0.48	0.157	1.467
Employment Status	0.773	0.479	2.602	1	0.107	2.166	0.847	5.542
Marital Status	-0.468	0.591	0.627	1	0.429	0.626	0.197	1.995
HTN Duration	0.14	0.525	0.071	1	0.789	1.151	0.411	3.222
HTN Control	-0.276	0.503	0.3	1	0.584	0.759	0.283	2.035
Retinopathy	-0.735	0.851	0.745	1	0.388	0.479	0.09	2.544
CKD	2.523	0.702	12.918	1	0	12.649	3.15	49.362
IHD	1.207	0.643	3.521	1	0.061	3.344	0.948	11.801
DM	-0.63	0.536	1.383	1	0.24	0.532	0.186	1.522
Hypothyroidism	-19.633	13236.193	0	1	0.999	0	0	-
Family history of HTN	-0.113	0.629	0.032	1	0.857	0.893	0.26	3.065

DISCUSSION

RLS was found in 15.8% in our study, indicating a considerable burden of RLS in this population, having an equal distribution among males and females ($p=0.986$). Although previous studies have reported higher prevalence rates, particularly when hypertension coexists with diabetes, our findings highlight that RLS remains a significant concern even in hypertensive patients as diagnosed by the NIH criteria, regardless of the presence of complications and co-morbid conditions. The prevalence in our study is less as compared to 49.3% reported by Masood et al. for people with hypertension.[7] These differences can be attributed to variability in the study population, methods or regional health profiles.[7] Among the clinical variables we examined, CKD had a strong and statistically significant link with RLS ($p < 0.001$). It also remained an independent predictor in logistic regression analysis (OR = 12.649, 95% CI: 3.150–49.362). This aligns with prior literature demonstrating a high RLS incidence in patients having impaired renal function, likely due to iron dysregulation, uremia or dopaminergic pathway disruption.[13,14,15] In contrast, other comorbid conditions such as diabetes, ischemic heart disease and hypothyroidism were not significantly associated with RLS in multivariate analysis, despite showing some trends in bivariate assessments. Interestingly, variables including gender, age, marital and employment status, duration of hypertension, and antihypertensive treatment regimens did not show a statistically significant relationship with RLS. While some previous studies have identified demographic factors like female gender or older age as potential risk factors,[16,17] our findings suggest that, in hypertensive patients, the presence of certain comorbidities particularly CKD may be more relevant predictors of RLS than sociodemographic characteristics.

The relatively high percentage of patients with uncontrolled hypertension (30.5%) and the observed trend of higher RLS prevalence among them (though not statistically significant, $p = 0.077$) point to a possible link between suboptimal blood pressure control and RLS symptoms. Poor hypertension control may contribute to microvascular changes or exacerbate comorbidities that could trigger or

worsen RLS symptoms.[18,19] Given that RLS is known to impair sleep quality, cause significant discomfort and reduce quality of life, its under-recognition in hypertensive patients is concerning.[20] The necessity of routine RLS screening in hypertensive people, particularly those with CKD or other contributing conditions, is reaffirmed by this study. Clinical results and quality of life may be enhanced by early diagnosis, which can enable prompt treatment with both pharmaceutical and non-pharmacological approaches. A comprehensive evaluation is the first step in managing RLS in order to find and address any underlying or contributing factors.[5] When RLS is secondary to other medical conditions, treatment of the underlying cause is essential. For individuals with primary RLS, the focus is on controlling symptoms.[21,22] In those with mild manifestations, non-pharmacological strategies are often sufficient. These include patient education on good sleep practices, physical techniques such as stretching, massage, walking, cognitive distraction and the use of hot or cold baths.[23,24] For patients experiencing moderate to severe symptoms, medication may be necessary. Common pharmacologic options include gabapentin, pregabalin, pramipexole, other dopaminergic agents or opioids, chosen based on symptom severity, comorbid conditions and the presence of pain or significant motor disturbances.[22,25]

This study has certain limitations that should be noted. Since it was carried out at a single healthcare institute, the results might not represent the wider population. For a clearer comprehension of the impact of RLS among hypertensive patients in Pakistan, further research involving larger and more diverse populations is warranted. The strengths of our study include use of an internationally validated diagnostic criterion for RLS, minimizing misclassification and ensuring accurate identification. Furthermore, our study encompassed both gender, wide age range and a detailed evaluation of complications and co-morbid conditions, allowing assessment of potential confounders and independent predictors. Although RLS is a treatable condition, it can considerably disrupt sleep and reduce overall quality of life. Raising awareness of RLS among healthcare professionals and patients is essential for promoting early diagnosis and timely treatment, which can help decrease the disease burden and improve patient outcomes.

CONCLUSION

RLS was detected in a significant percentage (15.8%) of hypertensive patients in our study. Among the different clinical and demographic variables that were analyzed, CKD had a good and statistically significant correlation with RLS and was an independent predictor. These findings highlight significance of RLS screening among hypertensive patients, particularly those having CKD, so that symptom management and overall quality of life may be improved.

Conflict of Interest
None to declare.
Disclaimer
None to declare.
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Author's Contribution:
BW, NIB, IK, and AB contributed to the conception and design of the study. Data collection was carried out by BK, NIB, IK, UW, and UJ. Data analysis, and interpretation was performed by BK, NIB, AB. Manuscript drafting and critical revision were undertaken by all authors. All authors approved the final manuscript.

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