Prevalence of restless leg syndrome in subjects with depressive disorder

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ABSTRACT

Background: Restless legs syndrome (RLS) is known to be associated with depression. We hypothesized that RLS in depression is linked to the severity, duration, and frequency of depressive episodes.

Materials and Methods: Subjects fulfilling DSM-IV-TR criteria of depressive disorders were included in this study after seeking informed consent. Using structured interview of MINI-Plus their demographic data and history were recorded. Severity of depression was assessed with the help of HAM-D. Insomnia was diagnosed following ICSD-2 criteria. RLS was diagnosed according to IRLSSG criteria. Descriptive statistics, Chi-square test, independent sample t test and MANOVA were computed with the help of SPSS v 17.0.

Results: RLS was reported by 31.48% of sample. There was no gender difference in prevalence of RLS ($\chi^2$=0.46; $P=0.33$). There was no difference in the age, total duration of depressive illness and number of depressive episodes between RLS and non-RLS groups ($F=0.44; P=0.77$; Wilk’s Lambda=0.96). The HAM-D score was higher in the non-RLS group ($P=0.03$). Onset of RLS symptoms was not related to onset of depressive symptoms.

Conclusion: RLS is prevalent in depressive disorder. However, onset of RLS is unrelated to age and number or duration of depressive disorders.

Key words: Adults, depression, prevalence, restless leg syndrome

INTRODUCTION

Restless legs syndrome (RLS) is a sensori-motor disorder that interferes with the sleep of the sufferers. This syndrome is characterized by four major symptoms including urge to move legs which is more in the evening and night, this urge is usually relieved by movement and increased by rest.\(^1\) Disruption in dopamine transmission in brain is hypothesized for this problem as it frequently responds to dopaminergic therapy.\(^2\)

RLS has been found to be associated with depression in clinical sample as well as epidemiological studies.\(^3\)\(^4\) Dopamine is implicated in the causation of depression and treatment of RLS is thought to improve depressive symptoms in RLS patients.\(^2\) Together, these facts suggest that there may be some overlap between these two disorders. Earlier studies have analyzed the presence of depression in RLS patients, but to the best of our knowledge no study has assessed the prevalence of RLS in depressed patients except one.\(^3\) This kind of study can throw more light on the patho-physiological underpinnings of both the disorders. Hence, the present study was planned.

MATERIALS AND METHODS

The present study was conducted in a tertiary care teaching institution after seeking approval from the institutional ethics committee. All subjects presenting to psychiatry OPD with complaints of depressive illness were included in this
study. Depressive illness included three categories – major depressive disorder (MDD) or dysthymia or recurrent depressive disorders fulfilling the DSM-IV-TR criteria were included in this study. [6] Mini International Neuropsychiatric Interview Plus (MINI-Plus) was used for structured clinical interview. [7] However, subjects suffering from any medical or neurological disorder that predisposes them to develop RLS, those ever suffered from any kind of psychotic disorder or currently taking antipsychotic drug; presently meeting RLS, those ever suffered from any kind of psychotic disorder or currently taking antipsychotic drug or disturbed sleep; those unwilling to participate; suffering from any other sleep disorder, e.g., sleep apnea, parasomnia or neurological disorder that predisposes them to develop RLS and sleep disorder were not included in this study. Similarly, pregnant females, those within post partum period (12 months since last childbirth) or those suffering from postmenopausal syndrome were also excluded from the study.

Subjects were explained the rationale of study before taking their informed written consent. Their demographic data were recorded and clinical history, drug history, and family history of psychiatric disorder, RLS, and sleep disorder were sought. Recurrent depression was diagnosed when a person suffered two or more episodes of depression with two asymptomatic months in between two consequent episodes. Any emergence of depressive symptoms during this period was considered as a continuing previous episode of major depressive disorder or dysthymia.

**Diagnosis of restless legs syndrome**
Restless leg syndrome was diagnosed according to criteria proposed by the international restless leg syndrome study group. [8] These criteria for adults include urge to move legs, relief in the urge by movement, increment of urge during rest, and circadian variation with maximum symptom during evening or night. Only those cases that fulfilled all of these four criteria were included in the present study.

**Diagnosis of insomnia**
Diagnosis of insomnia was made when anybody complained of either difficulty falling asleep, staying asleep or early morning awakening (at least 2 hours before their usual wake time) on most of the days for at least 1 month. These patients were further categorized into primary and secondary insomnia according to international classification of sleep disorder-2. [8]

**Severity of depressive episode**
After making clinical diagnosis of depressive disorder, severity of depressive episode was assessed using Hamilton Rating Scale for Depression (HAM-D). [9]

**Statistical analysis**
Analysis was performed using SPSS 17.0. Descriptive statistics was run. Chi-square analysis was done for the nonparametric variables. An independent sample t test was used to find out the difference between the means in two groups. One-way MANOVA was performed to analyze effect of age, total duration of depressive illness, number of depressive episodes, and duration of present depressive episode on RLS.

**RESULTS**
This study included 54 subjects. Prevalence of RLS in this group was 31.48%. There was no difference between the genders with regard to prevalence of RLS ($X^2=0.46; P=0.33$). Average duration of RLS was 35.58 (+33.22) months. Gender distribution ($X^2=0.46; P=0.33$) and frequency of primary insomnias (adjustment insomnia, psychophysiological insomnia, and paradoxical insomnia) was not different between subjects with and without RLS. However, insomnia secondary to RLS was more frequent in the RLS group ($X^2=24.82; P<0.001$). When we clubbed the primary and secondary insomnia, we did not find any difference in the frequency of insomnia in either groups (83.8% in non-RLS and 88.2% in the RLS group; $P=0.50$). Prevalence of psychiatric illness in family members was not different between groups ($X^2=2.52; P=0.16$). Only three subjects reported symptoms of RLS in their first-degree relatives, two in the RLS group, and another in the non-RLS group. Onset of MDD symptoms with relation to onset of RLS symptoms are shown in Figure 1. There was no significant difference with respect to age, total duration of depressive illness, number of episodes, and duration of present depressive episode on RLS between groups ($F=0.44; P=0.77$; Wilk’s Lambda$=0.96$; Partial eta squared$=0.03$).

Non-RLS subjects had higher HAM-D scores as compared to RLS subjects (non-RLS: 20.08+4.88; RLS: 16.58+3.23; $P=0.03$).

**DISCUSSION**
This study found that RLS was frequent in the persons...
suffering from depressive illness compared to the general population. Earlier studies have found that depression is more prevalent in subjects with RLS.\textsuperscript{[10,11]} Earlier studies addressing the prevalence of RLS in community sample suggested prevalence rates between 0.9% to 8.3% in Asian community and 17.7% in American community.\textsuperscript{[4,10,12]} Only one study has examined the frequency of RLS in depressed subjects and reported prevalence of 27%.\textsuperscript{[9]} We have found nearly similar prevalence in this study.

RLS has female predisposition in earlier studies.\textsuperscript{[10,11]} However, we did not find any difference between genders. Perhaps, sample selection might have played a role. Earlier studies have included RLS sufferers and then looked for depression while we did the opposite. Other epidemiological studies cannot be compared with this study as this study was clinic based.

Whether RLS leads to depression or depression leads to or aggravates RLS symptoms is a debatable issue. Previous studies suggested that psychiatric morbidity is frequent in subjects with RLS.\textsuperscript{[4,10,13,14]} However, contradictory data are also available, at least in subjects with mild RLS,\textsuperscript{[15]} Our study suggest that onset of RLS symptoms was unrelated to onset of depressive symptoms. A large, prospective study addressing this issue is warranted to reach to any conclusion. Present evidence indicates that RLS may either precede or follow depression.\textsuperscript{[16]}

RLS patients often suffer from chronic insomnia and its clinical presentation frequently masquerades or induce depression.\textsuperscript{[3,10,17]} thereby favoring the notion that RLS precedes depression. Hornyak et al.\textsuperscript{[17]} suggested that severity of RLS correlated with severity of insomnia but not with depression score. In addition, RLS subjects score high on only those items of depression rating scale which are consequent to insomnia\textsuperscript{[17]} corroborating lower HAM-D scores in the present study. Thus the present literature is inconclusive regarding the role of insomnia in the development of depression in RLS patients! Our results did not find any difference in the prevalence of insomnia (primary and combined) in either of the groups suggesting that insomnia may be an independent factor which does not affect RLS.

A number of factors during depressive illness may increase the likelihood of development of RLS. It is known that RLS symptoms are often aggravated during periods of stress and with the antidepressant therapy.\textsuperscript{[3,18]} Mirtazepine has been found to induce RLS more frequently compared to other antidepressants including SSRIs.\textsuperscript{[18,19]} In the present study, most of the patients had longstanding illness spanning upto 10 years and were taking antidepressants off and on. Since, RLS was never screened they were not able to recall its relationship with antidepressant therapy. This could be a confounding factor in present study. Our data suggest that depression may not predispose a person to RLS as total duration of depressive illness, duration of present episode, “number of depressive episodes” and family history of psychiatric illness were not different between two groups.

Pathophysiologically dopamine is implicated both in depression and RLS.\textsuperscript{[16]} Benes et al.\textsuperscript{[2]} concluded that dopaminergic treatment of RLS improved the depressive symptoms and antidepressants should be advised when resolution of RLS does not improve the depressive symptoms. This must also be kept in mind that dopaminergic agonists possess an antidepressant property.\textsuperscript{[20]} It may be a simplistic view as treatment of RLS actually improves sleep quality and abolishes insufficient sleep syndrome. The latter can masquerade depression, hence, we need more data to assess these issues.

This study has some methodological limitations. Firstly, the sample size is small owing to robust exclusion criteria and hence, results are difficult to be generalized. Secondly, the data were retrospective and recall bias cannot be excluded in this group. Thirdly, a number of subjects were taking antidepressants at the time of presentation which could have aggravated RLS. Fourthly, owing to cross-sectional design we could not evaluate the effect of treatment of RLS on depressive symptoms or vice versa.

Nonetheless, this study is still important as it throws light on the possible comorbidity in depressive illness that can reduce the chances of remission of depression or precipitate future episodes. Large-sample prospective studies in future are required to reach to a conclusion on this issue.

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