ORIGINAL ARTICLE

Frequency of Restless Leg Syndrome in Diabetic Patients and it's Impact on Quality of Life

ABDUL MANAN[1], ZUBAIR AHMAD[2], WASFA AIJAZ[3], MUHAMMAD KAMRAN[4], FAYAZ AHMED MEMON[5], FAIZAN AHMED[6]
[1]Final year medical student, Quaid e Azam Medical College Bahawalpur, Bahawal Victoria Hospital, Bahawalpur
[2]Training Medical Officer, Department of Medicine, Hayatabad Medical Complex, Peshawar.
[3]Consultant Physician and Endocrinologist, Medicine and Endocrine Department, Medical Unit II, JPMC.
[4]House Officer, Department of Medicine, Mayo Hospital, Lahore.
[5]Professor, Department of Medicine, Muhammed Medical College & Hospital, Mirpurkhas, Sindh.
[6]House Officer, Internal Medicine, Lahore General Hospital.
Corresponding author: Zubair Ahmad, Email: zubairahmadbuner@gmail.com

ABSTRACT

Objective: The purpose of this study was to assess the prevalence of RLS and its effect on quality of life in diabetic patients.
Study Design: Cross-sectional/Comparative study
Place and Duration: Department of Medicine, Hayatabad Medical Complex, Peshawar in the duration from June, 2022 to November, 2022.
Methods: There were 114 diabetic and non diabetic patients were presented in this study. After obtaining informed written consent detailed demographics of enrolled cases were recorded. Patients were distributed in two groups, group I had 57 diabetic patients and groups II had 57 diabetic patients. Both groups were diagnosed with RLS using the International RLS Study Group's diagnostic criteria. SPSS 23.0 was used to analyze all data.
Results: There were majority females 30 (52.6%) in group I and 33 (57.9%) in group II. Mean age of the patients in group I was 49.17±9.48 years and in group II mean age was 46.12±11.85 years. Frequency of HTN in group I was found in 22 (38.6%) cases and in group II its frequency was 13 (22.8%). RLS in group I was found in 19 (33.3%) cases and in group II found in 5 (8.8%) cases. Frequency of retinopathy, neuropathy and abnormal neck circumference was significantly higher in diabetic cases as compared to non-diabetic with p value <0.002.
Conclusion: This study's findings suggest a strong link between RLS and diabetes, as well as a negative impact on the quality of life, health outcomes, sleep, daytime activity, cognitive function, and mental health of diabetic patients. Additionally, they suggest that doctors and other healthcare professionals should be more aware of RLS.
Keywords: RLS, Diabetes, Retinopathy, Neuropathy, Quality of life

INTRODUCTION

Diabetes mellitus (DM) is still a growing global health concern.[1,2] Involuntary leg movement, particularly in the evening and after long periods of inactivity, is a hallmark symptom of restless legs syndrome (RLS), a common neurological sensorimotor disease.[3,4] Clinically documented by Ekbom in the early 1940s, the term "restless legs syndrome" was first mentioned by Willis in 1672.[5] Thus, "Willis-Ekbom disease" is another name for this condition. The International Restless Legs Study Group (IRLSSG) established four minimum diagnostic criteria for RLS, which were as follows: 1 An itch to move the affected limbs, as is common in paresthesias and dysesthesias. 2.0 Discomfort in the muscles. 3. Symptoms are exacerbated or present only when at rest (i.e., when resting or sitting), and are alleviated, albeit temporarily, during physical activity. 4. Nighttime is when symptoms are most prominent.[6]

RLS has been associated to a number of different conditions and illnesses [7], including renal insufficiency, iron deficiency, rheumatoid arthritis, polyneuropathy, cryoglobulinemia, and infection; however, RLS can also be idiopathic or run in families. The fact that up to two-thirds of people who have primary RLS have a family history of the ailment suggests that it is an autosomal dominant disorder; the secondary variety of RLS is more common in people who present with RLS for the first time later in life [8].

Despite efforts to raise awareness, [9] this neurological condition is still frequently misdiagnosed by medical professionals. Because clinical observation is the only test available for RLS, diagnosis is entirely dependent on the patient's symptoms.

More than five times a month is required for a positive diagnosis of restless legs syndrome [10], and all four of the NIH-mandated essential clinical diagnostic criteria for the condition must be met. Participants at a workshop as well as members of the executive committee of the International Restless Legs Syndrome Study Group worked together to establish and validate these criteria. People with diabetes exhibited a 4-4.4 fold greater likelihood of experiencing restless legs syndrome (RLS) [11], in comparison to the general population. Because diabetes has a role in the aetiology of both polyneuropathy and renal failure [10], the association between RLS and diabetes is not as strong as it may be.

Those who suffer from restless leg syndrome (RLS) have trouble falling asleep and staying asleep once they go into bed. Daytime sleepiness and exhaustion are the result of poor sleep quality, which is exacerbated by restless legs syndrome (RLS) symptoms, which are alleviated by movement and walking. Although its path may be unpredictable, permanent decline is unusual. You can have RLS as a secondary condition or as a primary one. Secondary RLS is commonly caused by pregnancy, iron insufficiency, and renal failure, but primary RLS can have any number of potential causes, including a positive family history or idiopathic aetiology.

New research has revealed the involvement of the cerebellum and cingulate cortex, two brain regions not directly responsible for movement or sensation. Both the anterior and posterior cingulate gyri as well as the cerebellum were engaged. Multiple neurotransmitter systems are at play here, not just the dopaminergic oxygen-sensing system [12]. This includes the opioid, glutamatergic, and serotonergic networks.

Restless legs syndrome is characterised clinically by a strong desire to move the limbs in response to an uncomfortable sensation that worsens during sleep and is alleviated by movement. Restless Legs Syndrome (RLS) may be an underlying medical condition or a symptom of another illness, such as iron deficiency anaemia or polyneuropathy. Despite their similarities, RLS and painful diabetic neuropathy are two separate entities that can be difficult to diagnose [13,14]. There are no diagnostic tests; therefore, the diagnosis is made only on clinical symptoms alone. There are four requirements that must be met on more than five occasions per month [15], as determined by the executive committee of the International Restless Legs Syndrome Study and Workshop group. This investigation focuses on T2DM patients and their experiences with RLS.

MATERIALS AND METHODS

This Cross-sectional/Comparative study was conducted at Department of Medicine, Hayatabad Medical Complex, Peshawar

in the duration from June, 2022 to November, 2022 and comprised of 114 patients. Included patients were diabetic and hypertensive cases and were aged between 20-70 years. Patients who were hesitant to participate, women who were pregnant, and persons with certain diseases were excluded.

Patients were distributed in two groups, group I had 57 diabetic patients and groups II had 57 diabetic patients. The International Restless Legs Syndrome Study Group's four minimum criteria for RLS were used to assess diagnostic criteria of RLS, and the physician collected the data from a checklist that included demographic information, diabetes-related variables, and diagnostic criteria of RLS. Age, sex, and BMI were used to create a balanced sample for each group. The duration and type of diabetes in a patient are established. Risk factors and diabetes subtype were examined using two-dimensional frequency tables and the tchouprov qualitative correlation coefficient. Test was used to compare the prevalence of RLS between the two groups, and means and standard deviations were used to summarise quantitative factors. The Mann-Whitney U test, the Fisher's exact test, and the chi-square test were employed to determine statistical significance when comparing two groups. Data analysis was performed in SPSS 23.0.

RESULTS

There were majority females 30 (52.6%) in group I and 33 (57.9%) in group II. Mean age of the patients in group I was 49.17±9.48 years with mean BMI 27.2±6.39 kg/m^2 and in group II mean age was 46.12±11.85 years and had mean BMI 26.4±7.26 kg/m^2. 37 cases in group I were smokers and in group II 21 cases were smokers.18 cases in group I and 31 cases in group II had physical activity >30 min/day.(table 1)

Table-1: Demographics data of the both groups

Variables	Diabetes (57)	Non-diabetes (57)
Mean age (years)	49.17±9.48	46.12±11.85
Mean BMI (kg/m^2)	27.2±6.39	26.4±7.26
Gender		
Male	27 (47.4%)	24 (42.1%)
Female	30 (52.6%)	33 (57.9%)
Smokers		
Yes	37 (64.9%)	21 (36.8%)
No	20 (35.1%)	36 (63.2%)
Physical activity		
>30mint per day	18 (31.6%)	31 (54.4%)
<30mint per day	39 (68.4%)	26 (45.6%)

Frequency of HTN in group I was found in 22 (38.6%) cases and in group II its frequency was 13 (22.8%).(figure 1)
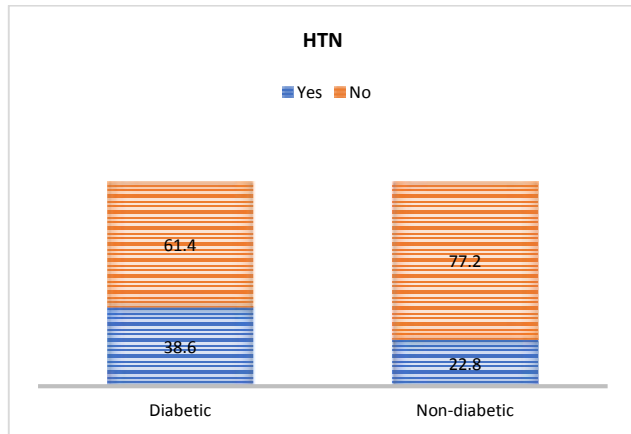

Figure-1: Hypertension among both groups

RLS in group I was found in 19 (33.3%) cases and in group II found in 5 (8.8%) cases.(table 2)

Table-2: Frequency of RLS among both groups

Variables	Diabetic (n=57)	Non-diabetic (n=57)
Restless Leg syndrome		
Yes	19 (33.3%)	5 (8.8%)
No	38 (66.75)	52 (91.2%)

Frequency of retinopathy, neuropathy and abnormal neck circumference was significantly higher in diabetic cases as compared to non-diabetic with p value <0.002.(table 3)

Table-3: Relation of diseases with diabetes

Variables	Group I	Group II
Comorbidities		
retinopathy	28 (49.1%)	10 (17.5%)
neuropathy	13 (22.8%)	6 (10.5%)
abnormal neck circumference	44 (77.2%)	12 (21.1%)

Sleep quality poor was found majority in RLS diabetic cases as compared to non-diabetic cases with p <0.003.(table 4)

Table-4: Sleep quality among both groups

Variables	Group I	Group II
Sleep Quality		
Poor	43 (75.4%)	8 (14.04%)
Normal	14 (24.6%)	49 (75.96%)

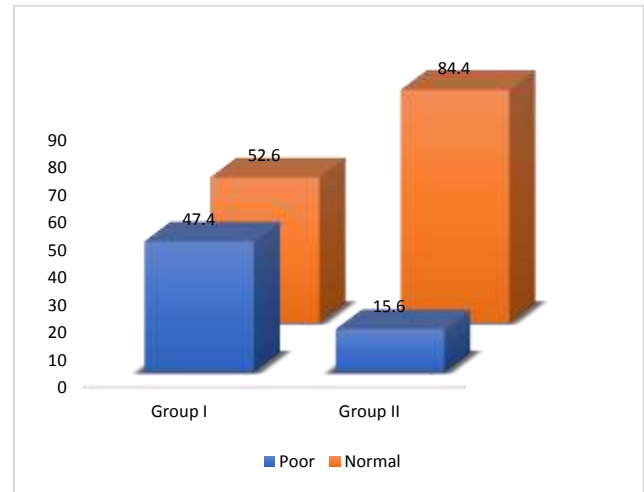Quality of life among RLS cases of both groups were affected negatively.(figure 2)

Figure-2: QoL comparison among both groups

DISCUSSION

Several studies have demonstrated that persons who have type 2 diabetes have a much higher prevalence of restless legs syndrome; however, this link cannot be simply attributable to the existence of peripheral neuropathy in these patients. Long-term sleep deprivation is associated with an increased risk of insulin resistance as well as metabolic abnormalities [16]. Another probable cause of insulin resistance and metabolic abnormalities is obesity. According to the findings, the prevalence of RLS among diabetics was 33.3%, whereas it was only 8.8% in the control group. The current result was superior than the finding that was made by Harashima et al. (8%), which was found in [17]. Results obtained in this investigation were comparable to those obtained in a study carried out by Zobeiri et al. [18], who discovered a prevalence of 28.6% in experimental individuals as opposed to 7.1% in control participants. In earlier study carried out in a variety of nations [19,20], it was shown that diabetic patients had a lower incidence of RLS than those without diabetes.

In a study that was conducted by Batool-Anwar et al.8, the participants were women between the ages of forty and fifty-one, and the researchers discovered that 33% of the individuals suffered from hypertension. These findings are consistent with those of other studies that have concluded there is a connection among RLS and hypertension and cardiovascular disease.[21,22] The fact that the prevalence of restless legs syndrome (RLS) is more than four times higher in diabetics than in non-diabetic controls suggests that there is a strong connection between RLS and diabetes. Given the association between neuropathy and RLS [23], the increased risk for RLS in diabetics may indicate repercussions of diabetic neuropathy rather than diabetes itself. This hypothesis is supported by the fact that diabetic neuropathy is associated with RLS. Cho et al. reveal a proven RLS prevalence in diabetics that is over two times more than control with osteoarthritis [23]. This was accomplished by performing in-person interviews using the 18-item Hopkins Diagnostic Questionnaire, which eliminates RLS mimics.

This conclusion contradicts the results of a prior study [24] that found no link between RLS and T2D. Different comorbidities and study designs could account for the varying prevalence of RLS . The current investigation confirmed a previously observed [25] link between peripheral neuropathy and restless legs syndrome. A misdiagnosis or delay in treatment may occur because the symptoms of restless legs syndrome and peripheral neuropathy are similar and can worsen each other's effects. Restless legs syndrome may also be associated with small fibre neuropathy [26]. The results of this study highlight the significance of detecting restless legs syndrome as soon as possible, as it is a curable illness that worsens diabetic neuropathy and has a detrimental impact on quality of life and sleep. The current finding of a numerically higher (not reaching statistical difference) glycated haemoglobin among patients with restless legs syndrome contradicts the conclusions of previous researchers who found that restless legs syndrome, through sleep disturbances and psychological factors, could impair glycemic control [27]. Similar to a survey that was conducted in Colombia [28,29] and reached the same conclusion, the current investigation revealed no association between RLS and sex, retinopathy, or neck circumference.

Diseases unrelated to sleep or the nervous system are common companions to RLS. Identifying patients might be challenging because their symptoms are often subtle.[30]

CONCLUSION

This study's findings suggest a strong link between RLS and diabetes, as well as a negative impact on the quality of life, health outcomes, sleep, daytime activity, cognitive function, and mental health of diabetic patients. Additionally, they suggest that doctors and other healthcare professionals should be more aware of RLS.

REFERENCES

1   Delanerolle G., Phiri P., Zeng Y., et al. A systematic review and meta-analysis of gestational diabetes mellitus and mental health among BAME populations. EClinicalMedicine. 2021;38
2   Li T., Providencia R., Mu N., et al. Association of metformin monotherapy or combined therapy with cardiovascular risks in patients with type 2 diabetes mellitus. Cardiovasc Diabetol. 2021;20(1):30.
3   Burman D. Sleep disorders: restless legs syndrome. FP Essent. 2017;460:29–32.
4   Allen R.P., Picchietti D., Hening W.A., et al. 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):101–119.
5   Odin P., Mrowka M., Shing M. Restless legs syndrome. Eur J Neurol. 2002;9(Suppl 3):59–67.
6   Allen R.P., Picchietti D.L., Garcia-Borreguero D., et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG)

consensus criteria–history, rationale, description, and significance. Sleep Med. 2014;15(8):860–873.
7   G. Merlino, L. Fratticci, M. Valente et al., "Association of restless leqs syndrome in type 2 diabetes: a case-control study," Sleep, vol. 30, no. 7, pp. 866–871, 2007.
8   P. E. Cotter and S. T. O'Keeffe, "Restless leg syndrome: is it a real problem?" Therapeutics and Clinical Risk Management, vol. 2, no. 4, pp. 465–475, 2006.
9   C. Sitaru, V. Cristea, and S. M. Florea, "Restless legs syndrome—relevant aspects for internal medicine specialists," Romanian Journal of Internal Medicine, vol. 37, no. 3, pp. 275–286, 1999.
10 R. P. Skomro, S. Ludwig, E. Salamon, and M. H. Kryger, "Sleep complaints and restless legs syndrome in adult type 2 diabetics," Sleep Medicine, vol. 2, no. 5, pp. 417–422, 2001.
11 S.-C. Lai and R.-S. Chen, "Restless legs syndrome," Acta Neurologica Taiwanica, vol. 17, no. 1, pp. 54–65, 2008.
12 Koo BB, Bagai K, Walters AS: Restless legs syndrome: current concepts about disease pathophysiology. Tremor Other HyperkinetMov (N Y). 2016, 22:401.
13 Trotti LM, Becker LA: Iron for the treatment of restless legs syndrome. Cochrane Database Syst Rev. 2019, 4:CD007834.
14 Kalra S, Gupta A: Diabetic painful neuropathy and restless legs syndrome in diabetes. Diabetes Ther. 2018, 9:441-447.
15 Allen RP, Picchietti D, Hening WA, et al.: 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, 4:101-119.
16 Greco D: Sindrome delle gambe senza riposo e diabete mellito: un'associazione casuale? [Article in Italian]. Recenti Prog Med. 2011, 102:212-216.
17 Harashima S, Nishimura A, Osugi T Wang Y, Liu Y, Takayama H, Inagaki N: Restless legs syndrome in patients with type 2 diabetes: effectiveness of pramipexole therapy. BMJ Support Palliat Care. 2016, 6:89-93.
18 Zobeiri M, Shokoohi A: Restless leg syndrome in diabetics compared with normal controls. Sleep Disord. 2014, 2014:871751.
19 Modarresnia L, Golgiri F, Madani NH, Emami Z, Tanha K: Restless legs syndrome in Iranian people with type 2 diabetes mellitus: the role in quality of life and quality of sleep. J Clin Sleep Med. 2018, 15:223-228.
20 Šiarnik P, Klobučníková K, Šurda P, Putala M, Šútovský S, Kollár B, Turčáni P: Excessive daytime sleepiness in acute ischemic stroke: association with restless legs syndrome, diabetes mellitus, obesity, and sleep-disordered breathing. J Clin Sleep Med. 2018, 15:95-100.
21 Chen NH, Chuang LP, Yang CT, Kushida CA, Hsu SC, Wang PC, et al. The prevalence of restless legs syndrome in Taiwanese adults. Psychiatry Clin Neurosci 2010;64:170-8.
22 Winkelman JW, Finn L, Young T. Prevalence and correlates of restless legs syndrome symptoms in the Wisconsin Sleep Cohort. Sleep Med 2006;7:545-52.
23 Y. W. Cho, G. Y. Na, J. G. Lim et al., "Prevalence and clinical characteristics of restless legs syndrome in diabetic peripheral neuropathy: comparison with chronic osteoarthritis," Sleep Medicine, vol. 14, pp. 1387–1392, 2013.
24 Sabic A, Sinanovic O, Sabic D, Galic G: Restless legs syndrome in patients with hypertension and diabetes mellitus. Med Arch. 2016, 70:116-118.
25 Merlino G, Fratticci L, Valente M, et al.: Association of restless legs syndrome in type 2 diabetes: a case-control study. Sleep. 2007, 30:866-871.
26 Harashima S, Nishimura A, Osugi T Wang Y, Liu Y, Takayama H, Inagaki N: Restless legs syndrome in patients with type 2 diabetes: effectiveness of pramipexole therapy. BMJ Support Palliat Care. 2016, 6:89-93.
27 Cuellar NG, Dorn JM: Peripheral diabetic neuropathy or restless legs syndrome in persons with type 2 diabetes mellitus: differentiating diagnosis in practice. J Am Assoc Nurse Pract. 2015, 27:671-675.
28 Merlino G, Valente M, Serafini A, et al.: Effects of restless legs syndrome on quality of life and psychological status in patients with type 2 diabetes. Diabetes Educ. 2010, 36:79-87.
29 Ruiz AJ, RondonSepúlveda MA, Franco OH, et al.: The associations between sleep disorders and anthropometric measures in adults from three Colombian cities at different altitudes. Maturitas. 2016, 94:1-10.
30 Ning P, Mu X, Yang X, Li T, Xu Y. Prevalence of restless legs syndrome in people with diabetes mellitus: A pooling analysis of observational studies. EClinicalMedicine. 2022 Mar 24;46:101357.