

Restless legs syndrome in adolescents: relationship with sleep quality, cardiorespiratory fitness and body fat

Christoforos D. Giannaki^{1,2*}
Georgios M. Hadjigeorgiou³
George Aphas¹
Marios Pantzaris²
Giorgos K. Sakkas⁴

¹ Department of Life and Health Sciences, University of Nicosia, Nicosia, Cyprus.

² The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus.

³ Department of Medicine, University of Thessaly, Greece

⁴ Faculty of Sport and Health Sciences, University of St Mark & St John, Plymouth, UK.

ABSTRACT

Objective: The aim of the current study was to investigate the relationship between restless legs syndrome (RLS) and cardiorespiratory fitness, body composition and sleep quality in a sample of adolescents. **Methods:** One hundred fifty seven volunteer adolescents (16.6 ± 0.7 yrs) participated in the study. Sleep quality was assessed by the Pittsburg sleep quality index. Cardiorespiratory fitness was assessed by the 20 m shuttle run test and body composition by bioelectrical impedance analysis. **Results:** The prevalence of RLS was 5.1%. The adolescents with RLS were found to exhibit significantly higher body fat levels ($p=0.019$) and poorer sleep quality score ($p=0.000$) compared with their free-RLS counterparts. **Conclusions:** Adolescents with RLS are subjects of higher body fat and impaired sleep quality compared with adolescents without RLS. Early diagnosis and appropriate management of RLS is essential in the adolescents.

Keywords: Sleep disorders; Body composition; Restless legs syndrome; Adolescent; Cyprus.

Corresponding author: Christoforos D. Giannaki. Department of Life and Health Sciences. University of Nicosia, Nicosia, Cyprus. 46 Makedonitiss Avenue, CY 1700. E-mail: giannaki.c@unic.ac.cy

Received: November 13, 2016;

Accepted: January 01, 2017.

INTRODUCTION

Restless legs syndrome (RLS) is a common sensory-motor neurological disorder affecting both the general adult population¹ and patients with chronic diseases².

In the last decade, several epidemiological and cross-sectional studies on adults' patients with RLS reveal a possible association between RLS and chronic diseases including cardiovascular and cerebrovascular diseases, chronic kidney disease, hypertension and diabetes³.

In brief, RLS induces a strong urge to move the lower extremities and usually accompanied by unpleasant sensations, the symptoms appear or become worsen during inactivity and rest periods and especially in the night, whilst the patients could relief by movement⁴. Interestingly, RLS symptoms could appear also from early age whilst it is considered to be a highly familial disorder⁵. Therefore, it is not surprising that published data document the occurrence of RLS symptoms in pediatric populations⁶. The prevalence of pediatric RLS has been reported to be between 2 and 4%⁶, however, higher prevalence such as 6-8% has been reported in recent studies as well⁷. Pediatric RLS is associated with low sleep quality and psychological distress, factors that may lead to significant impairments on overall health and quality of life⁷.

A number of published studies on adolescents show an association between poor sleep quality and quantity and increased risk for obesity⁸. As mentioned above, RLS could induce significant impairments on sleep and thus, could contribute to increased risk for obesity and weight gain. Interestingly, evidence derived from studies on adults, revealed an association between RLS and obesity indices such as the body mass index (BMI) and the waist to hip ratio (WHR- an index of abdominal obesity)⁹, suggesting that RLS could be considered as a risk factor for obesity. Similarly, the relationship between low physical fitness levels and RLS has been reported in large epidemiological studies in adults¹⁰. Still, there is a scarcity of published data regarding potential associations of those factors and RLS in adolescents.

The aim of the current cross-sectional study was to examine potential associations between RLS and cardiorespiratory fitness, BMI and body fat and sleep quality among a sample of adolescents.

MATERIALS AND METHODS

Participants

One hundred fifty-seven volunteer adolescents (16.6 ± 0.7 yrs) participated in this cross-sectional study. The adolescents derived by a single high-school located in the city of Limassol, Cyprus. RLS was diagnosed using the four basic essential criteria developed by the International RLS study group⁴. In addition, information regarding lifestyle habits was obtained such as amount of television viewing each day and studying time each day. Informed consent and parental permission was obtained by all the participants. The study was approved by both the

University of Nicosia Research Ethics Committee and the Ministry of Education of Cyprus educational authorities.

Sleep quality assessment

The students' subjective sleep quality was assessed by the Pittsburgh sleep quality index (PSQI)¹¹. A PSQI global score greater than 5 was classified as poor sleep quality.

Anthropometric examination

Height was measured using a standing stadiometer (Seca model 720, Germany). Body mass was recorded to the nearest 0.05 kg using a portable analogue scale (Seca model 755, Germany). BMI was calculated as body weight divided by height squared. Body fat levels were calculated using bioelectrical impedance analysis (BIA) method with a portable body composition system (Bodystat, Quadscan 4000).

Cardiorespiratory fitness assessment

Cardiorespiratory fitness levels were evaluated using the 20-meter shuttle run test¹². The students performed the test in groups and were instructed to run back and forth between two fixed lines 20 meters apart, according to audio signals dictating running speed. Initial running speed was $8.5 \text{ km} \cdot \text{h}^{-1}$, and then it increased by $0.5 \text{ km} \cdot \text{h}^{-1}$ every minute. The number of completed shuttles was recorded for each student.

Statistical Analysis

Unpaired t-tests were performed to compare differences between the students with RLS and students without RLS for continuous normally distributed variables. Chi squared was used in order to examine differences between the two groups for categorical variables. All the statistical analyses were performed by using the statistical package for social sciences (SPSS for windows version 19). All data are reported as mean \pm standard deviation and the level for statistical significance was set at $p < 0.05$.

Post hoc sample size calculations were conducted based in % body fat and BMI score values in our study. The current study had 94% power to detect differences in % body fat between the two groups at a $t=1.97$ and effect size $d=1.296$. The minimum required sample size to detect differences in BMI between the two groups was an average of 72 in RLS group and 1344 in Control group for the same power level (94%) for 2-sided type 1 and type 2 errors of 5%.

RESULTS

Eight out of the 157 students were found positive to all the four essential diagnostic criteria of RLS. The data regarding the students' anthropometric, cardiorespiratory fitness, sleep quality and lifestyle data are presented in Table 1. The students with RLS were found to experience higher body fat levels ($p=0.019$) and a poorer sleep quality score ($p=0.000$) compared with the students without RLS.

Table 1. Basic characteristics, anthropometry, cardiorespiratory fitness, sleep quality and lifestyle parameters data derived into the RLS and non-RLS groups.

Variable	RLS group (n= 8)	Non-RLS group (n=149)	p-value
Male/Female	2/6	73/76	0.280 ^a
Age	16.3±1.0	16.6±0.7	0.319
Body Weight (kg)	62.5±9.4	61.9±13.2	0.920
Height (cm)	161.8±5.0	166.6±8.0	0.154
Body mass index	23.9±3.7	22.2±4.2	0.363
Body fat (%)	33.1±2.9	25.9±7.3	0.019
Completed shuttles in the 20m shuttle run test	23.0±8.5	32.7±22.1	0.292
PSQI	12.2±2.8	3.9±3.4	0.000
Studying time per day (min)	55.5±53.6	64.0±59.2	0.658
Amount of television viewing per day (min)	124.2±74.3	79.2±75.3	0.113

RLS=restless legs syndrome; PSQI=Pittsburgh sleep quality index; ^a For categorical data a chi-square test performed.

DISCUSSION

The prevalence of RLS in this cohort of participants is 5.1%. The adolescents with positive RLS diagnosis were found to exhibit significantly higher body fat levels and poorer sleep quality score compared with their free-RLS counterparts. The current study examined the relationship between RLS, fitness and obesity indices as well as sleep quality and lifestyle habits among a sample of adolescents, however due to the nature of the studied population, the sample size of the current study is considered small and therefore the outcomes should be interpreted with caution.

The knowledge accumulated over the past few years reveal the great importance of good sleep on health, daytime function and quality of life of children and adolescents¹³. On the other hand, there is evidence to support the negative impact of sleep loss and sleep disorders on those parameters¹³. In agreement to our study, RLS is affecting approximately 2-4% of children and adolescents⁶ however, no association with cardiovascular risk factors have been made until now. Our study is the first to show some evidence of the association between the presence of RLS with future cardiovascular risk factors such as obesity and physical inactivity.

Impaired sleep quality and sleep loss induced by RLS in adolescents could contribute to the development, among others, of psychological distress and low quality of life levels⁷. Many studies have examined the relationship between sleep and obesity in children and adolescents, indicated that sleep loss and low sleep quality could be negatively associated with obesity and diabetes¹⁴. RLS on children and adolescents has been reported to be one of the main contributors for sleep loss⁷. However, there is a scarcity of published data regarding the relationship of sleep quality and body fat in adolescents.

In previous studies conducted in adults, obesity was shown to increase the risk for developing RLS. Obesity indices such as BMI and WHR were both found to be associated with the presence of RLS in two large studies conducted in adults⁹. Interestingly, the results revealed that greater BMI in the early adulthood (18-21 years) has been associated with even greater prevalence of RLS. Similarly, a more recent study from the same

group confirmed the association between RLS and obesity, indicated also an association between RLS and high cholesterol levels¹⁵.

However, we should note that obesity indices used in those studies did not evaluate body fat and body composition at all. The data of the current study reveal for first time in adolescents an association between RLS presence and high body fat. Interestingly, the mean value for body fat observed in the current study corresponds to high fat levels, significantly higher than the cut-off point value (>25% for male and >32% for female respectively)¹⁶.

The exact mechanism whereby obesity could lead to RLS or vice versa is still unknown. However, it is known that RLS has been associated with late sleep onset¹⁷ and nocturnal eating¹⁸, which both have been considered as a contributing factor for obesity¹⁹. RLS patients who exhibit also nocturnal eating are more likely to experience higher BMI compared to RLS patients who did not report episodes of nocturnal eating²⁰.

According to the literature, various biological and behavioral mechanisms may link obesity and sleep. Sleep loss has been linked to increased risk for obesity and diabetes with various hormonal abnormalities such as lower leptin levels²¹, increased ghrelin levels and increased evening cortisol levels²², and metabolic associated abnormalities such as impaired glucose tolerance¹⁹ and impaired insulin sensitivity²².

Moreover, sleep loss has been associated with habits that increase the risk for obesity such as an increase of time spend on sedentary activities such as watching television²³ and unhealthy eating behavior that favor obesity and weight gain⁸. In addition, number of studies indicates the negative effect of both sleep deprivation²⁴, RLS and an associated condition called periodic limb movements in sleep²⁵ on the development of hypertension, with the sympathetic nervous system over activity to be one of the major pathophysiological mechanisms responsible for the increase in nocturnal blood pressure levels observed in these conditions.

Finally, previous studies revealed an association between obesity and iron deficiency²⁶. It is known that iron deficiency is involved in the pathophysiology of RLS²⁷ and this may explain

in part the presence of RLS in the adolescents with high fat levels, found in the current study.

On the other hand, we should acknowledge the fact that other studies did not observe any associations between BMI or/and body fat with RLS in idiopathic²⁸ and uremic RLS patients²⁹. Therefore is clear that more research is needed in order to confirm potential associations between RLS and body fat in both pediatric and adult populations.

Similarly, the relationship between low physical fitness levels and RLS has been reported in large epidemiological studies in adults¹⁰, whilst, evidence exist regarding the beneficial effect of exercise training on RLS symptoms³⁰.

Habits such as watching TV (especially on bedtime) could have a negative impact on sleep in children and adolescents³¹. The data of the current study did not observe any associations between the hours spending every day on TV or reading respectively and RLS, confirming recent data in such populations⁷.

CONCLUSION

In conclusion, adolescents with RLS were found to experience higher body fat and impaired sleep quality compared with adolescents without RLS. Therefore, early diagnosis and appropriate management of RLS is essential in the adolescents. More research with larger sample is needed in order to support the hypothesis that RLS could be considered as a risk factor for the development of adolescent obesity and the physiological mechanisms which explain this association.

ACKNOWLEDGMENTS

We would like to thank all the students who volunteered for the purposes of the study as well as Mr. Yiannakis Ioannou and Mr. Aggelos Koumpounis for their help and support.

REFERENCES

- Allen RP, Picchietti DL, Garcia-Borreguero D, Ondo WG, Walters AS, Winkelman JW, et al.; International Restless Legs Syndrome Study Group. 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):860-73.
- Giannaki CD, Hadjigeorgiou GM, Karatzaferi C, Pantzaris MC, Stefanidis I, Sakkas GK. Epidemiology, impact, and treatment options of restless legs syndrome in end-stage renal disease patients: an evidence-based review. *Kidney Int.* 2014;85(6):1275-82.
- Trenkwalder C, Allen R, Hogl B, Paulus W, Winkelmann J. Restless legs syndrome associated with major diseases: A systematic review and new concept. *Neurology.* 2016;86(14):1336-43.
- Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J; Restless Legs Syndrome Diagnosis and Epidemiology workshop at the National Institutes of Health; International Restless Legs Syndrome Study Group. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med.* 2003;4(2):101-19.
- Picchietti MA, Picchietti DL. Advances in pediatric restless legs syndrome: Iron, genetics, diagnosis and treatment. *Sleep Med.* 2010;11(7):643-51.
- Picchietti DL, Bruni O, de Weerd A, Durmer JS, Kotagal S, Owens JA, et al.; International Restless Legs Syndrome Study Group (IRLSSG). Pediatric restless legs syndrome diagnostic criteria: an update by the International Restless Legs Syndrome Study Group. *Sleep Med.* 2013;14(12):1253-9.
- Silva GE, Goodwin JL, Vana KD, Vasquez MM, Wilcox PG, Quan SF. Restless legs syndrome, sleep, and quality of life among adolescents and young adults. *J Clin Sleep Med.* 2014;10(7):779-86.
- Miller AL, Lumeng JC, LeBourgeois MK. Sleep patterns and obesity in childhood. *Curr Opin Endocrinol Diabetes Obes.* 2015;22(1):41-7.
- Gao X, Schwarzschild MA, Wang H, Ascherio A. Obesity and restless legs syndrome in men and women. *Neurology.* 2009;72(14):1255-61.
- Phillips B, Young T, Finn L, Asher K, Hening WA, Purvis C. Epidemiology of restless legs symptoms in adults. *Arch Intern Med.* 2000;160(14):2137-41.
- Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 1989;28(2):193-213.
- Léger LA, Mercier D, Gadoury C, Lambert J. The multistage 20 metre shuttle run test for aerobic fitness. *J Sports Sci.* 1988;6(2):93-101.
- Gregory AM, Sadeh A. Sleep, emotional and behavioral difficulties in children and adolescents. *Sleep Med Rev.* 2012;16(2):129-36.
- Fatima Y, Doi SA, Mamun AA. Longitudinal impact of sleep on overweight and obesity in children and adolescents: a systematic review and bias-adjusted meta-analysis. *Obes Rev.* 2015;16(2):137-49.
- De Vito K, Li Y, Batoool-Anwar S, Ning Y, Han J, Gao X. Prospective study of obesity, hypertension, high cholesterol, and risk of restless legs syndrome. *Mov Disord.* 2014;29(8):1044-52.
- The Cooper Institute. *Fitnessgram & Activitygram test administration manual.* 3rd ed. Champaign: Human Kinetics; 2004.
- Phillips B, Hening W, Britz P, Mannino D. Prevalence and correlates of restless legs syndrome: results from the 2005 National Sleep Foundation Poll. *Chest.* 2006;129(1):76-80.
- Provini F, Antelmi E, Vignatelli L, Zaniboni A, Naldi G, Calandra-Buonaura G, et al. Association of restless legs syndrome with nocturnal eating: a case-control study. *Mov Disord.* 2009;24(6):871-7.
- Knutson KL, Spiegel K, Penev P, Van Cauter E. The metabolic consequences of sleep deprivation. *Sleep Med Rev.* 2007;11(3):163-78.
- Antelmi E, Vinai P, Pizza F, Marcatelli M, Speciale M, Provini F. Nocturnal eating is part of the clinical spectrum of restless legs syndrome and an underestimated risk factor for increased body mass index. *Sleep Med.* 2014;15(2):168-72.
- Boeke CE, Mantzoros CS, Hughes MD, L Rifas-Shiman S, Villamor E, Zera CA, et al. Differential associations of leptin with adiposity across early childhood. *Obesity (Silver Spring).* 2013;21(7):1430-7.
- Beccuti G, Pannain S. Sleep and obesity. *Curr Opin Clin Nutr Metab Care.* 2011;14(4):402-12.
- Patel SR, Blackwell T, Redline S, Ancoli-Israel S, Cauley JA, Hillier TA, et al.; Osteoporotic Fractures in Men Research Group; Study of Osteoporotic Fractures Research Group. The association between sleep duration and obesity in older adults. *Int J Obes (Lond).* 2008;32(12):1825-34.
- Guo X, Zheng L, Wang J, Zhang X, Zhang X, Li J, et al. Epidemiological evidence for the link between sleep duration and high blood pressure: a systematic review and meta-analysis. *Sleep Med.* 2013;14(4):324-32.
- Giannaki CD, Karatzaferi C, Hadjigeorgiou GM, George KP, Stefanidis I, Sakkas GK. Periodic limb movements in sleep and cardiovascular disease: time to act. *Front Neurol.* 2013;4:97.
- Aigner E, Feldman A, Datz C. Obesity as an emerging risk factor for iron deficiency. *Nutrients.* 2014;6(9):3587-600.
- Allen RP, Earley CJ. The role of iron in restless legs syndrome. *Mov Disord.* 2007;22 Supp 18:S440-8.
- Sarberg M, Josefsson A, Wiréhn AB, Svanborg E. Restless legs syndrome during and after pregnancy and its relation to snoring. *Acta Obstet Gynecol Scand.* 2012;91(7):850-5.
- Giannaki CD, Sakkas GK, Karatzaferi C, Hadjigeorgiou GM, Lavdas E, Liakopoulos V, et al. Evidence of increased muscle atrophy and impaired quality of life parameters in patients with uremic restless legs syndrome. *PLoS One.* 2011;6(10):e25180.
- Sakkas GK, Giannaki CD, Karatzaferi C, Maridaki M, Koutedakis Y, Hadjigeorgiou GM, et al. Current trends in the management of uremic restless legs syndrome: a systematic review on aspects related to quality of life, cardiovascular mortality and survival. *Sleep Med Rev.* 2015;21:39-49.
- Hale L, Guan S. Screen time and sleep among school-aged children and adolescents: a systematic literature review. *Sleep Med Rev.* 2015;21:50-8.