Restless Legs Syndrome in Aircrew

Ozge Arici Düz; Nesrin Helvaci Yilmaz; Oktay Olmuscelik

INTRODUCTION: Restless legs syndrome (RLS) is characterized by an uncomfortable sensation on the legs, which causes the urge to move the legs. The main cause is unknown but there are many risk factors, including geographical properties and high altitude. Our objective was to explore the frequency of RLS in aircrew.

METHODS: There were 301 Turkish aircrew who were admitted to Istanbul Medipol University Hospital Neurology Department for periodic examinations and 272 healthy (non-aircrew) subjects included in the study. The International RLS Study Group's Questionnaire and the International RLS Study Group Rating Scale (IRLSSGRS) were used to evaluate RLS. The participants filled the RLS questionnaire and then both groups were divided into two subgroups as having RLS or not. The subjects' years in the profession, average flight duration in a month, daily sleep duration, smoking, and coffee consumption were recorded. None of the subjects had previously been diagnosed with RLS.

RESULTS: The frequency of RLS was 6.7% in the aircrew group and 7.9% in the control group, and there was no significant difference between the two groups. Age, gender, daily duration of sleep, smoking, coffee consumption, family history of RLS, being a pilot or a flight attendant, years in profession, and monthly flight hours were similar in aircrew with and without RLS.

DISCUSSION: The RLS frequency in aircrew was similar to that of the control group. We can conclude flying at high altitude wasn't a risk factor for RLS.

KEYWORDS: RLS, aircrew, frequency, high altitude.

Düz OA, Yilmaz NH, Olmuscelik O. *Restless legs syndrome in aircrew.* Aerosp Med Hum Perform. 2019; 90(11):934–937.

Restless Legs Syndrome (RLS) is the name given to a disorder that causes uncomfortable sensations (paresthesia, prickling, burning, and pain) in the legs and the urge to move the legs, which occurs mainly in the evenings. These sensations emerge when the person is at rest, and the patient feels an urge to move their legs.[9]

The primary (idiopathic) RLS rate is 6%[10] for the general population in Turkey and between 40 and 65% of these patients have a family history.[23] Iron-deficiency anemia, kidney failure, diabetes mellitus, rheumatologic diseases, hypo/hyperthyroidism, chronic obstructive pulmonary disease, thrombophlebitis, neurological diseases such as Parkinson's disease, multiple sclerosis, polyneuropathies, drugs (tricyclic antidepressants, serotonin feedback inhibitors, dopamine antagonists), and pregnancy can be considered among the secondary causes of RLS.[5]

Geographical properties, high altitude, age, and gender were reported as factors that affect the frequency of RLS.[4] In studies performed in various regions around Turkey, it was found that RLS prevalence in the general population was between 3 and 9%.[8,24] This rate varies between 1 and 15% around the world.[15,19] Prevalence increases with age[28] and in women is twice that of men.[3] Prevalence of RLS in North America and Europe is higher than in Asian countries[19] and is higher at high altitudes.[4] In a study performed on those with chronic mountain sickness, it was found that presence of RLS can be an early symptom of hypoxia and can be correlated with maladaptation to high altitude.[27]

We were unable to locate any prior work that investigates the frequency of RLS among aircrew who travel at high altitudes.

METHODS

Subjects

A total of 301 actively flying Turkish aircrew (192 pilots, 109 cabin crew) and 272 age- and sex-matched healthy subjects

From the Istanbul Medipol University Faculty of Medicine, Istanbul, Turkey.

This manuscript was received in January 2019. It was accepted for publication in August 2019.

Address correspondence to: Özge Arıcı Düz, M.D., Istanbul Medipol University Faculty of Medicine, Neurology Department, TEM Göztepe çıkışı no:1 Bağcılar, Istanbul, Turkey; drozge2004@hotmail.com.

DOI: https://doi.org/10.3357/AMHP.5321.2019

were included in the study. Exclusion criteria were defined as follows: having any previous history of chronic illnesses like diabetes, hypo/hyperthyroidism, rheumatologic disease, chronic pulmonary disease, kidney and liver failure, iron deficiency anemia or any iron deficient state, using any drugs within the last month prior to enrollment, or being pregnant. The subjects' complete blood count test, urea, creatinine and ferritin levels and sedimentation rates were all within the normal range and were taken at the same time during the date of examination. All procedures performed in studies involving human subjects were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The ethical approval was taken from İstanbul Medipol University Ethics Committee.

Methods

The subjects' years in the profession, average flight duration in a month, daily sleep duration, smoking and coffee consumption were recorded. The daily sleep duration was recorded according to their statement. For the diagnosis of RLS, the International RLS Study Group's Questionnaire was used.[1] None of the subjects had previously been diagnosed with RLS. 'Patients who were diagnosed with RLS, who were admitted to Istanbul Medipol University Hospital Neurology Department for periodic examination, were assigned an International RLS Study Group Rating Scale (IRLSSGRS).[29] In this scale, which comprises a total of 10 questions, the answers were between 0–4 (0: none, 1: mild, 2: moderate, 3: severe, 4: very severe) and the total score was calculated based on the answers. Accordingly, 1–10 out of 40 (the maximum score) was classified as "mild", 11–20 was classified as "moderate", 21–30 was classified as "severe", and 31–40 was classified as "very severe". The family history of RLS was also recorded. Ethics committee approval was obtained from the local ethics committee of Istanbul Medipol University. This study was performed in accordance with the ethical standards detailed in the Helsinki Declaration. Written informed consent was taken from all subjects prior to the study.

Statistical Analysis

Data were analyzed using SPSS 11.0 for Windows (SPSS, Inc., Chicago, IL). Variable distributions were assessed by the Shapiro-Wilk normality test. As all the continuous variables were distributed nonnormally, they were expressed as median (range). The Mann-Whitney *U*-test was used to compare medians between two independent groups and the Kruskal-Wallis test was used to compare medians between more than two independent groups when needed. Correlation analyses were performed by using Spearman's coefficients. A *P*-value less than 0.05 was accepted as statistically significant.

RESULTS

Demographic parameters and clinical features of the aircrew and the control group are given in **Table I**. Monthly median flight duration of the aircrew was 80.0 h (20–139) per month and their median years in the profession were 8.0 yr (1–43). The frequency of RLS among the aircrew was 6.7% ($N = 19$) while it was 7.9% ($N = 20$) among the control group and there was no statistically significant difference between the two groups.

Table I. A Comparison of Demographic Details and Clinical Attributes of the Aircrew and the Control Group.

	AIRCREW ($N = 301$)	CONTROL GROUP ($N = 272$)	*P*-VALUE
Age (yr)	37.4 (24–63)	39.0 (23–63)	0.243
Female Gender (%)	22.6	26.1	0.339
Daily Duration of Sleep (hours)	8 (4–11)	7 (4–10)	<0.001
Smoking (%)	37.87	24.26	<0.001
Coffee Consumption (%)	60.4	56.2	0.307
Frequency of RLS	6.7	7.9	0.621
IRLSSGRS (%)	12 (6–21)	9 (6–18)	0.067

There was no statistically significant difference between the control group and the aircrew regarding age, gender, coffee consumption, or frequency of RLS and IRLSSGRS ($P > 0.05$). Although there was no statistically significant difference between the frequency of RLS in the two groups, smoking was more common and daily duration of sleep was also longer for the aircrew ($P < 0.05$) (Table I).

When assessing only the subjects with RLS in both groups, there was no significant difference in age, gender, daily duration of sleep, smoking, coffee consumption, family history of RLS and RLS severity between the aircrew with RLS and the control group with RLS ($P < 0.05$) (**Table II**). Although there was no statistical significance, RLS severity and frequency of smoking was higher in the aircrew with RLS when compared with the control group with RLS ($P < 0.05$).

The comparison between the aircrew with and without RLS showed that there was no significant difference in age, gender, daily duration of sleep, smoking, coffee consumption, being a pilot, years in the profession and monthly flight hours ($P < 0.05$) between groups (**Table III**). But having family history of RLS was statistically significant in aircrew who were diagnosed with RLS ($P < 0.05$).

DISCUSSION

The impact of being at a high altitude on RLS is controversial. Studies worldwide report that RLS prevalence is higher among people living at high altitudes in Africa than those living at sea level,[4] and the prevalence is approximately five times more in the Himalayas.[10] Nevertheless, a study was conducted on the correlation between RLS and chronic mountain disease but could not conclude a significant correlation, although RLS was associated with decreased oxygen saturation.[27] In RLS prevalence studies in Turkey, it was found that while the prevalence is lower at sea level (3%),[24,26] it can be as high as 6–7% in the rural areas and high altitudes.[11,31] In our study, the frequency of RLS was 6.7% among the members of the aircrew and was not different from the control group ($P < 0.05$). It is known that aircrew are

Table II. A Comparative Analysis of the Aircrew and Control Group with RLS.

	AIRCREW WITH RLS ($N = 19$)	CONTROL GROUP WITH RLS ($N = 20$)	*P*-VALUE
Age (yr)	34.0 (25–60)	37.5 (24–56)	0.667
Female Gender (%)	63.15	45.5	0.256
Daily Duration of Sleep (hours)	8 (4–11)	7.5 (5–10)	0.967
Smoking (%)	47.36	20	0.070
Coffee Consumption (%)	57.89	55	0.855
Family History of RLS (%)	21.05	45	0.113
RLS Severity	12 (6–21)	9 (6–18)	0.067

exposed to high altitudes for long time periods but the cabin pressure is not as high as geographically equivalent high altitudes.

In recent years, the role of peripheral hypoxia in RLS pathogenesis has been discussed.[22] Hypoxia induced pathways affect many cells in patients with RLS.[21] RLS is frequently observed in those with chronic obstructive pulmonary disease[13] and the RLS observed in those with chronic mountain sickness is shown to be correlated with decreased oxygen levels.[27] In oximetry studies performed in planes, it was found that oxygen saturation significantly decreases in passengers[14] and this decrease was 4%.[18] Thus, both the effect of hypoxia inside the cabin and long-term immobility at high altitudes may affect the RLS frequency among the aircrew members. However, it is known that air pressure and oxygen saturation inside the aircraft is kept close to nearly normal throughout the flight by means of mechanical equipment. Thus, both the effect of hypoxia inside the cabin and long-term immobility at high altitudes may affect the RLS because they maintain normal oxygen saturation throughout the flight. Therefore, they are affected by the oxygen alteration minimally and they do not have an RLS frequency which is different from the normal population.

Genetic factors, dysregulation of brain iron, and dopaminergic dysfunction play important roles in the pathogenesis of RLS.[7] Melatonin secretion is considered to be another factor. Melatonin is the hormone that is responsible for physiological sleep and is secreted from the epiphysis. Its secretion increases when it is dark and declines when there is light. Although it has been shown that there is no difference between those working at night and those working during daytime in terms of melatonin levels,[25] exposure to bright light at the wrong time of day causes internal desynchronization of the circadian rhythm.[6] Changes in melatonin secretion are known to cause increased sensory and motor symptoms in RLS patients. Melatonin also inhibits the central release of dopamine, thus aggravating the symptoms of RLS at night.[16] In our study, the aircrew had sufficient daily sleep duration with higher sleep duration compared to the control group, though they may have had impaired circadian rhythm functioning because of shiftwork-like schedules. Moreover, the comparison between aircrew and control with RLS, and aircrew with and without RLS displayed no significant differences in terms of daily duration of sleep. Thus, it is considered that the duration of sleep does not have any impact on the presence of RLS for aircrew. One limitation of this study is daily sleep duration was measured subjectively by self-reporting of the participants; objectively measured sleep gives more information about the relationship between RLS and being an aircrew member.

Table III. A Comparative Analysis of Parameters of the Aircrew for Presence of RLS.

	AIRCREW WITH RLS ($N = 19$)	AIRCREW WITHOUT RLS ($N = 282$)	*P*-VALUE
Age (yr)	34 (25–60)	36 (24–63)	0.251
Female Gender (%)	63.15	78.01	0.155
Daily Duration of Sleep (hours)	8 (4–11)	8 (4–10)	0.360
Smoking (%)	47.36	37.23	0.378
Coffee Consumption (%)	57.89	60.63	0.813
Family History of RLS (%)	21.05	4.96	0.020
Pilot (%)	47.36	64.53	0.132
Years in Profession	6 (1–35)	8 (1–43)	0.512
Monthly Flight Duration (hours)	80 (40–130)	80 (20–110)	0.531

RLS can be divided into two groups according to its etiology: primary (idiopathic) and secondary (symptomatic). Genetic factors are more influential in primary RLS while metabolic changes play a more important role in secondary RLS.[12] Genetic factors are important in the pathogenesis of RLS. While its inheritance is frequently reported as autosomal dominant, its inheritance pattern can also be autosomal recessive or non-Mendelian.[12,30] Young et al. reported that 40% of those who had RLS onset before the age of 35 have a family history, whereas 25% of those who had onset after the age of 35 have a family history.[32] In a study performed in Turkey, it was shown that first degree relatives of 15.3% of the patients diagnosed with RLS also have RLS symptoms.[26] In our study, the family history of RLS was 21.05% for the aircrew with RLS whereas it was 4.96% for the aircrew without RLS, which was statistically significant ($P < 0.05$).

In some studies, smoking and coffee consumption increased the severity of RLS.[2,20] However, other studies suggested that smoking wass not a risk factor for development of RLS.[17] In our study, frequency of smoking was higher in the aircrew compared to the control group; however, smoking did not differ between the groups with and without RLS ($P < 0.05$). Similarly, coffee consumption was not different between the control group and the aircrew and did not have any impact on RLS ($p > 0.05$).

To conclude, the RLS frequency in aircrew was 6.7%, which is similar to that of the normal population. It is considered that this similarity is due to modern technology which regulates and adjusts oxygen saturation and air pressure inside the aircraft throughout the flight.

ACKNOWLEDGMENTS

This study was not funded by any company. All authors declare that they have no conflict of interest.

Authors and affiliations: Ozge Arici Düz, M.D., and Nesrin Helvaci Yilmaz, M.D., Neurology Department, and Oktay Olmuscelik, M.D., Internal Medicine Department, Istanbul Medipol University Faculty of Medicine, Istanbul, Turkey.

REFERENCES

1. Allen RP, Picchietti DL, Garcia-Borreguero D, Ondo WG, Walters AS,. et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria–history, rationale, description, and significance. Sleep Med. 2014; 15(8):860–873.
2. Bayard M, Avonda T, Wadzinski J. Restless legs syndrome. Am Fam Physician. 2008; 78(2):235–240.
3. Berger K, Kurth T. RLS epidemiology - frequencies, risk factors and methods in population studies. Mov Disord Suppl. 2007; 22(Suppl. 18):S420–S423.
4. Castillo PR, Kaplan J, Lin SC, Fredrickson PA, Mahowald MW. Prevalence of restless legs syndrome among native South Americans residing in coastal and mountainous areas. Mayo Clin Proc. 2006; 81(10):1345–1347.
5. Chokroverty S. Differential diagnoses of restless legs syndrome/Willis-Ekbom disease: mimics and comorbidities. Sleep Med Clin. 2015; 10(3): 249–262.
6. Dumont M, Lanctôt V, Cadieux-Viau R, Paquet J. Melatonin production and light exposure of rotating night workers. Chronobiol Int. 2012; 29(2):203–210.
7. Earley CJ, Connor J, Garcia-Borreguero D, Jenner P, Winkelman J, et al. Altered brain iron homeostasis and dopaminergic function in restless legs syndrome (Willis–Ekbom Disease). Sleep Med. 2014; 15(11):1288–1301.
8. Erer S, Karli N, Zarifoglu M, Ozcakir A, Yildiz D. The prevalence and clinical features of restless legs syndrome: a door to door population study in Orhangazi, Bursa in Turkey. Neurol India. 2009; 57(6):729–733.
9. Garcia-Borreguero D, Williams AM. An update on restless legs (Willis-Ekbom disease): clinical features, pathogenesis and treatment. Curr Opin Neurol. 2014; 27(4):493–501.
10. Gupta R, Ulfberg J, Allen RP, Goel D. High prevalence of restless legs syndrome/Willis Ekbom Disease (RLS/WED) among people living at high altitude in the Indian Himalaya. Sleep Med. 2017; 35:7–11.
11. Güler S, Caylan A, Nesrin Turan F, Dağdeviren N, Çelik Y. The prevalence of restless legs syndrome in Edirne and its districts concomitant comorbid conditions and secondary complications. Neurol Sci. 2015; 36(10):1805–1812.
12. Jiménez-Jiménez FJ, Alonso-Navarro H, García-Martín E, Agúndez JAG. Genetics of restless legs syndrome: An update. Sleep Med Rev. 2018; 39:108–121.
13. Kaplan Y, Inonu H, Yilmaz A, Ocal S. Restless legs syndrome in patients with chronic obstructive pulmonary disease. Can J Neurol Sci. 2008; 35(3):352–357.
14. Kelly PT, Swanney MP, Frampton C, Seccombe LM, Peters MJ, Beckert LE. Normobaric hypoxia inhalation test vs. response to airline flight in healthy passengers. Aviat Space Environ Med. 2006; 77(11):1143–1147.
15. Merlino G, Valente M, Serafini A, Gigli GL. Restless legs syndrome: diagnosis, epidemiology, classification and consequences. Neurol Sci. 2007; 28(Suppl. 1):S37–S46.
16. Michaud M, Dumont M, Selmaoui B, Paquet J, Fantinni ML, et al. Circadian rhythm of restless legs syndrome: relationship with biological markers. Ann Neurol. 2004; 55(3):372–380.
17. Miri S, Rohani M, Sahraian MA, Zamani B, Shahidi GA, et al. Restless legs syndrome in Iranian patients with multiple sclerosis. Neurol Sci. 2013; 34(7):1105–1108.
18. Muhm JM, Rock PB, McMullin DL, Jones SP, Lu IL, et al. Effect of aircraft-cabin altitude on passenger discomfort. N Engl J Med. 2007; 357(1):18–27.
19. Ohayon MM, O'Hara R, Vitiello MV. Epidemiology of restless legs syndrome: a synthesis of the literature. Sleep Med Rev. 2012; 16(4): 283–295.
20. Oksenberg A. Alleviation of severe restless legs syndrome (RLS) symptoms by cigarette smoking. J Clin Sleep Med. 2010; 6(5):489–490.
21. Patton SM, Ponnuru P, Snyder AM, Podskalny GD, Connor JR. Hypoxia-inducible factor pathway activation in restless legs syndrome patients. Eur J Neurol. 2011; 18(11):1329–1335.
22. Salminen AV, Rimpilä V, Polo O. Peripheral hypoxia in restless legs syndrome (Willis-Ekbom disease). Neurology. 2014; 82(21):1856–18561.
23. Schormair B, Winkelmann J. Genetics of restless legs syndrome: mendelian, complex, and everything in between. Sleep Med Clin. 2011; 6(2):203–215.
24. Sevim S, Dogu O, Camdeviren H, Bugdayci R, Sasmaz T, et al. Unexpectedly low prevalence and unusual characteristics of RLS in Mersin, Turkey. Neurology. 2003; 61(11):1562–1569.
25. Sharifian A, Firoozeh M, Pouryaghoub G, Shahryari M, Rahimi M, et al. Restless Legs Syndrome in shift workers: A cross sectional study on male assembly workers. J Circadian Rhythms. 2009; 7:12.
26. Taşdemir M, Erdoğan H, Börü UT, Dilaver E, Kumaş A. Epidemiology of restless legs syndrome in Turkish adults on the western Black Sea coast of Turkey: A door-to-door study in a rural area. Sleep Med. 2010; 11(1):82–86.
27. Vizcarra-Escobar D, Mendiola-Yamasato A, Risco-Rocca J, Mariños-Velarde A, Juárez-Belaunde A, et al. Is restless legs syndrome associated with chronic mountain sickness? Sleep Med. 2015; 16(8):976–980.
28. Walters AS, Hickey K, Maltzman J. A questionnaire study of 138 patients with restless legs syndrome: the Night-Walker's Survey. Neurology. 1996; 46(1):92–95.
29. Walters AS, LeBrocq C, Dhar A, Henning W, Rosen R, et al. Validation of the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome. Sleep Med. 2003; 4(2):121–132.
30. Winkelmann J, Polo O, Provini F, Nevsimalova S, Kemlink D, et al. Genetics of restless legs syndrome (RLS): State-of-the-art and future directions. Mov Disord. 2007; 22(S18, Suppl. 18)S449–S458.
31. Yilmaz NH, Akbostanci MC, Oto A, Aykac O. Prevalence of restless legs syndrome in Ankara, Turkey: an analysis of diagnostic criteria and awareness. Acta Neurol Belg. 2013; 113(3):247–251.
32. Young JE, Vilariño-Güell C, Lin SC, Wszolek ZK, Farrer MJ. Clinical and genetic description of a family with a high prevalence of autosomal dominant restless legs syndrome. Mayo Clin Proc. 2009; 84(2):134–138.