RESEARCH ARTICLE

Prevalence and severity of restless leg syndrome in patients with spinal cord injuries

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Abstract

Objective: To determine the prevalence of restless leg syndrome in patients with spinal cord injury using a consensus criterion.

Method: The cross-sectional study was conducted from November 29, 2018, to February 28, 2021 at the departments of Neurology and Orthopaedic Surgery, King Edward Medical University, Mayo Hospital, Lahore, Pakistan, and comprised patients of either gender aged 18-80 years having spinal cord injuries. All the patients were interviewed using a 10-item questionnaire, and were assessed using the five-point consensus criteria of the International Restless Leg Syndrome Study Group. Data was analysed using SPSS 20.

Results: Of the 253 patients, 128(50.6%) were males and 125(49.4%) were females. The overall mean age was 38.6±14.2 years. Restless leg syndrome was present in 116(45.8%) patients, and 64(55.2%) of them were males ($p>0.05$). The mean duration of the symptoms was 18.9±16.9 months. Causes of spinal cord injury included metastasis 28(11.1%) multiple sclerosis 32(12.6%), neuromyelitis optica spectrum disorders 68(26.9%), tuberculous spondylitis 85(33.6%), trauma 24(9.5%) and viral myelitis 16(6.3%).

Conclusion: Restless leg syndrome was prevalent in less than half the patients having spinal cord injury. It was more prevalent in males compared to females, but the difference was not significant.

Key Words: Restless leg syndrome, Spinal cord injury, Leg pain syndrome.

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Introduction

A very common movement disorder is the restless leg syndrome (RLS) in which the patient has a strong and irresistible urge to move the legs. It usually happens in the mornings and evenings, when the patient is in a resting position. This condition may improve when patients continue to move their legs. Walking and stretching of legs also play a useful role[1]. A survey done among the general population showed that RLS prevalence was 3% in those aged 18-29 years, 10% in those aged 30-79 years, and 19% in those aged >80 years. The disease generally appeared between the third and the fourth decades of life[2]. Women are frequently affected by this disorder and the morbidity rate is significantly high. Also, dopamine deficiency and brain iron dysregulation are the principal abnormalities seen in RLS patients[3]. Patient's family history, the presence of periodic leg movements when awake or asleep, and a positive response to dopaminergic treatment are key diagnostic markers. RLS may cause severe sleep disturbances, low quality of life, depressive and anxiety symptoms, and may be a risk factor for cardiovascular disease (CVD)[4].

Spinal cord injuries (SCIs), both traumatic and non-traumatic, pose an enormous economic burden on the healthcare system due to their associated morbidity. Kumru H et al.[5] found a 17.9% frequency of RLS in traumatic SCI patients. RLS prevalence was reported at 19% among veterans with spinal cord lesions by Friday T et al.[6]. RLS diagnosis is quite challenging in patients with traumatic SCI because post-traumatic neuropathic pain is a common complication and the biggest mimic of RLS.[7,8] Many studies reported a higher prevalence of RLS in multiple sclerosis (MS) patients having spinal cord lesions.[9-11] Similarly, a couple of studies[12,13] found increased frequency and severity of RLS in patients with neuromyelitis optica spectrum disorders (NMOSD). In a recent study conducted in Iran,[14] prevalence rates of RLS were reported at 45.8% in NMOSD and 28.7% in MS. The current study was planned to evaluate the prevalence and severity of RLS in patients with various SCIs presenting at a tertiary care hospital in Pakistan.

Patients and Methods

The cross-sectional study was conducted from November 29, 2018, to February 28, 2021 at the departments of Neurology and Orthopaedic Surgery,

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King Edward Medical University, Mayo Hospital, Lahore, Pakistan. After approval from the institutional ethics review board, the sample size was calculated with 95% confidence level, 5% margin of error and expected RLS prevalence of 17.9% using online software openepi.[5,15]

The sample was raised using non-probability consecutive sampling technique. Those included were patients of either gender aged 18-80 years having SCIs. Pregnant females and patients with anaemia, uraemia, Parkinsonism and taking anti-psychotics or anti-depressants were excluded. Those mimicking conditions such as post-traumatic neuropathic pain, peripheral neuropathy and radiculopathy, peripheral artery disease, myalgia, venous stasis, leg oedema, arthritis, nocturnal leg cramps, painful legs and moving toes syndrome, meralgia paresthetica, positional discomfort and habitual foot-tapping were carefully investigated and excluded.

After taking informed consent from all the subjects, the same neurologist and orthopaedic surgeon interviewed and assessed all the patients for the presence and absence of RLS. All the patients were interviewed using a 10-item questionnaire, and were assessed using the five-point consensus criteria of the International RLS Study Group (IRLSSG)[16], including "an urge to move the legs that is present at rest, relieved by movement, demonstrates a circadian pattern with peak symptoms occurring at night or in the evening and the occurrences of the above features are not solely accounted for as symptoms primary to another medical or behavioural condition (e.g., myalgia, venous stasis, leg oedema, arthritis, leg cramps, positional discomfort, habitual foot tapping)". The severity of RLS was rated using the IRLSSG rating scale[17].

Data regarding gender, age, presence/absence and severity of RLS, duration of symptoms, level and cause of SCI were noted on a pre-designed proforma. Questions 1, 2, 4, 5, 6, 9 and 10 were assessed using a 5-point Likert scale; very severe, severe, moderate, mild and none. Question 3 was assessed with a 6-point Likert scale; no relief, mild relief, moderate relief, complete or almost complete relief, and no RLS symptoms, and the question does not apply. Question 7 was rated using a 5-point Likert scale; very often=6-7 days, often=4-5 days, sometimes=2-3 days, occasionally=<1 day, and never. For question 8, following Likert scale was used: very severe=8/24 hours, severe=3-8/24 hours, moderate=1-3/24 hours, mild=<1/24 hours, and none. The overall score of the questionnaire ranged from a minimum of zero to the maximum of 40.

Data was analysed using SPSS 20. Qualitative data was presented as frequencies and percentages, while quantitative data was presented as means and standard deviations. Data was stratified for age and severity of RLS. Post-stratification, chi-square test was applied. $P<0.05$ was taken as statistically significant.

Results

Of the 253 patients, 128(50.6%) were males and 125(49.4%) were females. The overall mean age was 38.6±14.2 years. The mean duration of the symptoms was 18.9±16.9 months. Causes of spinal cord injury included metastasis 28(11.1%) multiple sclerosis 32(12.6%), neuromyelitis optica spectrum disorders 68(26.9%), tuberculous spondylitis 85(33.6%), trauma 24(9.5%) and viral myelitis 16(6.3%) (Table 1).

Table-1: Demographic data of the gender, age, duration of the symptoms, level and cause of spinal cord injury.

Variables	Frequency (N=253)	Percent (%)
Gender of the patients		
●Male	128	50.6%
●Female	125	49.4%
Age of the patients in years (Mean±SD)	38.6±14.2	
Restless leg syndrome		
●Yes	125	49.4%
●No	137	54.2%
Duration of the symptoms (Mean±SD)	18.9±16.9	
Level of the spinal cord		
●Cervical	77	28.8%
●Thoracic	88	34.8%
●Cervicothoracic	44	17.4%
●Lumbar	16	6.3%
●Thoracolumbar	08	3.2%
●Lumbosacral	24	9.5%
Cause of spinal cord injury		
●Metastasis	28	11.1%
●Multiple sclerosis	32	12.6%
●Neuromyelitis optica spectrum disorders	68	26.9%
●Tuberculous spondylitis (Pott disease)	85	33.6%
●Trauma	24	9.5%
●Viral myelitis	16	6.3%

SD: Standard deviation.

Table-2: Gender distribution of patients with restless leg syndrome (RLS).

Restless leg syndrome	Gender of the patient		*p*-value
	Male (n=128) (%)	Female (n=125) (%)	
●Present	64 (55.2%)	52 (44.8%	0.180
●Absent	64 (46.7%)	73 (53.3%)	

RLS was present in 116(45.8%) patients, and 64(55.2%) of them were males ($p>0.05$) (Table 2). Responses to the RLS

Table-3: Rating scale for restless lest syndrome (RLS) questionnaire responses by the participants.

Variables	Very severe	severe	Moderate	Mild	None	N=253
Overall, how would you rate the RLS discomfort in your legs or arms?	08 (3.2%)	64 (25.3%)	36 (14.2%)	08 (3.2%)	137 (54.2%)	253 (100%)
Overall, how would you rate the need to move around because of your RLS symptoms?	08 (3.2%)	64 (25.3%)	36 (14.2%)	08 (3.2%)	137 (54.2%)	253 (100%)
Overall, how much relief of your RLS arm or leg discomfort did you get from moving around?	24 (9.5%),	20 (7.9%),	72 (28.5%),	00 (00%)	137 (54.2%).	253 (100%)
Overall, how severe was your sleep disturbance because of your RLS symptoms?	08 (3.2%),	24 (9.5%),	32 (12.6%),	52 (20.6%)	137 (54.2%)	253 (100%)
How severe was your tiredness or sleepiness because of your RLS symptoms?	08 (3.2%),	32 (12.6%),	48 (19.0%)	28 (11.1%)	137 (54.2%).	253 (100%)
Overall, how severe was your RLS as a whole?	24 (9.5%),	32 (12.6%),	56 (22.1%),	04 (1.6%)	137 (54.2%)	253 (100%)
How often did you have RLS symptoms?	8 (3.2%),	48 (19.0%),	48 (19.0%),	12 (4.7%)	137 (54.2%).	253 (100%)
When you had RLS symptoms, how severe were they on an average day?	00 (00%)	24 (9.5%),	40 (15.8%),	52 (20.6%)	137 (54.2%)	253 (100%)
Overall, how severe was the impact of your RLS symptoms on your ability to carry out your daily affairs (for example carrying out a satisfactory family, home, social, school, or work life)?	16 (6.3%)	24 (9.5%),	56 (22.1%),	20 (7.9%)	137 (54.2%)	253 (100%)
How severe was your mood disturbance because of your RLS symptoms (for example, angry, depressed, sad, anxious, or irritable)?	00 (00%)	32 (12.6%),	52 (20.6%),	32 (12.6%),	137 (54.2%)	253 (100%)

rating scale questionnaire were stratified (Table 3).

Discussion

The current study found RLS in 45.8% patients having SCIs, including both non-traumatic and traumatic causes; mostly prevalent in patients with tuberculous (TB) spondylitis (33.6%), followed by neuromyelitis optica spectrum disorders (26.9%) and multiple sclerosis (12.6%). Once thought to be a rare disorder, RLS is now known to be a common condition globally; the highest (5.5-11.6%) prevalence is reported in North America and Europe, while the least (1.0-7.5%) prevalence has been reported from Asia.[18] Females are affected about twice as often as males for mild as well as moderate-to-severe RLS.[19]

Since the advent of anti-TB therapy (ATT) and improved public health measures, spinal TB has been minimised in industrialised countries, although in developing nations it is still a significant cause of morbidity. Recently, an Indian study[20] reported 17% prevalence of poor sleep quality and 32% risk of RLS among TB patients, including pulmonary and extra-pulmonary disease. Similarly, the current study found RLS significantly prevalent (33.6%) in TB spondylitis (i.e. Potts disease) patients. The finding is consistent with the Indian study[20], probably because the two countries share the same region regarding environmental, socioeconomic, cultural and genetic factors. Moreover, there is a possibility that isoniazid, which is an essential firstline ATT, causes peripheral neuropathy, and peripheral neuropathy by itself is an independent risk factor for RLS and can mimic RLS, which could be the reason for the significantly high prevalence of RLS in TB spondylitis patients.

According to Hyun JW et al.,[12], the frequency and severity of RLS in NMOSD patients were significantly higher than in healthy controls, and NMOSD patients with RLS had a longer disease duration and more severe disability than those without RLS. Similarly, Bazegar M. et al.[13] reported lower quality of life, higher symptoms of anxiety and depression, and more RLS symptoms in NMOSD patients. In the current study, RLS was present in 26.9% of NMOSD and 12.6% of MS patients, contrary to much higher prevalence rates of RLS at 45.8% in NMOSD, 41.1% in clinically isolated syndrome (CIS) and 28.7% in MS, recently reported by Shaygannejad V et al.[14] Moreover, they found that MS patients had lower prevalence rates for RLS than CIS or NMOSD patients, which is in line with the current findings.

Sieminski M et al.[21] presented a comprehensive account of the high overlap between RLS and MS. Briefly, inflammatory processes in MS may lead to an upregulation of cytokines (Il-6, TNF), which causes intracellular iron retention, leading to cell destruction and iron deficiency in other brain areas. The unbalanced iron stores result in the downregulation of dopamine and myelination. Simultaneously, upregulation of nitric oxide suppresses myelin proteins' expression, which ultimately leads to demyelination and symptoms of both RLS and MS. It has been noticed that there is not a single theoretical or neurophysiological area that has offered any prevention for RLS occurrence among NMOSD patients. However, in comparison to their pathophysiological similarities with MS, the mechanism

explained for MS might also apply to NMOSD patients.

Kumru H et al.[5] found 17.9% frequency of RLS in traumatic SCI patients. Friday T et al.[6] subdivided SCI in the veteran population into four groups: MS, trauma, vascular, and other/unknown; with the prevalence rate of RLS at 55% in MS and 36% in trauma compared to 12.6% in MS and 9.5% in trauma. The current findings are in line with these results. While comparing RLS among the spinal cord levels (cervical, thoracic, lumbar and cervicothoracic), only the cervicothoracic subgroup showed a significant difference.

A few case reports[22] of RLS associated with viral myelitis are there in literature. Similarly, only a single case report[23] was found of RLS as an initial manifestation of metastatic conus medullaris lesion. Moreover, RLS cancer patients have significantly higher levels of anxiety and depression and more inferior quality of life.[24] RLS is a contributory factor in sleep disturbances in cancer patients undergoing chemotherapy.[25]

The present study is the first to report RLS prevalence in TB spondylitis (Potts disease) cases. It has some limitations as the sample was limited to patients having low socioeconomic status. A large and diversified sample size along with a control group would have made the study more robust and generalisable.

Conclusion

RLS was found in considerable large portion of the sample that comprised patients with SCIs. RLS is generally considered a trivial diagnosis, but it has a devastating effect on the patients' quality of life. Physicians should be aware of this condition so that overall RLS morbidity may be reduced.

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