Restless Legs Syndrome Symptoms in Primary Care

A Prevalence Study

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Background: There are relatively few studies on the prevalence of restless legs syndrome (RLS) in the general population, even fewer that used diagnostic questions covering all 4 essential diagnostic criteria defining the RLS symptom complex, and none that have reported on the 2 RLS phenotypes for patients seen by family physicians.

Methods: To determine the prevalence of the symptom complex, diagnostic for RLS in a primary care patient population, a prospective population-based single-center study was performed. Every adult patient presenting for care in a small rural primary care practice with mostly white patients was surveyed for a 1-year period using a validated RLS diagnostic questionnaire.

Results: A total of 2099 patients completed the questionnaire. Analysis revealed that 24.0% of these patients were positive for all 4 of the essential symptoms used to make the diagnosis of RLS and 15.3% reported these symptoms at least weekly. In addition, the RLS symptom complex was reported significantly more often by women than men and, as a whole, patients reporting the RLS symptoms were significantly older than patients without symptoms. The prevalence of symptoms increased with age until about 60 years and then showed a steady decrease thereafter. Further, early-onset RLS was significantly more common in women than men.

Conclusions: A high prevalence of RLS symptoms was observed in this primary care population. This finding supports the need for heightened awareness in both the medical community and general population regarding this disorder, which can often be effectively treated within the primary care practice.

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Although it has been estimated that 40 million Americans experience chronic sleep disorders, only a small proportion are adequately diagnosed and treated.1 Restless legs syndrome (RLS) is a sleep disorder that accounts for a significant proportion of patients with sleep complaints. The first modern medical description of RLS as a syndrome was provided by Ekbom2 in 1945. More detailed diagnostic criteria were developed by the International RLS Study Group (IRLSSG) in 1995,3 and were recently updated at an international diagnostic workshop at the National Institutes of Health in Washington, DC (May 2002). This most recent revision was approved by the IRLSSG. Currently, to be considered positive for RLS symptoms, the following 4 diagnostic criteria must be met: (1) the patient must have an urge to move the legs, usually accompanied by an unpleasant sensation in the legs; (2) RLS symptoms must be aggravated by rest; (3) RLS symptoms must be alleviated by movement and, in particular, walking; and (4) RLS symptoms must be worse in the evening or night either currently or in the past when the condition first started.

The diagnosis is based on clinical symptoms, and the primary care physician can provide both the diagnosis and the subsequent medical treatment for most cases. Current studies suggest that the prevalence of RLS is between 9% and 15%,4,6; however, the 2001 Sleep in America Poll conducted by the National Sleep Foundation7 found that only 3% of the poll participants with RLS symptoms have had this disorder diagnosed by a physician. If these patients are present among the patients being treated in a primary care practice, this result suggests a partial failure of the current system to address all the needs for these patients.

The objective of the present study was to determine whether these undiagnosed patients with RLS symptoms could be part of a primary care practice. Therefore, the study was designed to determine the prevalence of RLS symptoms in a specific pri-
primary care population. The practice used in this study had been previously surveyed using a general sleep disorders questionnaire. The item specific to RLS symptoms revealed that the symptoms were not only present among the patients, but represented an unexpectedly high proportion of the primary care population (29.3%).

The present study was designed to more accurately determine the prevalence and to assess the population characteristics of the patients with RLS in this primary care practice.

METHODS

SETTING AND PARTICIPANTS

The setting for the study was the Moscow Clinic, a 3-physician primary care practice in Moscow, Idaho. This rural community of approximately 22000 population is located in the northwestern United States and contains a major state university. The catchment area for the clinic within a 48-km radius includes approximately 60000 individuals. The clinic serves relatively few university students.

Every adult patient (18 years or older) with an appointment at the clinic between December 6, 1999, and December 5, 2000, was asked to complete the diagnostic Restless Legs Syndrome Questionnaire (RLSQ).§ Patients who were not approached during their appointment (due to medical distress or a large influx of patients at the same time) received the questionnaire by mail.

STUDY DESCRIPTION

After obtaining written consent, the on-site researcher distributed the RLSQ. The researcher was available to assist the patients in completing the questionnaires, as well as to answer any questions. The Stanford University Panel on Human Subjects reviewed and approved the study.

RLSQ SCORING

The RLSQ was validated as a 5-page questionnaire with stopping points on the first page for patients without RLS symptoms. In this study, the first page was used to determine the prevalence of RLS symptoms within this primary care population. The scoring algorithm was based on the 4 basic diagnostic criteria developed by the IRLSSG. Thus, to be considered positive for RLS symptoms, the patient had to respond positively to questions on each of the 4 diagnostic criteria previously described.

When the RLSQ was compared with expert clinical diagnoses for consecutive patients in a sleep disorder clinic, the questionnaire had a sensitivity of 92% and a specificity of 93%. Patients reporting all 4 basic symptoms of the RLSQ were assigned an RLSQ-positive score while patients who did not report all 4 symptoms were assigned an RLSQ-negative score. Unlike several prior studies, the criteria for an RLSQ-positive condition did not require any frequency of symptoms. However, to enable comparisons with the prior studies, the frequency of symptoms was obtained and entered into the analyses.

DATA ANALYSIS

All data from the RLSQ was entered into a computerized database to facilitate data analysis. The age and sex of patients who participated at the clinic were compared with those of the other 4 patient populations: participants responding by mail, those who refused to participate, those unable to participate because of the lack of current contact information, and those with medical conditions (eg, dementia) that precluded them from completing the questionnaire. Further, the participants were divided into 7 age groups representing each decade of life from 18 to 93 years, with the exception of 18 and 19 added to the youngest decade (18-29) and 90 to 93 added to the last decade (80-93). These divisions were made to assess any differences in age or sex using a standard analysis of variance. In addition, the percentage of patients with RLS symptoms was analyzed for those whose frequency of RLS symptoms was at least once a week, similar to the frequency criteria used in most prior studies. This permitted comparison with these prior studies. The severity of the RLS symptoms was also investigated. Finally, the age of onset of RLS symptoms was examined with an onset of RLS symptoms at or before age 45 years defined as early-onset RLS and an onset of symptoms after age 45 years defined as late-onset RLS. Past studies have shown that early-onset RLS generally has a high frequency of occurrence within families and a slow progressive development of symptoms over several years, while these are not the case for late-onset RLS. These 2 groups may represent 2 different phenotypes of the disorder.

RESULTS

POPULATION CHARACTERISTICS

Of the 2649 patients who visited the clinic in 1 year, approximately half were women (50.4%). Of those asked to participate (either on-site or by mail), a total of 2099 (79.2%) agreed to do so. Women comprised 51.7% (men, 48.3%) of the participants. A total of 1905 participated on-site and an additional 194 completed the RLSQ by mail. The 550 nonresponders included 82 patients who were unable to participate because of medical conditions, 52 patients unable to participate because of a lack of current contact information, and 416 who refused to participate. Figure 1 provides details on the order of study procedures and the number of patients completing each step of the process. The age of the responders ranged from 18 to 93 years with a mean (SD) age of 45.6 (18.9) years. The ethnicity of the responders was predominantly white (98.0%). The demographic characteristics for this clinic sample are typical for the geographic region and are summarized in Table 1.

The participants responding by mail were significantly older than the on-site participants (t = 5.01, P < .001), yet sex distribution did not differ significantly between these 2 groups. Exclusion of the responders by mail failed to significantly alter the other basic findings. Comparing all nonparticipating patients (those refusing or unable to respond) with those participating showed the nonparticipants were significantly older (mean ages, 52.7 vs 45.6 years, respectively; t = 5.94, P < .001) and included relatively fewer women (45.1% vs 51.7%, respectively; χ² = 3.84, P < .005) (Table 1). The nonparticipants were mostly patients who refused to participate (75.6%), although this lack of participation also occurred for 2 other reasons. Fifty-two (9.5%) mostly younger patients (mean [SD] age, 28.5 [12.5] years) did not participate while at the clinic, did not have current addresses on file, and therefore, could not be reached by mail. Another 82 (14.9%) mostly older patients (mean

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Sex and ethnic composition did not differ significantly among the 3 major nonresponder groups.

PREVALENCE

Based on the RLSQ, we found that 504 (24.0%) of the 2099 patients surveyed at the Moscow Clinic reported all 4 basic diagnostic symptoms of RLS. Once a frequency criterion was added, the prevalence decreased slightly. Of the patients surveyed, 15.3% had symptoms at least weekly and 20.6% had symptoms at least monthly (Table 2). In a more stringent condition when both a frequency (at least weekly) and a severity (RLS symptoms were at least mildly distressing when they occurred) criteria were included, the prevalence was 13.7% (Table 3). Additionally, the frequency and severity items correlated significantly with Spearman ρ (r = 0.18, P < .001), but the degree of variance accounted for by this correlation was not high. However, a definition involving severity and frequency of symptoms has not been used for other RLS prevalence studies. Instead, the frequency criterion has been seen as a surrogate measure for presence of a condition with a clinically significant severity. Therefore, only the frequency criterion was explored in greater detail in our study to allow comparison to prior studies.

SEX AND AGE EFFECTS

Upon analysis of the participants, the RLSQ-positive patients were older (mean age, 47.2 vs 45.0 years; t = 3.40, P < .003) and included relatively more women (59.5% vs [SD] age, 73.8 [21.2] years) were unable to participate because of medical complications. Sex and ethnic composition did not differ significantly among the 3 major nonresponder groups.

Table 1. Demographic Characteristics for Participants Who Completed the Restless Legs Syndrome Questionnaire vs Nonparticipants

<table>
<thead>
<tr>
<th>All Participants</th>
<th>Participants at Clinic Visit</th>
<th>Participants via Mail</th>
<th>Nonparticipants</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (total = 2649)</td>
<td>2099</td>
<td>1905</td>
<td>550</td>
</tr>
<tr>
<td>Men/women (% women)*</td>
<td>1012/1085 (51.7)</td>
<td>924/981 (51.5)</td>
<td>302/248 (45.1)</td>
</tr>
<tr>
<td>Age, y†</td>
<td>Mean ± SD 45.6 ± 18.9</td>
<td>45.0 ± 18.9</td>
<td>50.9 ± 16.1</td>
</tr>
<tr>
<td>Range</td>
<td>18-93</td>
<td>18-93</td>
<td>19-91</td>
</tr>
<tr>
<td>Ethnicity, % white‡</td>
<td>98.0</td>
<td>98.0</td>
<td>97.6</td>
</tr>
</tbody>
</table>

*Two participants via mail did not reveal their sex, so they were not included in the percentages.
†Four participants and 14 nonparticipants at clinic visit did not reveal their ages and were not included for the calculation.
‡Approximately 10% of the population in each sample did not complete the ethnicity question.

Table 2. Frequency of RLS Symptoms for the RLSQ-Positive Patients

<table>
<thead>
<tr>
<th>Frequency of RLS Symptoms*</th>
<th>RLSQ-Positive Patients, % (No. of Patients in Category)</th>
<th>Estimated Prevalence of RLSQ-Positive Patients With Symptoms of This Frequency or Greater, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 times per week</td>
<td>27.3 (95)</td>
<td>6.6</td>
</tr>
<tr>
<td>1-3 times per week</td>
<td>36.5 (127)</td>
<td>15.3</td>
</tr>
<tr>
<td>1-3 times per month</td>
<td>21.8 (76)</td>
<td>21.6</td>
</tr>
<tr>
<td>&lt;1 time per month</td>
<td>14.4 (50)</td>
<td>24.0</td>
</tr>
</tbody>
</table>

*This item was added to the Restless Legs Syndrome Questionnaire (RLSQ) after the start of the study and 156 RLSQ-positive patients did not complete this question. The estimated prevalence is given as cumulative for symptoms occurring at least as often as the given frequency and assumes the percentage of RLSQ-positive patients from this subset applies to the entire sample of all RLSQ patients.
Decades except the decades of 80 and older, in which RLS was a consistent decrease in prevalence after age 59. The percentage of patients with RLS symptoms (32.4%). There was a higher reporting of RLS symptoms in primary care populations compared with other studies, (3) that the RLSQ is either more sensitive or less specific for RLS symptoms than the methods used in prior studies, or (4) the RLSQ did not impose any minimum frequency criteria for symptoms as was used in most other studies.

Symptoms of RLS may prove to be more prevalent in a primary care population compared with a general population. The sleep deprivation often experienced by patients with RLS may contribute to other medical problems for which patients would typically seek treatment.

COMMENT

THE HIGH PREVALENCE OF RLS

To our knowledge, this is the first RLS prevalence study where the selected instrument covered all 4 of the diagnostic criteria for RLS and also had an established sensitivity and specificity for RLS detection. Upon using this instrument, we found a high prevalence of RLS symptoms in this primary care population. The percentage of primary care patients with symptoms of RLS (24.0%) was higher than the 9% to 15% previously reported for North American and European populations. There are at least 4 possible explanations for this higher prevalence: (1) a higher reporting of RLS symptoms in primary care patient populations than in the general population, (2) a geographic or demographic difference in this population compared with populations in other studies, (3) that the symptom is either more sensitive or less specific for RLS symptoms than the methods used in prior studies, or (4) the RLSQ did not impose any minimum frequency criteria for symptoms as was used in most other studies.

Symptoms of RLS may prove to be more prevalent in a primary care population compared with a general population.
individuals seeking medical attention may be more likely to have underlying medical problems or be taking medication that could cause or worsen RLS symptoms. Further confirmatory studies are necessary within the primary care setting to address these issues.

Another possible explanation for the increased prevalence of RLS within this patient population could be the location and/or demographics of the population. The ethnically homogeneous population at this clinic has primarily Northern European ancestry. Therefore, a founder effect could exist in this population, which would increase the prevalence of RLS. Another study from a somewhat ethnically homogeneous population of French Canadians showed an apparent founder effect with an overall RLS prevalence of 15.0%. A replication study in a more ethnically diverse primary care population from a different geographic area is currently under way. The findings from this study may help to discern whether the high prevalence of RLS symptoms from the present study exists due to its primary care setting, geographic location, ethnic composition, or a combination of all 3 factors.

The specificity and sensitivity of the RLSQ must also be addressed. The validation studies were performed in a sleep disorder clinic population, which included many patients with sleep-disordered breathing and RLS. However, there were few patients with the types of medical complaints seen in a primary care practice that might be mistaken for RLS. For example, the RLSQ fails to exclude patients with some leg symptoms that present like RLS symptoms, but are attributed to other causes (eg, leg cramps or positional discomfort). Yet, this can be a problem with other instruments as well.

A potentially more significant difference between this instrument and most others is that it did not require a minimum frequency of current symptoms. Thus, patients who only experience RLS symptoms rarely or under certain circumstances (eg, traveling long distances or attending a theater late in the day) are also included. We believe that the inclusion of patients with less frequent symptoms in our final results is justified because 79% of patients who reported symptoms less than once per week, also reported that the RLS symptoms that they did experience, albeit less frequently, were at least mildly distressing (Table 3). This is further supported by the low overall correlation between frequency and severity of symptoms (Spearman ρ=0.18) which, while significant, clearly indicates that frequency is a poor surrogate measure for severity of the symptoms when they are present. Also, little is known about the natural course of this

| Age Group, y | No. (%) With RLS Symptoms (RLSQ Positive) | Ratio of % of RLSQ-Positive Women to % of RLSQ-Positive Men | No. (%) With RLS Symptoms at Least Once per Week† | Ratio of % of RLSQ-Positive Women to % of RLSQ Positive Men‡ |
| 18-29 | 87/540 (16.1) | 1.44 (18.7/13.0) | 37/373 (9.9) | 1.73 (12.3/7.1) |
| 30-39 | 93/347 (28.2) | 1.23 (30.9/25.2) | 41/240 (17.1) | 1.64 (20.8/12.7) |
| 40-49 | 99/283 (25.8) | 1.45 (31.1/21.4) | 42/264 (15.9) | 1.55 (19.7/12.7) |
| 50-59 | 93/287 (32.4) | 1.48 (38.1/25.8) | 41/198 (20.7) | 0.99 (20.6/20.9) |
| 60-69 | 71/259 (27.4) | 1.46 (33.1/22.7) | 34/179 (19.0) | 1.33 (22.0/16.5) |
| 70-79 | 40/171 (23.4) | 1.50 (27.8/18.5) | 17/118 (14.4) | 2.18 (19.4/8.9) |
| 80-93 | 16/108 (14.8) | 0.92 (14.3/15.6) | 10/75 (13.3) | 0.71 (11.4/16.1) |
| All ages | 504/2095 (24.1) | 1.37 (27.6/20.2) | 222/1447 (15.3) | 1.38 (17.7/12.8) |

*Four participants did not report their ages and were not included in these percentages.
†Calculations were performed assuming that the percentage of Restless Legs Syndrome Questionnaire (RLSQ)-positive patients who meet the once-per-week frequency criterion applies to the entire sample.
disorder, so it is possible that some patients with infrequent RLS symptoms could eventually experience the symptoms more frequently. It is beneficial for the patient to be aware that successful therapies are available in the event that the RLS symptoms become more frequent or disturbing in the future.

Most patients from our study had symptoms at least once per month, and 15.3% reported symptoms at least once per week. In a study by Phillips et al, 9.4% of all responders reported an RLS complaint occurring more than once a week. Another study by Lavigne and Montplaisir reported bedtime leg restlessness occurring “often” or “very often” to be 15.0%. It is interesting to note that had the Phillips et al study not included a frequency criterion, their prevalence of RLS symptoms would have been 19.4% for individuals with even rare symptoms, which approaches the overall prevalence of 24.0% from our study. Thus, once adjusted to match frequency criteria, our prevalence data are similar to those from the 2 other major North American studies that also involved a primarily white population. When comparing our data with those of the Rothdach et al study from a German population, which did not require any set frequency of symptom occurrence, our overall prevalence is significantly higher than their overall prevalence of 9.8%.

Yet, the Rothdach survey included a set of questions that are likely to exclude RLS patients who report only an urge to move without any other abnormal sensations. It is unclear how many patients with RLS do not report the usual paresthesias.

Analysis of the data revealed a few other areas that could have artificially increased the prevalence. First, the population that completed the RLSQ via mail was significantly older than the population that completed the RLSQ in the clinic. Yet, exclusion of the participants responding by mail did not significantly alter the overall prevalence of RLS symptoms in this population. Second, the nonparticipants were significantly older than the participants. This may indicate that older patients are more likely to either decline participation or have a medical condition that prohibits them from participating. Finally, there were more female participants than male participants. This suggests that women are more inclined to participate in a questionnaire-based research project than men. However, this does not explain the sex differences in RLS prevalence noted in this and other studies.

SEX-RELATED FINDINGS

Upon analyzing the population, significant sex differences were observed. Women were 37% more likely to report RLS symptoms than men when looking at the entire population (Table 5). This sex difference has been reported for most RLS prevalence studies. More extensive age of onset analyses from our study also revealed a significant difference in sex for the 2 basic phenotypes. We found that 62% more women than men reported the early-onset form of RLS symptoms. In contrast, the late-onset form occurred for 121% more men than women. This difference may reflect some aspect of the genetics, an environmental component, or hormonal factors that contribute to the increased occurrence of this disorder in women. There could also be a difference in the primary form of the disorder for women with early-onset RLS, which could be explained by a genetic abnormality or polymorphism that alters the disorder and/or the risk of the disorder for women in the earlier years of life. This topic clearly deserves further attention in future studies. The surprising male predominance in the late-onset RLS group has not previously been reported. This may suggest that other male-related health factors contribute to this late-onset form of RLS. The difference in the male-female ratio between the prevalence studies on RLS may have partially occurred because of differences in the number of early- vs late-onset forms of RLS. Most prior studies were done before these 2 phenotypes of RLS were defined and thus did not report the information on this significant aspect of RLS. However, it should be noted that the sample size for the age and sex by age of onset of RLS symptoms in this study is smaller than desired for these type of analyses. Medical problems that mimic the symptoms of RLS could also interfere. Future confirmatory studies must be performed in a larger sample size before any conclusions are drawn.

AGE-RELATED FINDINGS

Additional age-related findings were also detected in this population. The RLSQ-positive patients were significantly older than the RLSQ-negative patients. This is consistent with findings that RLS is associated with increased age. It is noteworthy that the decrease in prevalence for the oldest age group identified in this study (80-93 years) was also observed in the Rothdach et al study, although the older than 75 age group showed the decrease in that study. Therefore, a decrease in prevalence with older age may occur for RLS. This could be an artifact from other medical conditions obscuring RLS symptoms, a response bias for older patients, or it may reflect an aspect of the natural course of RLS that is not yet understood such as spontaneous remission or decreased survival with age. A planned long-term follow-up on our patient population may help to address some of these unanswered questions about the natural course of this disorder.

RLS IN PRIMARY CARE

Our finding that almost a quarter of the patients in this primary care population have all 4 of the diagnostic RLS symptoms suggests that a large number of RLS patients may be seen by family doctors. Yet, one must be careful in extrapolating this finding to the entire nation due to the homogeneous nature of the population explored in this study. Additional RLS prevalence studies in more ethnically diverse primary care populations are necessary. However, if only 3% of patients with RLS symptoms have had the disorder diagnosed by a physician, and if our prevalence of RLS symptoms is confirmed by further studies, there may be a significantly large number of primary care patients who could potentially benefit from the diagnosis of RLS. The advantages include benefits from a possible treatment (many successful therapies are currently available) as well as benefits related to the medi-
cal management of these patients (eg, avoidance of medications or lifestyle activities known to exacerbate RLS symptoms). Increasing physician awareness about the identification, diagnosis, and treatment for RLS is essential to provide the best quality care for each patient.

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