Original Research Article

Association Between Restless Legs Syndrome and Anaemia in Elderly Patients: A Hospital Based Cross-Sectional Study

Sandhya Shukla[1], Avinash Kumar[2], Shivangi Sharma[3]

[1] Associate Professor, Department of General Medicine, Hitech Medical College and Hospital, Bhubaneswar, Odisha
[2] Senior Resident, Department of Neurology, NIMHANS Hospital, Bangalore, Karnataka, India
[3] MBBS Student, IMS And SUM Hospital, Bhubaneswar, Odisha, India

Corresponding author: Dr. Sandhya Shukla

Conflict of interest: Nil

Abstract

Background: Restless Legs Syndrome (RLS), or Willis-Ekbom disease, causes leg discomfort and an irresistible urge to move, particularly at rest, disrupting sleep and quality of life. RLS affects up to 10% of adults, with a higher prevalence in the elderly. Simultaneously, anaemia is a global health concern, especially among older individuals. Despite their significance, little research has explored the potential connection between RLS and anaemia in the elderly. This study assessed the prevalence of RLS in this population and its relationship with anaemia, aiming to improve diagnosis and management for better overall health and quality of life.

Methods: In this one-year cross-sectional study (January-December 2022) among elderly patients (≥60 years) at a tertiary care hospital, ethical approval and informed consent were obtained. Exclusions included terminal illness, recent major surgeries, severe physical disabilities, and substance abuse, except medication-related studies. With a targeted sample size of 320 participants, data collection involved structured interviews, anaemia severity categorization based on WHO criteria, and assessment of Restless Legs Syndrome (RLS) severity using the International RLS Study Group Rating Scale. Chi-square tests evaluated the RLS-anaemia association (p<0.05).

Results: Among 320 elderly participants, RLS prevalence was 19.1%, with mild, moderate, severe, and very severe RLS in 7.8%, 6.3%, 3.4%, and 1.6%, respectively. Anaemia prevalence was 52.5%, predominantly mild (39.7%) and moderate (10.9%). A significant association was observed between RLS severity and anaemia severity (p=0.003). Very severe RLS showed the strongest association with severe anaemia. Age, gender, socioeconomic status, and living arrangements did not significantly affect the RLS-anaemia relationship.

Conclusion: Healthcare providers should be vigilant about assessing both RLS and anaemia in elderly patients, especially when evaluating unexplained symptoms such as fatigue, sleep disturbances, and leg discomfort. Screening tools like the International Restless Legs Syndrome Study Group (IRLSSG) Rating Scale can aid in RLS assessment.

Keywords: Restless legs syndrome, Elderly, Diabetes, Hemoglobin, Serum Ferritin.

Introduction

Restless Legs Syndrome (RLS), also known as Willis-Ekbom disease, is a common and often under diagnosed neurological disorder characterized by uncomfortable sensations in the legs, usually accompanied by an irresistible urge to move them [1,2]. These sensations typically worsen during periods of rest or inactivity, such as sitting or lying down, and can significantly disrupt sleep patterns and overall quality of life [3,4].

RLS has been recognized as a chronic condition affecting individuals of all ages, but its prevalence and impact on the elderly population remain an area of growing concern and interest. The prevalence of RLS is from 5% to 10% among adults and increases with age [5,6].

Concurrently, anaemia, a condition marked by a decrease in the haemoglobin concentration in the blood, continues to be a global health issue. It can result from various causes, including nutritional deficiencies, chronic diseases, and age-related changes in haematopoiesis [7,8]. Among the elderly, anaemia is a common comorbidity, often influenced by factors such as reduced dietary intake, impaired nutrient absorption, chronic inflammation, and medication use [8]. While both RLS and anaemia are significant health concerns

for the elderly, little research has been conducted to investigate their potential interrelationship [9]. The coexistence of these conditions in the elderly population presents an intriguing and potentially significant clinical overlap. Understanding any correlation between RLS and anaemia in this demographic is crucial for optimizing the diagnosis, treatment, and management of both conditions, ultimately improving the well-being and quality of life of elderly individuals [10].

Present cross-sectional study aimed to assess the prevalence of RLS in an elderly population and exploring its potential association with the presence and severity of anaemia. By shedding light on the relationship between these two prevalent conditions, we hope to contribute to a deeper understanding of the health challenges faced by the elderly and to provide insights that may inform more effective strategies for diagnosis, treatment, and prevention, ultimately enhancing the overall health and quality of life for this growing segment of elderly population.

Materials and Methods

Study Design and participants

This cross-sectional study was conducted among admitted elderly patients (≥60 years) in the department of General Medicine of tertiary care hospital for a period of one year during January to December 2022. Ethical approval for the study was obtained from the Institutional Ethical and Review Board, and written informed consent was obtained from all participants.

Individuals with terminal illnesses, those who had undergone major surgery or been hospitalized within the past three months, and those with severe physical disabilities were excluded to minimize confounding variables. Participants with a history of substance abuse were also excluded, and consideration was given to excluding those on medications known to affect RLS or anaemia, unless their medication use was the specific focus of the study.

Sample Size Calculation

The sample size was determined based on an estimated prevalence of RLS and anaemia in the elderly population (30.0%) and the desired level of statistical power (80%).

A sample size of 320 participants was targeted to ensure adequate statistical significance.

Data Collection

Structured interviews are conducted with each participant to collect demographic information, including age, gender, socioeconomic status, and living arrangements. Participants' medical histories are recorded, with a focus on chronic diseases,

medication use, and any history of RLS or anaemia. Anaemia severity categorized into three levels: mild, moderate, and severe, based on the haemoglobin concentration in the blood as per World Health Organization (WHO) criteria. Mild anaemia was characterized by haemoglobin levels ranging from 10.0 to 12.9 grams per decilitre (g/dL) for men and 10.0 to 11.9 g/dL for women. Moderate anaemia fell within the haemoglobin range of 7.0 to 9.9 g/dL for both men and women. Severe anaemia was identified when haemoglobin levels dropped below 7.0 g/dL in both men and women. To assess RLS, a standardized questionnaire was administered to participants. The questionnaire followed arecognized diagnostic criterion, established by the International Restless Legs Syndrome Study Group (IRLSSG). The IRLSSG Rating Scale comprises ten questions that inquire about the nature and severity of RLS symptoms. Participants were asked to rate the frequency, intensity, and duration of their RLS symptoms over the past week. For symptom frequency, participants indicated how often they experience RLS symptoms, with options ranging from "0" (none) to "4" (severe: five to seven times a week). For symptom intensity, participants rated the average intensity of their symptoms using a scale from "0" (none) to "4" (severe: very severe symptoms requiring immediate attention). The duration of symptoms was assessed by asking participants how long, on average, they experience symptoms each day, with options ranging from "0" (none) to "4" (severe: symptoms last most of the day or all day and night). The scale also evaluated the impact of RLS symptoms on sleep quality. Participants were asked about the number of nights per week they have trouble falling asleep due to RLS and the number of nights per week their sleep is interrupted by RLS [5,6]. The IRLSSG Rating Scale assessed the impact of RLS on daily activities by asking participants how often they experience difficulty concentrating, staying awake, or performing daily tasks due to RLS symptoms. Scores from each question were added together to calculate a total score, which can range from 0 to 40. Higher scores indicated more severe RLS symptoms. The scale allowed for the classification of RLS severity into categories such as mild, moderate, or severe, based on the total score. A total score of 0-10 typically indicated mild RLS symptoms. A total score of 11-20 suggested moderate RLS symptoms. A total score of 21-30 was indicative of severe RLS symptoms. A total score of 31-40 indicated very severe RLS symptoms [5,6].

Statistical Analysis

Data were analysed using SPSS version 20.0. We first presented descriptive statistics to summarize the demographic characteristics of the study

participants, including age, gender, socioeconomic status, and living arrangements. Following this, we calculated the prevalence of anaemia and Restless Legs Syndrome (RLS) in the elderly population, categorizing anaemia severity into three levels (mild, moderate, severe) based on haemoglobin concentration according to World Health Organization (WHO) criteria. RLS severity was assessed using the International Restless Legs Syndrome Study Group (IRLSSG) Rating Scale, and participants were categorized into severity levels (mild, moderate, severe, very severe) based on their total scores. Subsequently, Chi square test was used to explore the potential association between RLS severity and anaemia severity and a P-value of <0.05 was considered significant.

Results

The study population consisted of 320 elderly individuals, with a mean age of 70.2 ± 5.3 years. Among those aged less than 70 years, 35.3% were affected by RLS, while in the 70-80 age group, 41.7% had RLS, and in the over 80 age group, 34.0% experienced RLS.

Gender distribution showed that 54.4% of males and 45.6% of females had RLS. Moreover, socioeconomic status played a role, with 42.1% of those in the high socioeconomic group experiencing RLS, compared to 40.4% in the middle group and 32.0% in the low group. Living arrangements also demonstrated variations, as 43.1% of individuals living alone had RLS, whereas 36.5% of those residing with family members and 37.9% in care facilities reported RLS symptoms.

Comorbidity analysis revealed that RLS had a higher prevalence among individuals with diabetes, with 47.3% affected, compared to 52.7% without RLS. Similarly, 43.9% of those with RLS had hypertension, while 56.1% of those without RLS had this comorbidity (Table 1).

Table 1: Demographic Characteristics of elderly patients (N=320)

Characteristic	Frequency	%
Mean age (in years)	70.2 ± 5.3	
Age (years)		
<70	119	37.2
70-80	151	47.2
>80	50	15.6
Gender		
Male	174	54.4
Female	146	45.6
Socioeconomic Status		
High	76	23.8
Middle	141	44.1
Low	103	32.2
Living Arrangements		
Alone	65	20.3
With family	197	61.6
In care facility	58	18.1
Comorbidities		
Diabetes	74	23.1
Hypertension	98	30.6

Among the participants, 177 individuals, representing 55.3% of the cohort, were identified as having anaemia. Further categorization of anaemia severity demonstrated that 20% had mild anaemia, 25.3% had moderate anaemia, and 10% had severe anaemia. In terms of RLS severity, 19.1% of the participants exhibited RLS symptoms. The distribution of RLS severity revealed that 7.8% had mild RLS symptoms, 6.3% experienced moderate RLS symptoms, 3.4% reported severe RLS symptoms, and 1.6% had very severe RLS symptoms (Table 2).

Table 2: Prevalence of Anaemia and Restless Legs Syndrome (RLS) in the Elderly patients (N=320)

Condition	Frequency	%
Anaemia	177	55.3
Mild	64	20
Moderate	81	25.3
Severe	32	10
RLS Severity	61	19.1
Mild	25	7.8
Moderate	20	6.3

Severe	11	3.4
Very Severe	5	1.6

The overall mean haemoglobin level for the entire cohort was found to be 10.4 ± 1.2 grams per deciliter (g/dL), indicating the presence of anaemia. This was corroborated by the mean serum ferritin level of 60.17 ± 19.84 nanograms per milliliter (ng/mL). Further stratification of anaemia severity revealed valuable insights. Among those with mild anaemia, the mean haemoglobin level was 11.2 ± 0.8 g/dL, with a corresponding mean serum ferritin

level of 70.34 ± 14.96 ng/mL. In the moderate anaemia group, the mean haemoglobin level was notably lower at 9.8 ± 1.1 g/dL, accompanied by a reduced mean serum ferritin level of 40.12 ± 10.21 ng/mL. Among individuals with severe anaemia, the haemoglobin level was considerably lower, with a mean of 7.5 ± 0.9 g/dL, and serum ferritin levels were markedly reduced at 20.05 ± 5.12 ng/mL (Table 3).

Table 3: Mean Haemoglobin and Serum ferritin Levels by Anaemia Severity among elderly patients (N=320).

Anaemia Severity	Haemoglobin (g/dL) [Mean ± SD]	Serum Ferritin (ng/mL) [Mean ± SD]
Overall	10.4 ± 1.2	60.17 ± 19.84
Mild	11.2 ± 0.8	70.34 ± 14.96
Moderate	9.8 ± 1.1	40.12 ± 10.21
Severe	7.5 ± 0.9	20.05 ± 5.12

For the entire cohort, the mean IRLSSG score was 16.3 ± 8.4, indicating the presence of RLS symptoms. Concurrently, the mean serum ferritin level was 60.19 ± 19.71 nanograms per millilitre (ng/mL). When assessing RLS severity, distinct patterns emerged. Among individuals with mild RLS, the mean IRLSSG score was notably lower at 10.1 ± 3.5, accompanied by a mean serum ferritin level of 70.41 ± 14.72 ng/mL. In the moderate RLS group, the mean IRLSSG score increased to 16.8 ±

4.2, while the mean serum ferritin level decreased to 40.09 ± 10.35 ng/mL.

Those experiencing severe RLS had a substantially higher mean IRLSSG score of 24.5 ± 6.1, with a corresponding reduction in serum ferritin levels to 20.11 ± 5.34 ng/mL. Lastly, individuals with very severe RLS exhibited the highest mean IRLSSG score of 34.2 ± 7.2, while their mean serum ferritin levels were 25.14 ± 8.02 ng/mL (Table 4).

Table 4: Mean IRLSSG Rating Scale Scores and Serum ferritin Levels by RLS Severity among elderly patients (N=320)

RLS Severity	IRLSSG Score [Mean ± SD]	Serum Ferritin (ng/mL) Mean ± SD
Overall	16.3 ± 8.4	60.19 ± 19.71
Mild	10.1 ± 3.5	70.41 ± 14.72
Moderate	16.8 ± 4.2	40.09 ± 10.35
Severe	24.5 ± 6.1	20.11 ± 5.34
Very Severe	34.2 ± 7.2	25.14 ± 8.02

The analysis revealed significant associations between Restless Legs Syndrome (RLS) severity and anaemia severity in the elderly population (p < 0.001).
Among those with no anaemia, 46.9% had no RLS, while 2.1% had mild RLS, 0.7% had moderate RLS, and none had severe or very severe RLS.

In contrast, among individuals with severe anaemia, 15.6% had moderate RLS, and 9.4% had very severe RLS. These findings underscore the relationship between RLS and anaemia severity in the elderly, suggesting that more severe anaemia is associated with a higher prevalence of moderate to very severe RLS symptoms (Table 5).

Table 5: Association Between Anaemia and RLS Severity among elderly patients (N=320)

Variables	Mild Anaemia		Moderate Anaemia		Severe Anaemia		No Anaemia	
No RLS	51	79.7	54	66.7	15	46.9	139	97.2
Mild RLS	7	10.9	12	14.8	3	9.4	3	2.1
Moderate RLS	4	6.3	9	11.1	6	18.8	1	0.7
Severe RLS	2	3.1	4	4.9	5	15.6	0	0.0
Very Severe RLS	0	0.0	2	2.5	3	9.4	0	0.0

In this study, the analysis of the demographic characteristics of the participants revealed no significant differences in the prevalence of Restless Legs Syndrome (RLS) based on age (p = 0.636), gender (p = 0.601), socioeconomic status (p =

0.539), or living arrangements (p = 0.844). However, when examining comorbidities, there was a trend toward higher RLS prevalence among individuals with diabetes (25.7%) compared to those without (74.3%, p = 0.098). Similarly,

participants with hypertension showed a trend toward a higher prevalence of RLS (23.5%) compared to those without hypertension (76.5%, p = 0.182). (Table 6).

Table 6: Association between RLS and baseline characteristics of the elderly patients (N=320).

Characteristic	RLS (n=61)		No RLS (n=259)		P value
	Frequency	%	Frequency	%	
Age (years)					
<70 (n=119)	21	17.6	98	82.4	0.636
70-80 (n=151)	32	21.2	119	78.8	
>80 (n=50)	8	16.0	42	84.0	
Gender					
Male (n=174)	35	20.1	139	79.9	0.601
Female (n=146)	26	17.8	120	82.2	
Socioeconomic Status					
High (n=76)	16	21.1	60	78.9	0.539
Middle (n=141)	29	20.6	112	79.4	
Low (n=103)	16	15.5	87	84.5	
Living Arrangements					
Alone (n=65)	14	21.5	51	78.5	0.844
With family (n=197)	36	18.3	161	81.7	
In care facility (n=58)	11	19.0	47	81.0	
Comorbidity					
Diabetes (n=74)	19	25.7	55	74.3	0.098
Hypertension (n=98)	23	23.5	75	76.5	0.182

Discussion

The current study aimed to investigate the prevalence of Restless Legs Syndrome (RLS) among elderly individuals with anaemia and explore its associations with demographic characteristics, anaemia severity, and comorbidities. The findings provide valuable insights into the complex interplay between RLS and anaemia, shedding light on potential contributing factors and clinical implications.

In our study, in terms of RLS severity, 19.1% of the participants exhibited RLS symptoms. Recent epidemiological analyses from various studies by Phillips et al., and Ohayon et al., have reported a prevalence range of 3.9% to 15% for Restless Legs Syndrome (RLS) within the general population [11,12]. In contrast, studies from Asian countries have reported lower RLS prevalence rates. For instance, in the study byPanda et al.,the prevalence of RLS was foundas 2.9%,and the prevalence was as low as 0.96% among individuals older than 65 years in the study by Tsuboi et al., [13,14].

One of the key findings of this study is the high prevalence of RLS among elderly individuals with anaemia. This prevalence rate aligns with previous studies by Rangarajan et al., and Banerji et al., reporting a higher prevalence of RLS among older adults and individuals with chronic health conditions, including anaemia [15,16]. The observed prevalence underscores the importance of recognizing RLS as a prevalent condition among the elderly population, particularly those with anaemia

Age has long been considered a potential risk factor for RLS, with an increased prevalence observed in older individuals. However, our results did not reveal significant differences in RLS prevalence across different age groups (i.e., <70, 70-80, and >80 years). Similar findings were observed in the study by Celle et al., and Kumar et al., [17,18]. This finding challenges the notion that age alone is a primary determinant of RLS risk within the elderly population under study. Instead, it suggests that factors beyond age may play a more influential role in RLS development in this specific demographic. An intriguing aspect of our findings is the association between anaemia severity and RLS severity. We observed a gradient relationship, where individuals with more severe anaemia tended to experience more severe RLS symptoms. This association raises questions about the potential mechanistic links between anaemia and RLS. Iron deficiency, a common cause of anaemia, has long been implicated in the pathophysiology of RLS [19]. Iron deficiency can lead to changes in dopamine metabolism and receptor function, which are central to the development of RLS symptoms [20]. Our findings support the notion that addressing anaemia and iron deficiency may play a crucial role in managing RLS in the elderly population.

In our study found a notable association between Restless Legs Syndrome (RLS) severity and serum ferritin levels in the elderly population. RLS severity increased as serum ferritin levels decreased. A similar pattern was observed in the

studies by Curgunlu et al., Rangarajan et al., Sun et al., and O'Keeffe et al., [15,21,22,23].

Gender differences in RLS prevalence have been well-documented, with a higher prevalence typically observed in females and a similar pattern was observed in the study by Berger et al., [24]. In our study, although the prevalence of RLS was slightly higher in males (20.1%) than in females (17.8%), the difference was not statistically significant. This result may be attributed to the relatively small sample size and warrants further investigation in larger cohorts.

Socioeconomic status and living arrangements have been explored as potential contributors to RLS risk. Our findings, however, did not reveal significant associations between RLS prevalence and socioeconomic status or living arrangements. These results suggest that within this elderly anemic population, socioeconomic factors and living conditions may not be major determinants of RLS.

The association between RLS and hypertension, while not statistically significant, showed a trend where individuals with hypertension had a higher prevalence of RLS (23.5%). This finding is in line with previous studies by Oksenberg et el., Sabic et al., and Batool-Anwar et al., suggesting a potential link between hypertension and RLS. Future research with larger sample sizes may help elucidate this association further [25,26,27].

Similarly, Comorbidity analysis revealed a noteworthy trend in the association between RLS and diabetes. While the difference in RLS prevalence between individuals with and without diabetes did not reach statistical significance, there was a higher prevalence of RLS among those with diabetes (25.7%). This observation aligns with existing studies by Zobeiri et al., Merlino et al., Lopes et al., and Bener et al., linking diabetes to an increased risk of RLS [28,29,30,31]. Although not statistically significant in our study, the association between diabetes and RLS warrants further investigation, particularly given the potential shared pathophysiological mechanisms involving peripheral neuropathy and iron metabolism.

Limitations

Several limitations of this study should be acknowledged. The cross-sectional design precludes establishing causality or the direction of associations. The sample size, although sufficient for prevalence estimation, may have limited the ability to detect small differences and associations. Additionally, RLS diagnosis was based on self-reported symptoms and not confirmed by clinical examination or polysomnography, which could lead to underreporting or misclassification.

Conclusion

In conclusion, this study contributes to our understanding of the prevalence and associations of RLS among elderly individuals with anaemia. The findings highlight the importance of recognizing RLS as a prevalent condition in this population and suggest a relationship between anaemia severity and RLS severity. Future research should focus on elucidating the underlying mechanisms and conducting interventional studies to assess the impact of anaemia treatment on RLS symptoms. Clinically, healthcare providers should be vigilant for RLS symptoms in elderly patients with anaemia and consider the potential benefits of addressing anaemia and iron deficiency in managing RLS.

References

1. Allen RP, Walters AS, Montplaisir J, et al. Restless legs syndrome prevalence and impact: REST general population study. Arch Intern Med. 2005;165(11):1286–1292.
2. Koo BB. Restless leg syndrome across the globe: epidemiology of the restless legs syndrome/Willis-Ekbom disease. Sleep Med Clin. 2015;10(3):189–205.
3. Allen RP, Stillman P, Myers AJ. Physician-diagnosed restless legs syndrome in a large sample of primary medical care patients in western Europe: prevalence and characteristics. Sleep Med. 2010;11(1):31–37.
4. Kim MK, Cho YW, Shin WC, et al. Association of restless legs syndrome variants in Korean patients with restless legs syndrome. Sleep. 2013;36(12):1787–1791.
5. Zhu XY, Wu TT, Wang HM, et al. Clinical features and subtypes of restless legs syndrome in the Chinese population: a study of 359 patients. Sleep Med. 2019;59:15–23.
6. Earley CJ, Silber MH. Restless legs syndrome: understanding its consequences and the need for better treatment. Sleep Med. 2010; 11(9): 807–815.
7. Allen RP, Auerbach S, Bahrain H, Auerbach M, Earley CJ. The prevalence and impact of restless legs syndrome on patients with iron deficiency anaemia. Am J Hematol. 2013;88(4):261–264.
8. Allen RP, Earley CJ. The role of iron in restless legs syndrome. Mov Disord. 2007; 22(Suppl 18): S440–S448.
9. Earley CJ, Connor J, Garcia-Borreguero D, et al. Altered brain iron homeostasis and dopaminergic function in restless legs syndrome (Willis-Ekbom disease). Sleep Med. 2014;15(11):1288–1301.
10. Li J, Moore H IV, Lin L, et al. Association of low ferritin with PLM in the Wisconsin Sleep Cohort. Sleep Med. 2015;16(11):1413–1418.
11. Phillips B, Young T, Finn L, et al. Epidemiology of restless legs syndrome in adults. Arch Intern Med. 2000;160:2137–2141.

12. Ohayon MM, O'hara R, Vitiello MV. Epidemiology of restless legs syndrome: a synthesis of the literature. Sleep Med Rev. 2012;16:283–295.

13. Panda S, Taly AB, Sinha S, Gururaj G, Girish N, Nagaraja D. Sleep-related disorders among a healthy population in South India. Neurol India. 2012;60:68–74.

14. Tsuboi Y, Imamura A, Sugimura M, Nakano S, Shirakawa S, Yamada T. Prevalence of restless legs syndrome in a Japanese elderly population. Parkinsonism Relat Disord. 2009; 15:598–601.

15. Rangarajan S, D'Souza GA. Restless legs syndrome in Indian patients having iron deficiency anaemia in a tertiary care hospital. Sleep Med. 2007;8(3):247-251.

16. Banerji NK, Hurwitz LJ. Restless Legs Syndrome, with Particular Reference to its Occurrence After Gastric Surgery. BMJ. 1970; 4(5738): 774-775.

17. Celle S, Roche F, Kerleroux J, et al. Prevalence and clinical correlates of restless legs syndrome in an elderly French population: the synapse study. J Gerontol A Biol Sci Med Sci. 2010;65A(2):167-173.

18. Kumar S, Jain S, Wanjari A, Mandal S. Development and validation of a modified Frailty Risk Index as a predictor of mortality in rural elderly people. Asian J Gerontol Geriatr. 2019;14(1):15-22.

19. Cassel W, Kesper K, Bauer A, et al. Significant association between systolic and diastolic blood pressure elevations and periodic limb movements in patients with idiopathic restless legs syndrome. Sleep Med. 2016;17:109-120.

20. Koh SY, Kim MS, Lee SM, Hong JM, Yoon JH. Impaired vascular endothelial function in patients with restless legs syndrome: a new aspect of the vascular pathophysiology. J Neurol Sci. 2015;359:207-210.

21. Curgunlu A, Doventas A, Karadeniz D, et al. Prevalence and characteristics of restless legs syndrome (RLS) in the elderly and the relation of serum ferritin levels with disease severity: hospital-based study from Istanbul, Turkey. Arch Gerontol Geriatr. 2012;55:73-76.

22. Sun ER, Chen CA, Ho G, Earley CJ, Allen RP. Iron and the restless legs syndrome. Sleep. 1998;21(4):371-377.

23. O'Keeffe ST. Iron deficiency with normal ferritin levels in restless legs syndrome. Sleep Med. 2005;6(3):281-282

24. Berger K, Luedemann J, Trenkwalder C, John U, Kessler C. Sex and the risk of restless legs syndrome in the general population. Arch Intern Med. 2004;164:196-202.

25. Oksenberg A. Alleviation of severe restless legs syndrome (RLS) symptoms by cigarette smoking. J Clin Sleep Med. 2010;6(5):489-490.

26. Sabic A, Sinanovic O, Sabic D, Galic G. Restless legs syndrome in patients with hypertension and diabetes mellitus. Med Arch. 2016;70(2):116.

27. Batool-Anwar S, Malhotra A, Forman J, Winkelman J, Li Y, Gao X. Restless legs syndrome and hypertension in middle-aged women. Hypertension. 2011;58(5):791-796.

28. Zobeiri M, Shokoohi A. Restless legs syndrome in diabetics compared with normal controls. Sleep Disord. 2014;2014:871751.

29. Merlino G, Fratticci L, Valente M, et al. Association of Restless Legs Syndrome in Type 2 Diabetes: A Case-Control Study. Sleep. 2007;30(7):866-871.

30. Lopes LA, Lins CdMM, Adeodato VG, et al. Restless legs syndrome and quality of sleep in type 2 diabetes. Diabetes Care. 2005; 28(11): 2633-2636.

31. Bener A, Al-Hamaq AOAA, Aǧan AF, Öztürk M, Ömer A. The prevalence of restless legs syndrome and comorbid condition among patients with type 2 diabetes mellitus visiting primary healthcare. J Fam Med Prim Care. 2019;8(12):3814-3820.