

Restless Leg Syndrome in Patients Referred for Obstructive Sleep Apnea

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Abstract

Background: Restless leg syndrome (RLS) or Willis-Ekbom disease is a common disorder. It may present with excessive daytime sleepiness (EDS). EDS is seen often in obstructive sleep apnea (OSA) as well. Obesity and diabetes mellitus (DM) can be associated with both RLS and OSA.

Aim: To study the prevalence of RLS among patients with suspected OSA.

Material and Method: A retrospective evaluation of data was performed from proforma of patients referred for polysomnographic evaluation of OSA from January 2015 to December 2015 at a tertiary care post-graduate teaching institute. The sleep proforma through which the data was collected also had RLS diagnostic criteria.

Result: Out of 69 patients who underwent the sleep study for suspected OSA, 9 (13%) patients fulfilled the diagnostic criteria of RLS. The majority of the patients i.e. 7/9 (78%) were women while 2/9 (22%) were men. The mean age was 50 ± 3.5 years. History of excessive daytime sleepiness (EDS) was positive in 8 cases with the Epworth sleepiness score (ESS) of > 8 . History of snoring was present in all 9 cases. Six out of 9 cases had a history of insomnia. The mean body mass index (BMI) was 34.5 ± 4.2 kg/m². On polysomnography, three patients were diagnosed to have OSA with an apnea-hypopnea index of 5.2, 15 and 42 per hour. Periodic limb movement in sleep (PLMS) was documented in 7/9 (78%) patients. Eight out of 9 cases had secondary RLS, 4 due to diabetes, 2 had iron deficiency and the remaining 2 patients had RLS because of chronic obstructive pulmonary disease.

Conclusion: RLS is common among patients suspected with OSA. Screening of RLS should be done in all OSA suspect cases to prevent misdiagnosis and mismanagement of RLS in patients.

Keywords: Restless leg syndrome (RLS), Periodic limb movement in sleep (PLMS), Obstructive sleep apnea (OSA).

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Introduction

Restless leg syndrome (RLS) or Willis-Ekbom disease is a disorder that leads to an abnormal sensation in the extremity, especially in legs¹. The prevalence of RLS varies from 2.7% to 10% worldwide²⁻⁴. The limited studies available from India have shown the prevalence of RLS at around 2%^{3,5}. Insomnia, sleep disturbance or excessive daytime sleepiness (EDS) can be its presenting manifestation. It is often associated with periodic leg movements in sleep (PLMS). Definite diagnostic criteria have been laid down and evidence-based guidelines are available for its management^{6,7,8,9}. Diabetes, obesity and excessive daytime sleepiness, which are associated with obstructive sleep apnea (OSA), can also be associated with RLS. Hence this can be easily missed if not proactively looked for in patients referred for OSA.

Materials and Methods

A retrospective observation study was conducted at a tertiary care center, in New Delhi. We analyzed the prevalence of restless leg syndrome (RLS) from January 2015 to December 2015 in patients who underwent polysomnography for suspected OSA. During the study period, 69 patients suspected of OSA on basis of obesity, snoring &/or excessive daytime sleepiness had undergone polysomnography. The proforma of our department includes diagnostic criteria for RLS as well^{8,9}. The patients who fulfilled all four essential criteria for RLS i.e. an unpleasant sensation in the legs with an urge to move the legs, circadian variation, relief of the symptoms by movement and aggravation after rest were diagnosed as RLS. The available data of Epworth sleepiness score (ESS) and history of insomnia were noted down from the records. Also, the general physical examination including body mass index (BMI) and readings of the respiratory examination conducted at the time of screening was noted from the available records. The routine hematological and biochemical investigations, chest radiograph, thyroid function test (TFT), electrocardiography, 2D echocardiography and spirometry were also available in the proforma as per the department's sleep study protocol.

Results

Out of 69 patients who underwent polysomnography for suspected OSA during the study period, 9(13%) patients

fulfilled the diagnostic criteria of RLS. The majority of the patients 7/9 (78%) were women while 2/9 (22%) were men. The mean age of the study population was 50 ± 3.5 years. History of EDS was positive in 8/9 cases with ESS of ≥ 8 . History of snoring was present in all 9 (100%) cases. Six (67%) out of 9 cases had a history of insomnia. Three patients were smokers. The baseline mean SpO₂ was 97% on room air. General and respiratory examinations were normal in all cases. The mean body mass index (BMI) was 34.5 ± 4.2 kg/m². The routine hematological, biochemical investigations were normal in all 9 patients. The chest radiograph was normal in 7 cases. The other two chest radiographs were suggestive of old treated pulmonary tuberculosis and sarcoidosis. Eight cases had normal thyroid function while one showed hypothyroidism. Electrocardiogram and 2-dimensional echocardiography were normal in all cases. Spirometry showed an obstructive pattern in 3 cases, the restrictive pattern in 4 cases and normal in 2 cases.

During polysomnography three patients were diagnosed to have OSA one each of mild, moderate and severe OSA, with apnea-hypopnea index (AHI) of 5.2, 15 and 42 respectively. PLMS was documented in 7 (78%) out of 9 patients. Among the 9 cases, one had primary RLS and 8 had secondary RLS. Among secondary cases, 4 had RLS due to diabetes mellitus, 2 had RLS due to COPD and 2 suffered from iron deficiency. Only 2 out of 9 cases required pharmacological treatment, the others were managed conservatively or by treatment of underlying cause. Detailed demography of RLS patients is given in Table 1.

Discussion

Restless leg syndrome is purely a clinical diagnosis based on International RLS Study Group diagnostic criteria⁹. There is a limited data on RLS from the Indian population. The available data shows the prevalence of around 2% in general population. In our study, the prevalence of RLS among patients referred for polysomnography was 13%. Obesity and diabetes are predisposing factors for RLS, possibly due to that the prevalence was higher than that reported in general population. In our sample group, there was a clear female predominance like the other national and international studies^{3,10}.

Table 1: Demographic Profile of RLS patients

Case No	Age (years)	Sex	BMI	Neck circumference	Sleep (hrs)	Spo2 (RA)	EDS	Medical illness	RLS History	AHI	PLMS	Sleep disturbance					
												Snoring	Sleep fragmentation	Unfresh sleep	Insomnia	Natural choking	Nocturia
1	55	F	36.95	37.50	6	97	Yes	HTN, GERD, BA	Yes	42.8	—	Yes	Yes	Yes	No	No	Yes
2	40	F	29.50	33.00	5	98	Yes	GERD, BA	Yes	2.8	831	Yes	Yes	Yes	Yes	Yes	Yes
3	42	F	31.64	36.00	7	97	Yes	DM, GERD	Yes	2.5	321	Yes	Yes	Yes	Yes	No	Yes
4	63	F	36.44	39.50	6	98	Yes	HTN, DM	Yes	2.0	736	Yes	Yes	Yes	Yes	Yes	Yes
5	58	F	40.00	36.00	7	97	Yes	HTN, DM, GERD	Yes	3.4	636	Yes	Yes	Yes	yes	No	Yes
6	40	M	—	41.00	8	98	No	GERD, COPD	Yes	5.2	482	Yes	No	No	No	Yes	No
7	66	M	28.60	40.50	6	96	No	COPD	Yes	1.0	463	Yes	No	Yes	Yes	No	No
8	43	F	31.40	37.00	7	98	Yes	Sarcoidosis	Yes	15	183	Yes	Yes	Yes	Yes	No	Yes
9	50	F	41.73	40.00	4	98	Yes	GERD, DM	Yes	0.9	—	Yes	Yes	Yes	No	Yes	Yes

BMI: *Body mass index*, RA: *Room air*, EDS: *Excessive daytime sleepiness*, RLS: *Restless leg syndrome*, AHI: *ApneaHypopnea Index*, PLMS: *Periodic Leg Movement during Sleep*, HTN: *Hypertension*, GERD: *Gastroesophageal reflux disease*, DM: *Diabetes mellitus*.

The diagnosis of RLS is difficult and is usually missed not only at primary care level but also by secondary/tertiary specialists even in developed countries. Allen RP et al¹¹ in a study among primary care physicians found that RLS was undiagnosed at the primary care level and that 91% of the patients were never given a diagnosis of RLS. Another study found that only one-fourth of RLS sufferers was diagnosed by their physicians¹². In another study, Allen RP et al¹¹ found that more than 80% of RLS sufferers who had moderate to severe disease reported RLS symptoms to their physicians, but only 6% were given the diagnosis of RLS¹³. In a multi-national study from the developed world it was observed that, among 65% of the RLS patients who had consulted their primary care physicians, only 13% were given a diagnosis of RLS¹⁴. Our patients also would have missed diagnosis, if RLS was not proactively looked for during routine screening.

Comorbid diseases like diabetes and obesity can be associated with both RLS and obstructive sleep apnea (OSA). Sleep symptoms like excessive daytime sleepiness, sleep fragmentation, non-refreshing sleep, insomnia, leg pain with limb movement, snoring can be associated with both RLS and OSA. So the diagnosis of

RLS is more difficult among patients with suspected OSA. In our study, all the cases had more than two of above presenting symptoms. Polysomnography also may not help if the patient has OSA and PLMS, because PLMS can be associated with OSA. History of RLS obtained initially or after the study is the only way to diagnose RLS. There is a study, which has shown that patients who do not endorse any OSA symptoms, had endorsed insomnia or restless legs symptoms, and were found to have OSA¹⁵. But no study has so far demonstrated that those who endorse symptoms similar to OSA can also have RLS.

EDS is known to persist even after treatment of OSA. RLS can be one of the causes of symptom persistence. It is better to look for these causes prior to prescription of continuous positive airway pressure (CPAP) rather than later to prevent low compliance or failure of OSA treatment¹⁶. If the diagnosis of RLS is missed in OSA patients, it can lead to residual symptoms and can cause anxiety, depression, stress and increase the financial burden on the non-OSA patients in form of excessive investigation and treatment^{3,17}.

Periodic limb movements (PLM) are types of motor disorder that occur typically in sleep called periodic leg

movements of sleep (PLMS). Both PLMS and RLS are a somatosensory network disorder with an urge to move and usually, but not exclusively, affects the legs. The relationship between PLMS, RLS and OSA is complex. Patients with both RLS and OSA can have PLMS. It is essential to identify what is causing PLMS because the one that occurs due to OSA disappears with CPAP and the other one due to RLS needs a diagnosis and appropriate treatment¹⁸. The diagnosis of RLS is totally clinical, while the diagnosis of PLMS is based on polysomnography. While 80-90% of patients with RLS have PLMS, only 30% of PLMS patients have RLS¹⁹. As in present study 78% of RLS patient showed PLMS on polysomnography.

On the basis of etiology RLS can be divided into idiopathic or secondary. The secondary occurs most commonly due to iron deficiency²⁰. The patient should be screened for serum ferritin level and those with aferritin level of <50ug/dl should be treated with oral/injectable iron^{1,20}. The treatment can be pharmacological or non-pharmacological. The non-pharmacological treatment includes avoidance of alcohol, caffeine, and smoking with good sleep hygiene^{6,20}. The pharmacological treatment is required in patients with symptoms that seriously impair quality of life. Both pharmacological and non-pharmacological treatment may be given to those with secondary RLS where the symptoms of RLS persist despite the treatment of underlying cause. Among 9 cases with RLS, 8 had secondary RLS, 4 cases had RLS due to diabetes mellitus, 2 cases had underlying COPD and 2 had aferritin level of <50ug/dl. Only 2 of these patients required pharmacological treatment for the management of RLS.

Conclusion

RLS is common in patients referred for evaluation of OSA. It is more difficult to diagnose among those suspected with OSA since the symptoms are similar to OSA. Patients are likely to be incompletely managed if not enquired about RLS along with sleep history. Hence, screening of RLS should be done in all OSA suspect cases. PLMS is commonly associated with RLS. The management of RLS consists of treatment of underlying cause.

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