

Relationship between Demographic Characteristics, Depression and Insomnia with Restless Legs Syndrome: a Study of Adults Aged 17-70 Years in Yazd 2019

Mohammad Hossein Sorbi ^{1*} , Ali Issazadegan ¹ , Esmail Soleimani ¹ ,
Hamid Mirhosseini ² 

1. Department of Psychology, Faculty of Humanities, Urmia University, Urmia, Iran
2. Research Center of Addiction and Behavioral Sciences, Shahid Sadoughi University of Medical sciences, Yazd, Iran

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Corresponding Author:

Mohammad Hossein Sorbi
Sorbih@gmail.com

ABSTRACT

Introduction: Restless legs syndrome (RLS) is a neurological-motor disorder in which most patients tend to shake their legs during sleep and describe it as an unpleasant feeling. The aims of this study were to determine the prevalence of RLS, its relationship with demographic characteristics, depression, and insomnia and comparison of the mentioned variables in the group with and without RLS.

Methods: This was a case-control analytic study. The sample consisted of 429 adults aged 17-70 years who had referred all the psychiatric and neurological clinics of Yazd (center of Iran) in 2019. Participants were selected by cluster sampling method. Research tools included a demographic questionnaire, the Beck Depression Inventory (BDI-II), Insomnia Severity Index (ISI), and an International Restless Legs Syndrome Questionnaire (IRLSQ). The data were analyzed by SPSS-21, chi-square, Pearson correlation coefficient, independent t-test, and linear regression. Significant level was considered 0.05.

Results: The mean and standard deviation of the age of participants was 34.43 ± 10.82 . Furthermore, the mean and standard deviation of the age group with RLS was 36.07 ± 10.95 while in group without RLS was 33.92 ± 10.75 . Prevalence of RLS in adults was 23.5% (n= 101), in women was 32% (n= 66) and in men was 28.7% (n= 35). The t-test showed patients with RLS had a higher degree of depression and insomnia than those without RLS ($p < 0.05$). Multiple linear regression also showed that insomnia ($\beta = 0.36$), age ($\beta = 0.13$), and depression ($\beta = 0.15$) had a significant effect on RLS score.

Conclusion: The prevalence of RLS among adults in Yazd is high. Severe insomnia, depressed mood, and aging are considered as important factors in predicting this disease. According to what was mentioned early detection, prevention, and treatment of this disorder in adults is necessary.

Keywords: Restless legs syndrome, Depression, Insomnia, Age distribution, Body Mass Index

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Introduction

Restless Legs Syndrome (RLS) is a motor-neurological disorder and patients with the syndrome have a severe tendency to move their legs during sleep, describing it as an unpleasant feeling that inactivity worsens it and often it causes insomnia (1, 2). This tendency to shake legs is associated with an unpleasant feeling that patients liken them as the feeling of worm movement on the skin, the presence of insects in bone, the presence of water on the legs, and the electrical flow in the legs (1). This syndrome is one of the most common sleep disorders that, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), has become a complete disorder (3), but is often not diagnosed or misdiagnosed (4). According to reports, about 80 percent of patients with this disorder visit doctors due to their symptoms, but only 6 percent of them are diagnosed as RLS. After diagnosis, only 13% of patients are treated with appropriate medications. The disease has four diagnostic criteria developed by the international restless legs syndrome study group (IRLSSG) include 1) the tendency to shake legs to reduce the unpleasant feeling of the legs, 2) Symptoms begin with sitting and inactivity, 3) the symptoms of the disease relieve by moving the legs and 4) onset or exacerbation of symptoms at night (4, 5). Patients often walk at night to relieve the unpleasant symptoms of their legs and sleep early in the morning, thereby experiencing sleep deprivation and daily drowsiness that may interfere with their daily functioning (1, 2).

RLS has many side effects that reduce the quality of sleep and life, increase the risk of cardiovascular disease and even death, and is closely associated with depressive disorder (6). The results of some studies have shown a significant relationship between RLS and depression. It seems that this syndrome impedes patients to enjoy their life and has negative effects on the social activities of their family life and occupation. For example, these patients are reluctant to engage in activities that require

prolonged sitting periods because prolonged periods of rest exacerbate the unpleasant symptoms of their legs (2). However, RLS is not as life-threatening as heart disease or diabetes; it causes chronic insomnia and daily drowsiness, and affects patients' sleep quality (3). Mucsi et al. (7) also stated in their study that RLS reduces patients' quality of life due to sleep disorder. However, in some studies, such as the study by Al-Arabi et al. (8), no relationship was found between RLS and depression.

Therefore, considering the contradictory findings about the relationship between depression, sleep disorders, and RLS and lack of similar internal study on Iranian society, research in this field seems necessary. Reports indicate that the disorder is present in 2 to 15 percent of the general population and that the risk for women is about 11 to 27 percent higher than men (9). In a meta-analysis study performed in Iran, the overall prevalence of RLS was 30% (95% CI: 23-37) in adult (10). However, Hosseini et al. (11) reported 27.9% prevalence of this syndrome in cardiovascular patients and Amiri et al. (12) reported 67.2% prevalence in hemodialysis patients. Given the aforementioned, few studies have been conducted in Iran on factors such as demographic status, depression, and insomnia in RLS patients, which need to be investigated. Therefore, the aims of this study were to determine the prevalence of RLS and its relationship with demographic characteristics, depression, and insomnia among adults aged 17-70 years living in Yazd to obtain a report on the overall prevalence of this disorder in Iranian society and its related factors.

Methods

Study Type and Sampling Method

This case-control analytic study was conducted from May 10 to September 12, 2019. The study population included all patients with RLS disorder who had referred to the psychiatric and neurological clinics of Yazd in 2019. According to the 2016 census statistics, the city

had a population of about 1,200,000 (28). Using Cochran's formula, a sample size of 384 was needed for the study, but since the questionnaire may not be fully completed by adults, a sample size of 450 was considered. Cluster sampling was used as the sampling method. This means that among the entire districts in this city, districts 1 and 2 of Yazd were randomly selected. Then, two neighborhoods were randomly selected from each district, and adults from these neighborhoods were examined. The sample size was calculated using the following Cochran's formula:

$$n = \frac{\frac{z^2 pq}{d^2}}{1 + \frac{1}{N} \left(\frac{z^2 pq}{d^2} - 1 \right)}$$

N= 1200000; Z= 1.96; p= q= 0. 5; d= 0.05

Selection Criteria

After obtaining permission from the Ethics Committee of Yazd University of Medical Sciences (Code: IR.SSU.REC.1398.051), the researcher referred to the research's neighborhoods and explained to everyone the aims of the research and if the individual wishes to participate in the study then the interview was done. Inclusion criteria for RLS subjects were: 1) mild to high syndrome severity score (scores between 5 and 12) in IRLSQ, 2) diagnosis of RLS prescribed by a psychiatrist or neurologist, 3) 18 to 75 years of age, and 4) lack of the history of cardiovascular, renal and diabetes disease (self-reporting). Exclusion criteria were: 1) mild to low syndrome severity score (scores between 0 to 4) in IRLSQ, 2) having some kind of motor or perceptual disability that could interfere with completing the questionnaire, and 3) not having consent to participate in the research. Healthy subjects were also selected based on criteria such as: being old enough (18 to 75 years), completing informed consent, and psychiatric examination for not having RLS or mental disorder.

Instruments

The following tools were used to collect data.

a) Demographic Information: This was a researcher-made questionnaire for collecting demographic data of adults such as age, sex, educational status, economic status, marital status, income, weight, and height.

b) International Restless Legs Syndrome Questionnaire (IRLSQ): This questionnaire was developed by the International Study Group for RLS, which examines RLS and its severity and has 4 questions. The questionnaire was designed based on a four-point Likert scale where the choices are always= 3, most often= 2, rarely= 1 and never= 0. To calculate the total score of the questionnaire, the score of all questionnaire questions were summed up. The range of this questionnaire was between 0 and 12. The more points obtained from this questionnaire, the greater the degree of RLS and its severity, and vice versa. A score below 4 means the absence of RLS; a score between 4 and 8 indicates a mild severity of the syndrome, and a score between 8 and 12 indicates a severe severity of RLS. This questionnaire is a standard tool and its validity and reliability have been measured in previous studies (13). For example, Hemmati and Alidousti (14) have obtained its reliability of 0.95 using Cronbach's alpha. In this study, Cronbach's alpha coefficient was 0.89 for this questionnaire.

c) Beck Depression Inventory (BDI-II): For the past 35 years, the Beck Depression Inventory has been the most widely used diagnostic tool for depression in patients who have received a clinical depression diagnosis. BDI-II is a newer version of the original Beck Depression Inventory, which was designed to measure depression in adults and adolescents above 13 years of age and measure symptoms in the last two weeks. Because the original BDI covered only 6 of the 9 depression criteria, it was revised in 1996 to further align with the DSM-IV. The questionnaire has 21 items that each item is scored from 0 to 3 and each score can range from 0 to 63. People fall into four groups: 0 to 13 (minimum score), 14 to 19 (low depression), 20 to 28 (mild depression), and 29 to 63 (severe

depression). This standard questionnaire is validated worldwide and its Cronbach's alpha coefficient is 0.87 and test-retest reliability is 0.74 (15). In this study, Cronbach's alpha coefficient was 0.93 for this questionnaire.

d) Insomnia Severity Index (ISI): The Insomnia Severity Index (ISI) was designed by Morin in 1993. It is a brief self-assessment tool that measures the patient's perception of insomnia in nighttime sleep. The scale consists of seven items that assess difficulty in starting and maintaining sleep (nighttime and early morning wakefulness), satisfaction with the current pattern of sleep, interference with daily functioning, severity of the damage attributed to sleep problems and the degree of disturbance or worry caused by a sleep problem. Participants estimate their perception of ISI items on a 5-point scale (0= never and 5= very high). Scores range from 0 to 28. In the ISI, the range of scores is from 0 to 28. Higher scores indicate more perception of insomnia. This scale had an excellent internal consistency (Cronbach's alpha= 0.90). Also, the intraclass correlation coefficient presented an excellent agreement in the English version (ICC= 0.762, CI= 0.481–890) (16). The alpha coefficient of this questionnaire was 0.92 in the present study.

Data analysis

SPSS-21 was used to analyze the data. At the data entry stage, from the 450 questionnaires collected, 21 questionnaires were excluded from the study due to incompleteness. Next, 429 questionnaires were examined using descriptive statistics such as frequency (N) and percentage (%), mean (M), and standard deviation (SD). Finally, the data were analyzed using inferential

statistics such as chi-square, Pearson correlation coefficient, independent t-test, and linear regression.

Results

Demographic information of participants

The number of adults evaluated in this study was 429, ranging from 17 to 70 years. The mean and standard deviation of age of participants was 34.43 ± 10.82 . The results showed that 63.4% (n= 272) of the subjects were women and 36.6% (n= 157) were men. Of these, 65.5% (n= 281) were married, 31.7% (n= 136) single, and 2.8% (n= 12) divorced. 70.9% (n= 304) of participants had middle economic status, 15.9% (n= 68) had lower economic status and 13.2% (n= 57) had upper-middle economic status. However, 46.4% (n= 199) had middle income, 39.4% (n= 169) had lower income and 14.2% (n= 61) had upper income. In terms of education, 49.2% (n= 211) had an academic degree, 29.6% (n= 127) had a diploma and 21.2% (n= 91) had a diploma, and only 14% (n= 60) of the subjects were smoker.

Adult characteristics with and without RLS

Table 1 showed the demographic characteristics of the participants with and without RLS. The mean and standard deviation of the age group with RLS was 36.07 ± 10.95 and the group without RLS was 33.92 ± 10.75 . The prevalence of RLS in adults was 23.5% (n= 101), that was 32% (n= 66) in women and 28.7% (n= 35) in men.

The Chi-square test showed that there are no significant differences between gender, economic status, marital status, income, and smoking among participants with and without RLS ($p > 0.05$).

Table 1. The comparison of demographic characteristics in two groups with and without RLS (N = 429)

| Variables | RLS (-) | | RLS (+) | | p*. |
|---------------------|---------|------|---------|------|-------|
| | N | % | N | % | |
| Gender | | | | | |
| Male | 122 | 37.2 | 35 | 34.7 | 0.643 |
| Female | 206 | 62.8 | 66 | 65.3 | |
| Economic status | | | | | |
| Lower | 52 | 15.9 | 16 | 15.8 | 0.990 |
| Middle | 232 | 70.7 | 72 | 71.3 | |
| Upper-middle | 44 | 13.4 | 13 | 12.9 | |
| Education Level | | | | | |
| Middle School | 64 | 19.5 | 27 | 26.7 | 0.299 |
| High School Diploma | 99 | 30.2 | 28 | 27.7 | |
| Undergraduate | 165 | 50.3 | 46 | 45.5 | |
| Income | | | | | |
| Lower | 137 | 41.8 | 32 | 31.7 | 0.105 |
| Middle | 143 | 43.6 | 56 | 55.4 | |
| upper | 48 | 14.6 | 13 | 12.9 | |
| Smoking | | | | | |
| No | 45 | 13.7 | 15 | 14.9 | 0.774 |
| Yes | 283 | 86.3 | 86 | 85.1 | |

*Chi-square test

Correlation matrix of main research variables

Before determining the prediction of the dependent variable, it is necessary to test the linear relationships between the independent and dependent variables. To do so, Pearson's correlation coefficient was used. As seen in Table 2, in most cases (except socioeconomic status),

there was a significant positive correlation between all independent variables of the study and RLS ($p < 0.05$). Therefore, the greater the depression or the severity of insomnia in adults, the more RLS is in them ($p < 0.01$). On the other hand, the older the people were or the higher their body mass index (BMI), the severity of RLS ($p < 0.05$) was greater.

Table 2. The correlation matrix of variables

| Variables | 1 | 2 | 3 | 4 | 5 | 6 |
|------------------------------------|--------|--------|---------|--------|--------|------|
| 1. Age | - | | | | | |
| 2. Body mass index (BMI) | 0.26** | - | | | | |
| 3. Socioeconomic status (SES) | -0.02 | 0.09 | - | | | |
| 4. Beck inventory depression (BDI) | -0.01 | - 0.02 | -0.18** | - | | |
| 5. Insomnia severity index (ISI) | 0.007 | 0.01 | -0.14** | 0.54** | - | |
| 6. Restless legs syndrome (RLS) | 0.13** | 0.10* | 0.01 | 0.30** | 0.37** | - |
| Mean | 34.43 | 24.56 | 6.0 | 12.0 | 7.46 | 2.92 |
| Standard Deviation | 10.83 | 4.30 | 1.32 | 10.70 | 5.25 | 2.67 |

* $P < 0.05$, ** $P < 0.01$ Pearson correlation coefficient

The status of the main research variables

The Kolmogorov-Smirnov and Shapiro-Wilk showed that research variables had a normal distribution ($p > 0.05$), so the data were analyzed by parametric tests. The results of Table 3, obtained from the t-test, showed that there was a significant difference between depression and

insomnia severity in the two groups with and without RLS. This means that patients with RLS have more severe depression and insomnia than those without RLS ($p < 0.05$) but there were no significant differences between age, BMI, and SES among the two groups (Figure 1).

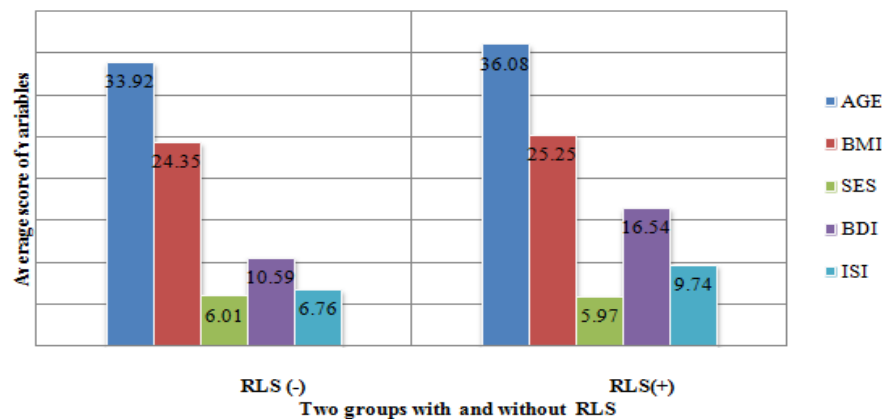


Figure 1. The comparison of age, body mass index (BMI), socioeconomic status (SES), Beck Depression Inventory (BDI) and Insomnia Severity Index (ISI) between RLS (-) and RLS (+)

Table 3. The comparison of main research variables in two groups with and without RLS

| Variables | RLS (-) | | RLS (+) | | p* |
|---------------------------------|---------|-------|---------|-------|----------|
| | Mean | SD | Mean | SD | |
| Age | 33.92 | 10.75 | 36.08 | 10.96 | 0.080 |
| Body mass index (BMI) | 24.35 | 4.18 | 25.25 | 4.64 | 0.066 |
| Socioeconomic status (SES) | 6.01 | 1.32 | 5.97 | 1.34 | 0.781 |
| Beck inventory depression (BDI) | 10.59 | 9.79 | 16.54 | 12.21 | < 0.0001 |
| Insomnia severity index (ISI) | 6.76 | 4.97 | 9.74 | 5.50 | < 0.0001 |

RLS- = 328; RLS+ = 101 * Independent t test

Finding of Regression Analysis in RLS

The contents of Tables 4 were obtained by stepwise regression analysis in which RLS were selected as the dependent variable and age, BMI, socioeconomic status, depression, and insomnia were the predictor variables. Initially, the error-independent values of the Durbin-Watson test showed that the DW= 1.86 was between 1.5 and 2.5, indicating a lack of autocorrelation in the errors so the observation independence assumption

is accepted. Therefore, it can be said that the fitted model is a suitable one. On the other hand, the values of Tolerance and variance inflation factor (VIF) were close to 1 and above 0.7. Also, the maximum VIF in the regression was calculated as 1.4 which is far from 2. Therefore, it can be said through these two indices that the co-linearity between the independent variables is low and the standard error of the regression coefficients has a low inflation.

Table 4. The summary of stepwise regression to predict RLS variable

| Model | Variable | R | R ² | B | Std. Error | Standardized Beta | F | t | Tolerance | VIF | 95% CI |
|-------|------------|------|----------------|-------|------------|-------------------|--------|--------|-----------|-----|------------|
| 1 | Insomnia | 0.36 | 0.13 | 0.186 | 0.023 | 0.365 | 65.80* | 8.112* | 1 | 1 | 0.14- 0.23 |
| 2 | Insomnia | 0.39 | 0.14 | 0.185 | 0.023 | 0.365 | 37.48* | 8.163* | 1 | 1 | 0.14- 0.23 |
| | Age | | | 0.031 | 0.011 | 0.127 | | 2.841* | | | |
| 3 | Insomnia | 0.41 | 0.16 | 0.145 | 0.027 | 0.285 | 28.09* | 5.432* | 0.71 | 1.4 | 0.09- 0.20 |
| | Age | | | 0.032 | 0.011 | 0.129 | | 2.911* | | | |
| | Depression | | | 0.037 | 0.013 | 0.149 | | 2.841* | | | |

* p< 0.01

Initially, the results of Table 4 show that the three steps of insomnia, age, and depression ($F= 28.9$; $R^2= 0.16$; $P= 0.01$) can predict 16% of the RLS variable. In addition, stepwise regression results show that the insomnia variable with $\beta= 0.36$ (95% CI: 0.14-0.23) has the most capability for predicting RLS. This means that 13% of the insomnia variable is predicted by RLS. However, depression with $\beta= 0.15$ (95% CI: 0.011-0.06) and age with $\beta= 0.13$ (95% CI: 0.01-0.05) had significant predictive power of RLS, respectively. The other variables not mentioned in Table 4 are excluded because of their lack of a significant role in predicting competence perception.

Discussion

The present study was a cross-sectional study that investigated the prevalence and psychological factors associated with RLS in Yazd. Initial results indicated that the prevalence of RLS was 23.5% in adults (32% in women and 28.7% in men). In a study of the Iranian adult population, Fereshtehnejad et al. (17) reported an average prevalence of RLS (6%) and reported that 6 out of every 1000 Iranians had RLS. Compared to the World Report, the prevalence of the syndrome in North America and Europe is reported to be between 5.5% and 11.6% and in the Asian population between 1% and 7.5% (18). Overall, the results indicate that US and Asian studies report a higher prevalence of RLS than European studies. Although this syndrome is found in all races, many believe it to be more prevalent in white races (12).

Other results indicated that there was no significant difference between gender, economic status, marital status, income, smoking, age, body mass index, and socioeconomic status among participants with and without RLS. However, there was a significant difference between depression and insomnia severity in the two groups with and without RLS, meaning that patients with RLS had more depression and insomnia than the group without RLS. Yilmaz et al. (19) showed RLS patients were found to have greater anxiety and depression scores compared

with the control group. According to Theorell-Haglöw et al. (20), depression and insomnia are more common in women in the population, which is expected to make more women than men with these symptoms. Consistent with the reported results, no significant difference was reported between the prevalence of RLS and gender (21), but in two large studies worldwide, the prevalence of RLS has been reported in women more than men (22, 23). In their study, Farajzadeh et al. (9) reported that depression rates in RLS patients were higher than those without syndromes. On the other hand, Habibzadeh et al. (24) reported that the quality of sleep in RLS patients was significantly more disturbed and worse than those without the syndrome. Insomnia, which comes with RLS, is characterized by dissatisfaction with the sleep quantity or quality and is accompanied by symptoms such as difficulty starting or maintaining sleep (frequent waking or returning to sleep) or early morning waking up with disabilities back to sleep (25).

Other results showed that there was a significant positive correlation between age, body mass index, depression and insomnia and RLS. The older the people are or the higher body mass index (BMI), the greater the risk of RLS with a 95% probability. On the other hand, with a 99% probability, the higher the degree of depression or the severity of insomnia in adults the prevalence of RLS is greater is. Other research results showed that insomnia variable with $\beta= 0.36$ (95% CI: 0.14-0.23), depression with $\beta= 0.15$ (95% CI: 0.011), and age with $\beta= 0.13$ (95% CI: 0.01-0.05) were able to predict RLS, respectively. The results are consistent with the previous studies. For example, Saraji et al. (26) found that body mass index in patients with RLS was significantly higher than in patients without this syndrome. On the other hand, in European and American societies, the prevalence of RLS increases in the general population with aging, but there is no change in the prevalence of RLS in Asian countries through aging (22, 27). Yilmaz et al. (19) showed RLS was associated with depression, anxiety, and sleep disturbance. RLS symptoms

are regulated by a circadian rhythm that was worsen at night, and thus have a profound effect on the onset of sleep and return to sleep and the increased risk of developing depression and anxiety (20). The most important advantages of this study were the novel results, offering complete results without bias and appropriate sample size. The limitations of this study were that this was a cross-sectional study, the information of some studies was insufficient, and there were no objective experiments in collecting information in this field.

Conclusion

The aim of this study was to determine the prevalence and factors associated with RLS in Yazd. The results showed that the prevalence of RLS in Yazd was 23.5%. That means that out of every 100 people, about 23 are suffering from RLS and this disorder is more prevalent in women. Compared to reports in similar studies, important factors such as severe insomnia, depressed mood, and old age are important factors in predicting the disease. This requires attention to the early detection of the disorder, timely treatment, and the provision of appropriate

preventive measures in Iranian adults, especially women.

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Authors' contribution

M.H.S. conceived of the presented idea. M.K.Z. developed the theory and performed the computations. M.H.S. and M.K.Z. verified the analytical methods. M.H.S. encouraged M.K.Z. to investigate [a specific aspect] and supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

Conflict of Interest

The authors declare that there is no conflict of interest.

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