Epidemiology of Restless Legs Syndrome in Korean Adults

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Study Objectives: To investigate the prevalence of restless legs syndrome (RLS) in Korea.

Design: A large population-based telephone interview method using the Korean version of the Johns Hopkins telephone diagnostic interview for the RLS.

Setting: A computer aided telephone interview method

Participants: A total of 5,000 subjects (2,470 men and 2,530 women) were interviewed in depth. A representative sample aged 20 to 69 years was constituted according to a stratified, multistage random sampling method.

Interventions: N/A

Measurements and Results: Of the respondents, 373 respondents (7.5%) of the population (pop) met the criteria for the definite or probable RLS groups: 194 (3.9% of pop) respondents fulfilled the criteria for definite RLS and 179 (3.6% of pop) respondents fulfilled the criteria for probable RLS. The prevalence of RLS was generally higher for women than men (4.4% vs. 3.3% for definite, 8.7% vs. 6.2% for definite plus probable). About 90% of RLS individuals were experiencing symptoms at the time of the interview and this was similar for both RLS groups. Seventy-four respondents (1.48%) reported symptoms were moderately or severely distressing and were therefore classified as RLS "sufferers." Of those with a diagnosis of RLS sufferer, 24.3% reported being treated for their symptoms, compared to 12.4% of RLS not designated a "sufferer."

Conclusion: RLS is common and underdiagnosed in Korea with nearly 1% of the population reporting disturbed sleep related to their RLS. These results are comparable to other countries.

Keywords: Epidemiology, Korea, prevalence, restless legs syndrome.

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RESTLESS LEGS SYNDROME (RLS) IS A COMMON SENSORIMOTOR DISORDER.[1] SINCE EKBOM FIRST REPORTED THIS SYNDROME IN 1945,[2] THE PREVALENCE of RLS has been reported with a wide variation, as there were no standard diagnostic criteria for the syndrome. It was not until 1995 that the International RLS Study Group (IRLSSG) developed standardized criteria for the diagnosis of RLS,[3] which were updated to clarify the criteria in a consensus workshop held at the United States National Institutes of Health (NIH).[4] Using these criteria, the prevalence of RLS determined from population-based samples ranges from 7.2 % to 11.5% in Europe and the United States.[5-11] One population-based study from a region of Turkey reported a 3.2% prevalence of RLS occur-ring at least monthly.[12] Other studies not listed here had limitations such as the target population being restricted, or the diagnostic methods did not cover the full NIH-IRLSSG diagnostic guidelines. As far as Asian epidemiologic studies, there are few population-based epidemiologic studies.[13,14]

Therefore, we performed an epidemiologic study of RLS in a large Korean adult population, using the NIH-IRLSSG diagnostic criteria.[4] In addition, we also provided data on the frequency and severity of RLS symptoms.

METHODS

Preparation of the Instrument

We developed the Korean version of the Johns Hopkins telephone diagnostic interview (JHTDI) questionnaire for the RLS after obtaining permission from the original authors.[15,16] The JHTDI questionnaire is a structured interviewing tool developed for establishing the prevalence of disease in a large populations of individuals who were unlikely to have ever seen a doctor for these symptoms, let alone have a diagnosis of RLS. It contains 17 first-order questions and 32 second- or third-order questions that are used, based upon the individual's response to the first-order questions. The JHTDI contains 9 specific "diagnostic" questions in which are contained the essential 4 criteria necessary to establish the diagnosis of RLS (Table 1).[4] These 9 "key" questions were used to establish "degrees" of disease burden for purposes of genetic analysis in the population studies by the Johns Hopkins RLS Center Study. The categories included "definite" RLS, "probable" RLS, "possible" RLS, not RLS, and un-

Table 1—The Primary Questions That Were Used To Establish the Diagnosis of Restless Legs Syndrome

Q1.   Have you ever had unpleasant or uncomfortable feelings in your legs that occurred mainly while you were either sitting or lying down?
Q3.   Have you ever felt the need or urge to move your legs that occurred mainly while you were sitting or lying down?
Q5.   If you had these feelings and you got up to walk -- while you are actually walking around, do you get any relief from these feelings?
Q5b.   Will these feelings return while you continue to walk?
Q5c.   If you move your legs, do you get any relief from these feelings, even temporarily?
Q7.   Do these feelings occur more often when you are sitting or more often when you are lying down?
Q7a.   Would it be true to say that you have these feelings almost exclusively when you are sitting?
Q8.   Are these feelings in your legs worse at night or in the evening than other times of the day?
Q8a.   Was there ever a time in your life when these feelings were worse at night than other times of day

Table 2—The Criteria for Interpreting the Primary Diagnostic Questions in the JHTDI Questionnaire

Criteria for defining "Definite" RLS

Guide	1	3	5	5b	5c	7	7a	8	8a
1	y	y	y	n/dk	-	ml/as	-	y	-
2	y	y	dk	-	y	ml/as	-	y	-
3	y	y	y	n/dk	-	ml/as	-	n	y
4	y	y	y	n/dk	-	ms	n	y	-
5	y	y	dk	-	y	ml/as	-	n	y
6	y	y	dk	-	y	ms	n	y	-
7	y	y	dk	-	y	ms	n	n	y
8	y	y	y	n/dk	-	ms	n	n	y

Criteria for defining "Probable" RLS

Guide	1	3	5	5b	5c	7	7a	8	8a
1	n	y	y	n/dk	-	ml/as	-	y	-
2	n	y	dk	-	y	ml/as	-	y	-
3	n	y	y	n/dk	-	ml/as	-	n	y
4	n	y	y	n/dk	-	ms	n	y	-
5	n	y	dk	-	y	ml/as	-	n	y
6	n	y	dk	-	y	ms	n	y	-
7	n	y	dk	-	y	ms	n	n	y
8	n	y	y	n/dk		ms	n	n	y
9	y	y	y	n/dk	-	ms	y	y	-
10	y	y	dk	-	y	ms	y	y	-
11	y	y	dk	-	y	ms	y	n	y
12	y	y	y	n/dk	-	ms	y	n	y

Interpretation of abbreviation: yes (y), no (n), do not know (dk), more sitting (ms), about the same (as), more lying (ml).

known. Because the Korean Study is an epidemiological study, only the definite and probable RLS categories were segregated out, with "not RLS" the default category. The criteria used to interpret the questions and define the two categories of RLS are shown in Table 2. In brief, to have a definite RLS diagnosis, the individual must meet all 4 criteria (questions 1, 3, 5 [or 5b or 5c] and 8 [or 8a]) and not have symptoms exclusively while sitting. To have a probable RLS diagnosis, questions 3, 5 (or 5b or 5c) and 8 (or 8a) have to be answered appropriately, but either no sensation was reported (question 1) or symptoms occurred almost exclusively with sitting, not with lying (questions 7 and 7a). The other questions in the JHTDI questionnaire are used to eliminate potential false positives (e.g., muscle cramps), establish effects on sleep, define duration and frequency of the disease, and give a broader view of the symptoms such that a separate reviewer of the final JHTDI questionnaire could make an accurate and independent judgment of the diagnosis. Other general criteria that were used in the final interpretation of the questionnaire are: (1) the subjects must have symptoms ≥once a month for 3 consecutive months or ≥20 lifetime episodes to qualify for RLS; (2) The subjects with less than daily symptoms must have a circadian pattern in current symptoms; (3) if all symptoms are cramps, the diagnosis is not RLS.

To prepare a Korean version of the questionnaire, the original JHTDI questionnaire was translated from English into Korean and then translated back into English by three sleep specialists and one linguist. We compared the original and the translated version in creating the preliminary Korean version. After developing the Korean version of the interview form, we did the validation study using it. And finally we standardized the Korean version of the JHTDI questionnaire for the RLS.[17] This form was used for the current study.

Subjects, Survey Procedures, and Analysis

After developing the telephone interview form, we conducted the interviews using a computer-aided telephone interview method. We chose 5,000 people in order to give a low sampling error of ± 1.39 points within 95% confidence intervals.

A representative sample, aged 20 to 69 years, was constituted according to a stratified, multistage random sampling method (sex, age groups, economics, and occupations of the population). Samples were established by region (5 Korean regions), by the population of place of residence, by sex, by age (5 strata: 20 to 29 y, 30 to 39 y, 40 to 49 y, 50 to 59 y, 60 to 69 y), by occupation, and by income based on the 2000 Korean Census.[18]

Overall, 42,641 telephone numbers were used to complete the sample size of 5,000. We were unable to use 68% because the line was either busy or gave no answer, disconnected, hung up, or was a business, a fax, or a number not in service. There were 3,819 participants who were ineligible because the potential respondents did not meet eligibility criteria for either age or gender, did not speak Korean, or had a language or physical disability that precluded them from completing the telephone interview; 4,826 respondents refused before hearing the introduction or first qualifying question. Therefore, we finally had 5,000 respondents who participated.

This survey was conducted by interviewers from Taylor Nelson Sofres (TNS), who received in depth training about RLS as well as interviewing techniques. Data collection was done with a software package designed specially for this type of computer assisted phone survey. Responses were analyzed to produce an

Table 3—Prevalence of Definite, Probable, and all RLS with Gender, Age of Symptom Onset, Current Age, Region, or Occupation as a Factor

	Total	Definite RLS	Probable RLS	All RLS
Number	5000	194 (3.9%)	179 (3.6%)	373 (7.5%)
Sex				
Men	2470	82 (3.3%)	71 (2.9%)	153 (6.2%)
Women	2530	112 (4.4%)	108 (4.3%)	220 (8.7%)
Age of onset (years)				
<45		137 (70.6%)	125 (69.8%)	262 (70.2%)
≥45		57 (29.4%)	54 (30.2%)	111 (29.8%)
Age group (years)		Mean: 45.2±13.0	Mean: 43.8±13.9	Mean: 44.5±13.4
20-29	1075	25 (2.3%)	39 (3.6%)	64 (6.0%)
30-39	1235	45 (3.6%)	28 (2.3%)	73 (5.9%)
40-49	1155	51 (4.4%)	49 (4.2%)	100 (8.7%)
50-59	784	40 (5.1%)	31 (4.0%)	71 (9.1%)
60-69	751	33 (4.4%)	32 (4.3%)	65 (8.7%)
Region (Province)				
Seoul/GyeongGi/GangWon	2550	95 (3.7%)	103 (4.0%)	198 (7.8%)
Pusan/GyeongNam	820	26 (3.2%)	26 (3.2%)	52 (6.3%)
Daegu/GyeongBuk	540	21 (3.9%)	15 (2.8%)	36 (6.7%)
Gwangju/JeonLa/Jeju	590	33 (5.6%)	19 (3.2%)	52 (8.8%)
Taejeon/ChungCheong	500	19 (3.8%)	16 (3.2%)	35 (7.0%)
Occupation				
Agriculture/ fishery/ forestry	269	12 (4.5%)	10 (3.7%)	22 (8.2%)
Self employed	603	23 (3.8%)	22 (3.6%)	45 (7.5%)
Blue collar	504	24 (4.8%)	24 (4.8%)	48 (9.5%)
White collar	974	26 (2.7%)	32 (3.3%)	58 (6.0%)
Housewife	1614	76 (4.7%)	55 (3.4%)	131 (8.1%)
Student	518	14 (2.7%)	20 (3.9%)	34 (6.6%)
Unemployed / Others	518	19 (3.9%)	16 (3.2%)	35 (7.1%)

* The numbers in parentheses indicate percent of the population.

estimate of prevalence of RLS symptoms of any frequency and sleep disturbance. The sleep disturbance was defined as either the inability to go to sleep due to leg discomfort, or trouble getting back to sleep after waking in the night. All of the analyses were performed by using SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL).

RESULTS

Study Population

The total sample size of the study was 5,000 (2,470 men and 2,530 women) and by age groups; 1,075 twenties 1,235 thirties, 1,155 forties, 784 fifties, and 751 sixties. The study groups were well representative of the general Korean adult population.

Prevalence of RLS and Characteristics of Subjects

Of the 5,000 respondents, 373 (7.5% of the population [pop]) met the criteria for definite or probable RLS groups: 194 (3.9% of pop) respondents fulfilled the criteria for definite RLS and 179 (3.6% of pop) respondents fulfilled the criteria for probable RLS (Table 3). The age at which symptoms were first present has been considered an import phenotype in subcategorizing those with RLS.[19] In our population, 70.2% of all RLS designatees reported symptoms before 45 years of age and thus would be considered early-onset phenotype. This was the same for both definite and

probable RLS groups (Table 3). The prevalence of RLS increased with age, reaching a peak prevalence of 9.1% in the 6th decade of life (50-59 y). There was a slight drop in prevalence in the following decade (8.7%), which is of unclear significance. The prevalence of RLS was generally similar in each occupation and each region of Korea (Table 3). The prevalence of RLS was generally higher for women than men (8.7% vs. 6.2%) and this gender difference remained relatively proportional in the definite and probable RLS groups and across the ages, at least when all RLS categories were used (Table 3; Figure 1).
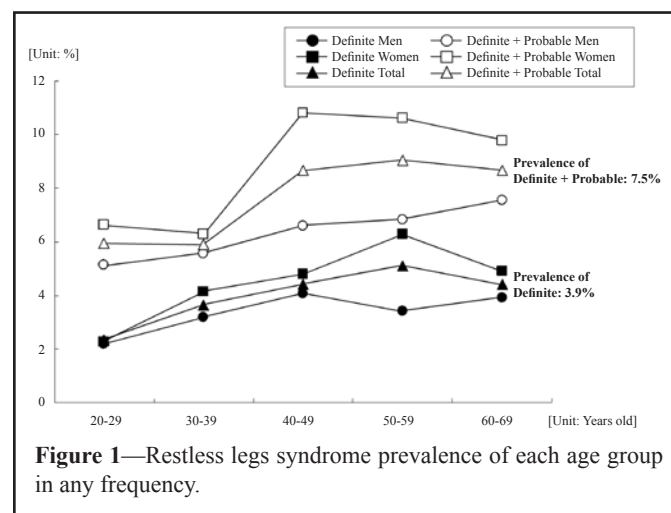

Figure 1—Restless legs syndrome prevalence of each age group in any frequency.

Table 4—Prevalence of Definite, Probable, and all RLS by Frequency of Symptom Occurrence and by Severity and Presence of Sleep Disturbance

Prevalence of RLS symptoms, No.(%)	Definite RLS	Probable RLS	All RLS
Any frequency	194 (3.9%)	179 (3.6%)	373 (7.5%)
Currently	174 (3.5%)	149 (3.0%)	323 (6.5%)
>1/week (≥5/month)	99 (2.0%)	68 (1.4%)	167 (3.3%)
≥2/week	83 (1.7%)	57 (1.1%)	140 (2.8%)
≥2/week and moderately or severely (RLS sufferers)	51 (1.0%)	23 (0.5%)	74 (1.5%)
≥2/week and moderately or severely and sleep disturbance	36 (0.7%)	8 (0.2%)	44 (0.9%)

About 90% of RLS individuals were experiencing symptoms at the time of the interview, and this was similar for both RLS groups (Table 4). Where the two RLS groups appear to diverge, as regards prevalence, is with increasing disease severity. Those individuals with a diagnosis of either category of RLS who reported that their RLS symptoms were moderately or severely distressing and had symptoms occurring at least twice weekly, were designated RLS "sufferers." These are the same criteria used in the RLS Epidemiology, Symptoms, and Treatment (REST) general population study to establish a subpopulation for whom disease burden was likely to require treatment.[8] Of 140 (2.85% of pop) RLS individuals who reported ≥2 nights per week of symptoms, roughly half (74; 1.48% of pop) reported symptoms were moderately or severely distressing and were therefore classified as RLS "sufferers." Those with definite RLS (51; 1.02% of pop) were twice as likely to be RLS sufferers as those with probable RLS (23; 0.46% of pop). Of those with a diagnosis of RLS sufferer, 24.3% reported being treated for their symptoms compared to 12.4% of RLS not designated as "sufferer."

If the presence of reported sleep disturbance is added as another level of RLS severity (Table 4), then 44 RLS individuals were identified indicating that close to one percent (0.88%) of the population interviewed has clinically relevant disease expected to significantly reduce quality of life. Given the criteria used to define probable RLS, it is not unexpected that those with probable RLS represent a relatively small number (8; 0.16% of pop) of those with reported sleep disturbance and that the definite RLS group constitutes the majority (36; 0.72% of pop).

Approximately 63% of the definite RLS group and 66% of the probable RLS group did not report any other related disorders that could constitute a secondary cause of the RLS. Of the 2024 women respondents with pregnancy histories, 332 (16.4%) reported that they had an uncomfortable feeling in their legs while they were lying down and they had an urge to move their leg while they were lying down during pregnancy.

DISCUSSION

This survey is the first systematic nationwide survey of RLS in Korean adults following the revised IRLSSG criteria.[4] More importantly it is the first population-based survey to use a complex questionnaire to exclude potential false-positive conditions. In our telephone survey, the response rate was 11.8%, which is lower than usually occurs with face to face interviews. In our survey, most nonparticipants did not want a phone interview and did not give us any information about the demographic characteristics; thus, we could not compare participants to nonparticipants. This is a common limitation with the telephone interview method. However, the telephone interview method has its own advantages, such as easier access to people of an entire area, permitting use of a stratified multistage random sampling method, and encouraging more candid responses than face to face interviews. Moreover, to assure the accuracy of our survey, we chose the TNS Company, a well-known international survey company that has its own quality control system.

The REST general population study, being an example of the most thorough of the presently published population surveys, only used a total of 6 questions.[8] The current survey is the only survey of an Asian population to use at least 4 questions as well as validating the translation of those questions. One previous Korean study used a single question and found a prevalence of 12.1%.[13] A study in Japan used 2 questions and reported the prevalence of RLS to be about 5% to 6%.[20] A study in Singapore (0.1% prevalence was reported) and a study in Mersin, Turkey (3.2% prevalence was reported) both reported using the 4 criteria outlined by the International RLS Study Group, but neither reported the actual questions or how translations of the English questions were validated.[12-14,21]

Because of the more complex set of questions that were used in this survey, we were able to categorize individuals into definite or probable RLS groups. We believe that the "probable" RLS category more likely has "true" RLS than they have "not" RLS and therefore have included them in the analysis of all RLS affected. We present both RLS categories so the reader can at least see the data separately. In the NIH workshop paper,[4] it was noted that some patients are not aware of the sensory component, and others cannot distinguish the urge to move from sensation, thus making question 1 (unpleasant sensation in the leg) likely to produce false negatives. The Johns Hopkins RLS Center group who developed the JHTDI questionnaire, used question 7 (7a) to reduce false positives in the definite RLS group. Individuals who truly have positional complaints (e.g., patient complains of legs discomfort when he is sitting with his leg crossed for a long time) would be an example. But it is also the clinical experience of the Hopkins group that patients with mild RLS symptoms may only report symptoms when sitting for long periods of time. Therefore, the "probable" RLS definition was developed to tract what was felt to be highly likely RLS individuals that did not meet the strictest criteria for RLS ("definite").

A total of 7.5% of the population met the criteria for definite or probable RLS groups; this is comparable to the 7.2% prevalence of the REST general population study, which was composed mostly of those of European ancestry.[8] If we are conservative in our assessment of the population burden of the disease by requiring only those criteria used to establish "definite" RLS, we still see a significant portion of the population (3.9%) reporting

RLS symptoms. If we are even more conservative, as was done in the REST general population study,[8] and only consider those with definite RLS and ≥2 nights per week of moderate or severe symptoms (RLS "sufferers") then about 1.0% of the population appear to be affected. The percentage of RLS sufferers including the probable as well as definite RLS was 1.5%. In the REST study the average prevalence of RLS sufferers was somewhat higher at 2.7% but it ranged from 1.3% in Germany to 4.2% in France.

The prevalence of RLS in the present study appears to increase with age until the 6th decade. But another view of the data is that there is no difference between the 5th and the 7th decades. There is a numerical increase in prevalence rates between the 5th and 6th decades (8.7% to 9.1%) and then a numerical decrease in the 7th decade (9.1% to 8.7%). The question is whether these numerical differences are statistically meaningful. One could easily argue that in fact the prevalence of RLS in the Korean population plateaus after the 5th decade. This differs from European surveys, which reported a somewhat steeper increase in prevalence with age, peaking slightly later between 6th to 8th decades.[5,11]

Also, distinctly different in the Korean RLS population from that reported in the European/American population is the gender differences. Almost all of the European/American population studies found women almost twice as likely to report RLS than men.[5,6,8-11,22] In our study, the prevalence is higher for women than for men in both the definite or probable RLS groups, however the difference is only about 40% higher, somewhat less than that in the Europe studies.[8]

In this survey, we found RLS is common in Korea and the prevalence of RLS is comparable to western countries. It also affects sleep considerably. Our results showed respondents with any RLS symptoms in Korea have similar clinical characteristics to those of other countries. It is surprising that so few of the RLS sufferers take any treatment, even when it is distressing and significantly disturbs sleep. This confirms that RLS is still underdiagnosed, as has been observed elsewhere, although it has a high prevalence in Korea. We clearly need to announce the RLS disorder to the public and have complementary education concerning the diagnosis and management of RLS for physicians.

ACKNOWLEDGMENTS

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