Original Article

Quality of sleep in patients with end-stage renal failure

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Key words:
- Restless Legs Syndrome,
- End-Stage Renal Disease,
- Sleep Quality

Abbreviations
RLS: Restless Legs Syndrome
PSQI: Pittsburgh Sleep Quality Index
CKD: Chronic Kidney Disease
IRLSSG: International Restless Legs Syndrome Study Group
PTH: Parathyroid Hormone
HTC: Hematocrit
B_2M: B_2 Microglobulin

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SUMMARY

INTRODUCTION: Restless syndrome (RLS) is a common disorder of the lower limbs, characterized by an intense need for continuous movement and accompanied usually by unpleasant sensations. In patients with End-Stage Renal Disease (ESRD) under hemodialysis and under peritoneal dialysis, the syndrome has not been thoroughly studied, particularly in the Greek population. The aim of the study was to assess the prevalence of RLS in ESRD. **MATERIALS AND METHODS:** ESRD patients underwent laboratory examinations and completed the Pittsburgh Sleep Quality Index (PSQI) questionnaire. It is a cross sectional study and the syndrome RLS was diagnosed according to the International Restless Legs criteria. **RESULTS:** RLS prevalence was 30% among ESRD patients with a higher prevalence among patients under peritoneal dialysis. The value of urea, β2-microglobulin and parathyroid hormone was related to the scores of the individual components of the PSQI questionnaire. Gender was not statistically associated with the presence of RLS. **CONCLUSIONS:** The current study demonstrated that 3 out of 10 patients with ESRD suffer from RLS, with the relative risk being increased in patients with high levels of parathyroid hormone. No association was found between hematocrit levels and hemodialysis characteristics. The value of urea, β2- microglobulin and parathyroid hormone was related with the scores of the individual components of the PSQI.
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INTRODUCTION

Restless Legs Syndrome (RLS) is a common neurological disorder characterized by lower limb paresthesia[1]. Predominant theories on the pathophysiology of the syndrome include dysfunction of the dopaminergic system and iron deficiency. It occurs mainly in the evening hours, causing arousals and disrupting the sleep architecture[2,3]. The diagnosis is based on the International Restless Leg Syndrome Study Group (IRLSSG) criteria and

its impact on the general population in Greece is 3.9%, similar to that of South Eastern Europe[4]. Chronic Kidney Disease (CKD) is a progressive, irreversible reduction of renal function, while End-Stage Renal Disease (ESRD) is defined by glomerular filtration rate (GFR) <15ml/min, or when mechanical support of renal function is required (kidney transplantation, dialysis)[6]. Recent studies, using the IRLSSG criteria, reveal a close relationship between ESRD and RLS, probably due to iron deficiency anemia, inadequate rehabilitation treatment and secondary hyperparathyroidism frequently present in patients with severe nephropathy. The development of micro-inflammation favors the onset of the syndrome and results in insomnia, decreased sleep quality, poor quality of life, and increased use of sleeping medications. These conditions may ultimately lead to cardiovascular complications and reduced survival[7]. The purpose of the present study was to record and describe the epidemiological characteristics of RLS in patients with ESRD undergoing hemodialysis and peritoneal dialysis. Secondary objectives of the study were to establish possible predisposing factors of the syndrome in the various subgroups of patients.

MATERIAL AND METHODS

The study included a total of 100 patients with ESRD (65 men and 35 women), 74 under artificial kidney (hemodialysis) and 26 under peritoneal dialysis. Included patients were on rehabilitation therapy at the Nephrology Clinic of General Hospital "PAPAGEORGIOU" Thessaloniki. Patients were divided into four groups according to the form of renal recovery and whether diabetic nephropathy was present. Analytically:

- Group 1 (DM): Artificial kidney patients without diabetic nephropathy (N = 59)
- Group 2 (PD): Patients under peritoneal dialysis without diabetic nephropathy (N = 19)
- Group 3 (DMDR): Artificial kidney patients with diabetic nephropathy (N = 15)
- Group 4 (PDDR): Peritoneal dialysis patients with diabetic nephropathy (N = 7)

All patients underwent laboratory blood testing for the hematocrit, urea, β2-microglobulin and parathyroid hormone (Immulite 2000 analyzer, SIEMENS®) and completed the Pittsburgh Sleep Quality Index (PSQI) questionnaire. The Diagnosis and Severity Scale that which was distributed and supplemented in one single visit to the Nephrology Clinic with a personal interview.

The PSQI measures the quality of sleep in adults over the last month evaluating components. It includes seven components: 1) Subjective sleep quality, 2) sleep latency, 3) sleeping period, 4) average sleep efficiency, 5) sleep disorders, 6) use of sleep medications, 7) daily dysfunction[8]. Each item is weighted on a 0–3 scale. The overall PSQI score is then calculated with the sum of the seven component scores, providing a total score ranging from 0 to 21 with lowest scores suggesting a better quality of sleep. The Diagnostic and Gravitational Restlessness Syndrome Scale was established in its final form in 2012 by the International RLS Study Group (IRLSSG). The basic criteria for diagnosis are four: 1) the need for legs movement due to an unpleasant sensation, 2) the onset or worsening of an uncomfortable sensation in the legs at rest, 3) the improvement or complete relief of symptoms after movement, 4) aggravation of symptoms and tendency to move in the afternoon or evening compared with the rest of the day. Diagnosis of RLS requires the presence of all criteria[9]. The severity of RLS is determined by ten questions with scores ranging 0 to 4 and is related to the subjective assessment of sleep quality due to the symptoms of restless legs as well as the incidence of symptoms in the daily activities and the patient's psycho-emotional state. Scores from 1 to 10 indicates mild syndrome, 11 to 20 moderate, 21 to 30 severe and 31 to 40 the most severe syndrome. A statistical analysis was done with the SPSS22.0 statistical software, and the MS Excel accounting software. A statistical significance level was set at 0.05. The statistical methods used were: binomial control, Pearson coefficient and Spearman coefficient. The linear regression model and control X were applied.

RESULTS

Results demonstrated a statistically significant increase in RLS prevalence in patients receiving peritoneal dialysis treatment (groups 2 and 4) ($p < 0.05$). RLS was not predominant in patients undergoing artificial kidney therapy (groups 1 and 3). A comparison was made between artificial kidney and peritoneal dialysis for the presence and severity of RLS. Results showed increased rates of RLS among patients receiving peritoneal dialysis compared with those of patients treated with artificial kidney (Figure 1).

There was a correlation of the renal recovery method with the RLS severity, which revealed significant statistical dependence and in particular patients on peritoneal

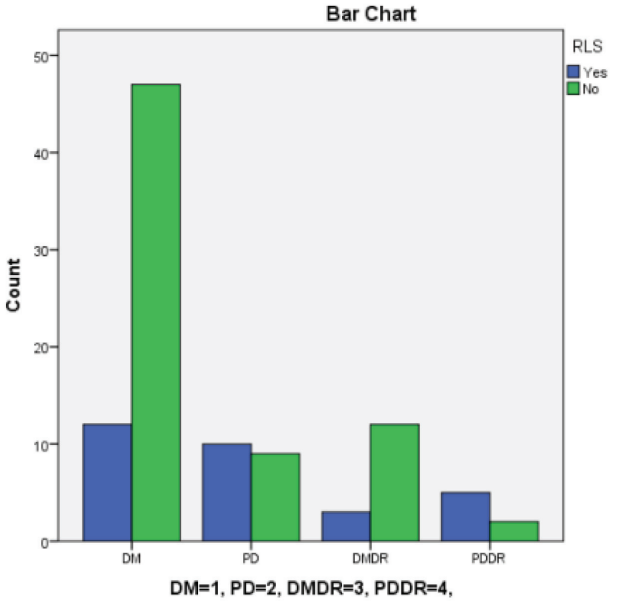

FIGURE 1. Prevalence of RLS depending of the type of renal recovery.

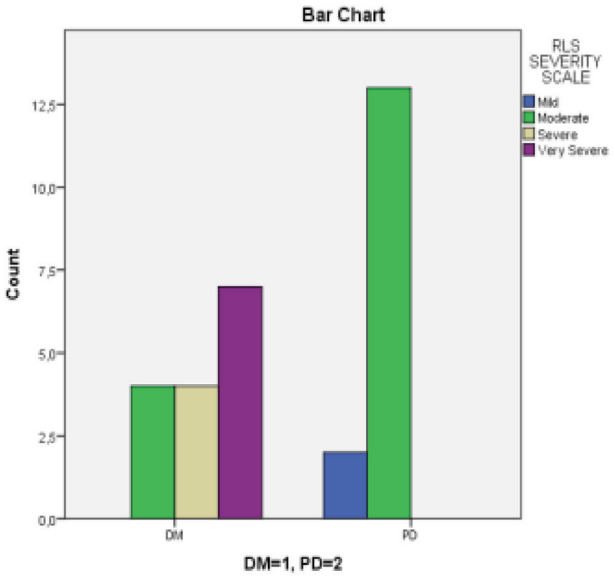

FIGURE 2. Correlation of renal recovery and RLS severity.

dialysis exhibit much higher rates of moderate degree of RLS severity compared with those of the artificial kidney patients (Table 1 and Figure 2).

A binomial control (NPar Test) was performed in order to estimate RLS in the study population divided into Group 1 (kidney patients with RLS) and Group 2 (kidney patients without RLS). It has been shown that the prevalence of RLS in end-stage renal disease was significantly higher compared with RLS prevalence in the general population ($p < 0.001$) (Table 2).

The quantitative variables studied are listed in Table 3, which includes mean values and standard deviations.

TABLE 1. RLS severity rates relative to the type of renal recovery.

	Mild RLS	Moderate RLS	Severe RLS	Very severe RLS	Total
DM	0	4	4	7	15
PD	2	13	0	0	15
TOTAL	2	17	4	7	30

TABLE 2. Results of NPar test.

Patient Groups	RLS Existence	N	RLS% in End Stage Renal Disease	RLS% in general population	p
1	YES	30	0.30	0.390	<0.001
2	NO	70	0.70		
TOTAL		100	1.00		

The investigated laboratory indicators were linearly related to the seven classes of PSQI. The correlation was plotted at the linearity level with the aid of the Pearson coefficient, but the Spearman coefficient was based on the order of the values. There was a statistically significant positive correlation between the increase in urea value and the second category of the PSQI questionnaire, or else the category referring to the difficulty of sleep initiating (Table 4 and Figure 3, 4). Additionally, a statistically significant positive correlation was found between the increase in the PTH value and the fifth category of the PSQI questionnaire, or else the category referring to the

TABLE 3. Mean values and standard deviations of quantitative variables.

	Age	Urea	PTH	HCT	B2M
N	100	100	100	100	100
Mean±SD	65,96 ± 12.70	135.91 ± 34.68	297.78 ± 169.57	32.77 ± 3.99	18.715 ± 3.15

presence of sleep disorders (Table 5 and Figure 5, 6). There was a statistically significant correlation between the increase in the β2 microglobulin value and the third category of the PSQI questionnaire referring to sleep duration (Table 6 and Figure 7, 8). Finally, no significant correlation emerged between the hematocrit and the individual classes of PSQI (Table 7 and Figure 9, 10).

DISCUSSION

The importance of sleep for the normal functioning of the body is fundamental. During this time, vital functions

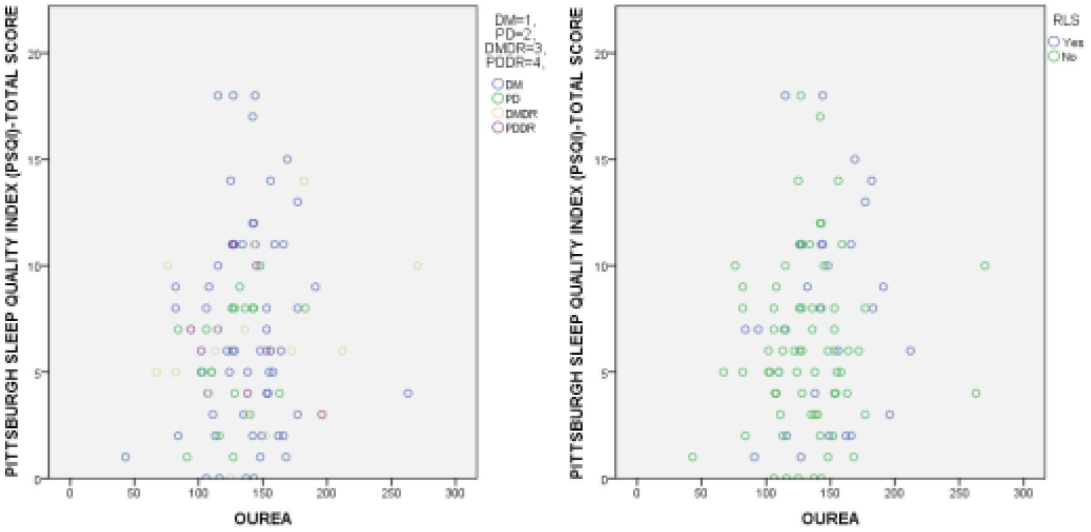

FIGURE 3 and 4. Correlation of urea values and PSQI.

TABLE 4. Correlation between Urea and PSQI questionnaires.

	PSQ1	PSQI2	PSQI3	PSQI4	PSQI5	PSQI6	PSQI7
r	0.137	0.196	0.157	-0.051	-0.055	0.071	0.062
p	0.175	**0.050**	0.119	0.612	0.586	0.484	0.542

TABLE 5. Correlation between PTH and PSQI questionnaires.

	PSQ1	PSQI2	PSQI3	PSQI4	PSQI5	PSQI6	PSQI7
r	0.090	0.109	-0.021	-0.090	0.299	0.148	0.150
p	0.375	0.279	0.837	0.373	**0.003**	0.142	0.135

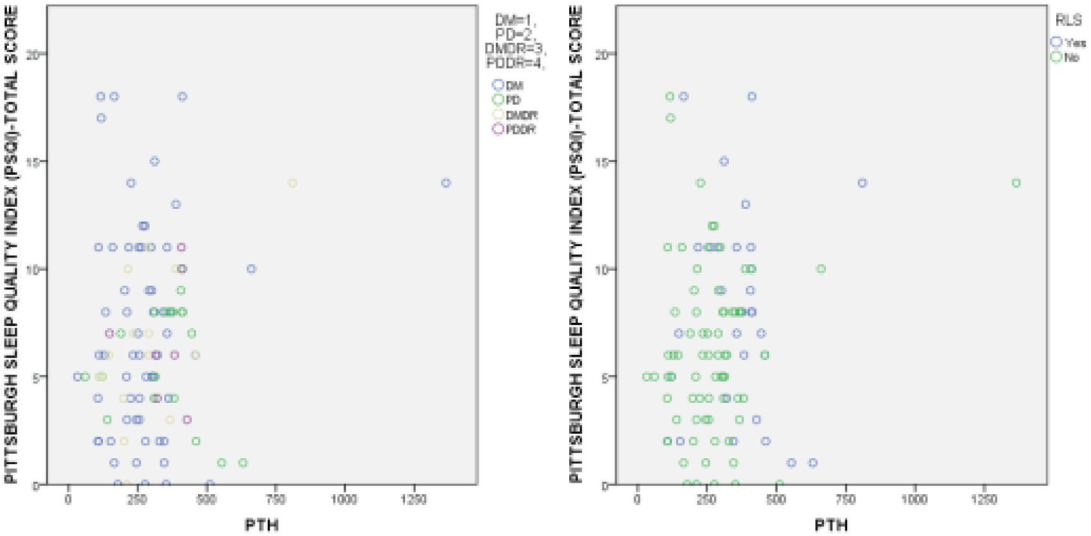

FIGURE 5 and 6. Correlation of PTH values and PSQI.

and consciousness are both reduced in order to enable reposal and the ability to cope with metabolic needs during vigilance. Sleep deprivation adversely affects quality of life, reduces performance in daily activities, causes sleepiness and malaise and leads to both physical and emotional disturbances. In recent years, interest has grown over the pathophysiology of sleep, because it has become common knowledge that its disorders lead with

TABLE 6. Correlation between β2 microglobulin serum levels and components of PSQI questionnaire.

	PSQ1	PSQI2	PSQI3	PSQI4	PSQI5	PSQI6	PSQI7
r	0.119	-0.039	0.201	0.157	-0.127	0.054	0.142
p	0.237	0.696	**0.045**	0.119	0.209	0.593	0.159

TABLE 7. Correlation between hematocrit levels and components of PSQI questionnaire.

	PSQ1	PSQI2	PSQI3	PSQI4	PSQI5	PSQI6	PSQI7
r	-0.068	-0.079	-0.040	0.034	0.014	-0.117	-0.139
p	0.504	0.435	0.691	0.737	0.891	0.248	0.166

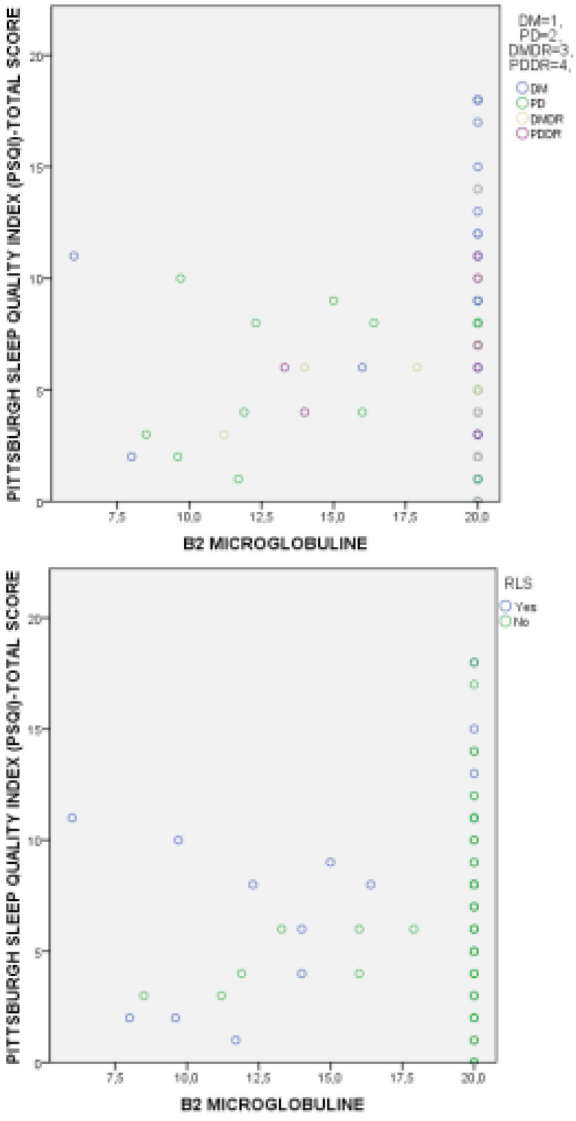

FIGURE 7 and 8. Correlation between β2 microglobulin serum levels and PSQI total score.

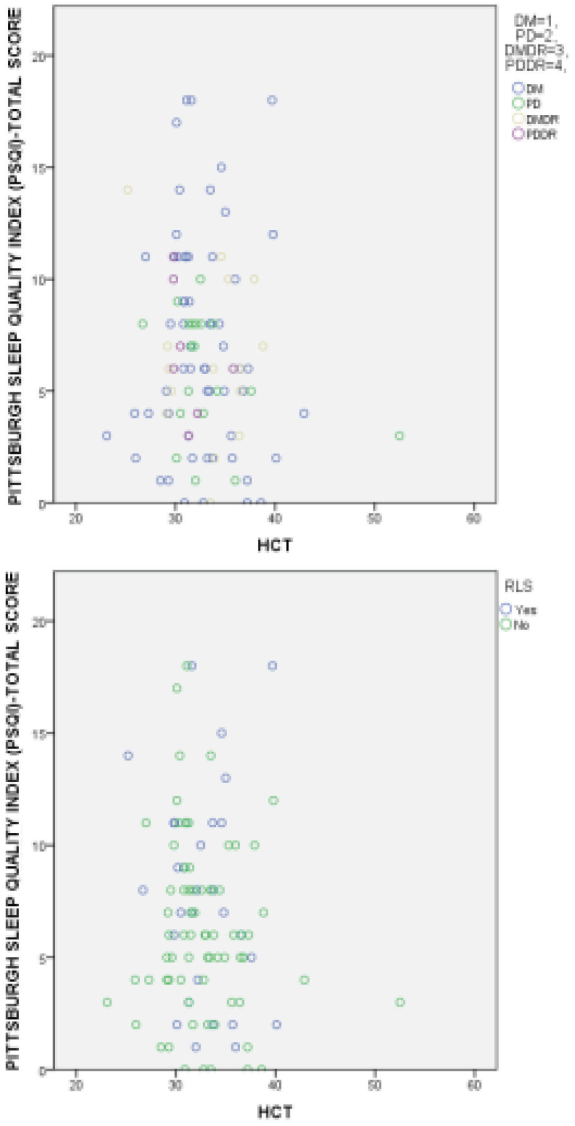

FIGURE 9 and 10. Correlation between hematocrit levels and PSQI total score.

mathematical precision to a variety of physical and mental disorders through complex neurophysiological changes[10].

This study was designed for patients with ESRD. These patients have special human body functioning due to renal insufficiency but also due to the consequences resulting from renal recovery, whether treated with artificial kidney, or undergoing peritoneal dialysis. Results from the current study suggest that RLS, which is a kinetic disorder of the lower limbs during sleep, is present in significantly higher percentage of 30% among patients with ESRD, compared to the proportion in the general population in Greece which is estimated at approximately 3.9%. This prevalence is similar to other studies, although a wide range of RLS prevalence has been acknowledged. It is worth mentioning that in a study conducted in Greece, the reported prevalence of RLS in patients on renal replacement therapy was 26.6% (154 out of 579 hemodialysis patients)[9]. Araujo et al[11], in a study of 400 hemodialysis patients from Brazil reported RLS prevalence of 21.5%. Al-Jahdali et al[16] in a study from Saudi Arabia reported a 50.2% prevalence of the syndrome. Gigli et al[17] from Italy evaluated the prevalence of RLS at 21.5% and La Manna et al[18] at 31.5%. Moreover, Cengic et al[20] in a study conducted in found that the prevalence of RLS in HD patients was 20.5%, while in a study from Japan that included 490 hemodialysis patients, the reported prevalence of RLS was 12.2%. Finally, in Glasgow, Siddiqui et al[19] in a study including 227 hemodialysis patients estimated the prevalence at 45.8%. Thus, one could argue that the prevalence of RLS reported in the current study (30%) is the average of the international bibliography.

Additionally, some interesting results, reported for the first time in the Greek population, emerge in our study. According to these, the proportion of with RLS was higher in patients on peritoneal dialysis and moderate in severity, while the proportion of RLS in patients under treatment with artificial kidney was lower, but of increased severity. The fact that the percentage of patients who had RLS was higher in patients on peritoneal dialysis is in agreement with the study of Losso et al[22], where 50% of patients under peritoneal dialysis had RLS while the prevalence of RLS among patients on artificial kidney therapy was 23%. In our study, the respective percentages were 58% and 25%, and thus are in accordance with the existing data.

An important finding in our study is that also parathyroid hormone levels increased in line with, the risk of RLS occurrence. This finding is consistent with previous data, and in the study of Gade et al[12] there was also a significant correlation between parathyroid hormone levels and the risk of RLS. These results are confirmed by the work of Santos et al[13] who reported a decrease in the prevalence of RLS from 52% to 21% in ESRD patients under hemodialysis after parathyroidectomy, which caused a decrease in parathyroid hormone serum levels.

The B2-microglobulin has been shown to be positively associated with PSQI Questionnaire component 3, relative to, the duration of sleep.

A positive correlation between the increase of the urea serum levels and the PSQI component No 2, which refers to the difficulty of initiating sleep was also observed. The abnormally elevated urea value may reflect only partial renal rehabilitation. End-stage renal disease and renal recovery have been shown to be associated with increased rates of sleep disorders compared to the general population[23-27]. Consequently, our finding regarding the association of increased urea serum levels and the increased likelihood of presenting RLS, is consistent with previous observations. Of note, this is the first time that such an observation has been reported in a Greek population of end stage renal disease patients.

Significant positive correlation between the increase in the serum levels of parathyroid hormone and PSQI component 5, or else the component relative to the presence of sleep disorders was also observed. Accordingly to previous observations regarding urea serum levels, as well as the significant pathological increase of parathyroid hormone is the result of extraterritorial clearance. Previous studies reported a correlation between increased parathyroid hormone levels and augmented risk of RLS. As a result, while RLS rate increase in this specific population, it is perfectly reasonable to expect a greater proportion of sleep disorders, something which has been clearly demonstrated in the present study. It is worth mentioning that this is the first time that an association between PSQI component 5 and parathyroid levels is reported in a Greek population of end stage renal disease patients.

The type of renal recovery of every patient with end-stage renal failure proved to be unrelated to sex. Men and women follow dialysis by artificial kidney and peritoneal dialysis, similar to the current study, after medical recommendation and with respect to the personal desire of the patient.

It is worth mentioning that the prevalence and severity of RLS is significantly reduced in patients who have undergone kidney transplantation, while exhibiting correlations, such as with hemoglobin or ferritin serum levels are similar to the non-uremic form of the syndrome[15]. It is also known that kidney transplantation significantly

improves secondary hyperparathyroidism, neuropathy and amyloidosis of hemodialysis, decreasing β2-microglobulin levels and generally the «uremic profile» exhibited by hemodialysis patients. It could therefore be assumed that the inability of conventional dialysis to eliminate all «uraemic toxins» makes this theory a potential pathogenetic mechanism of the RLS, as this improves along with their removal by kidney transplantation[14].

Overall, the results of this study are considered significant. Some of these are, of course, already mentioned in the previous studies and the fact that the prevalence of RLS reported in our study is similar, leads to further enhance the viewpoint of previous researchers. However, some statistical correlations were made for the first time and yielded results with statistical significance that has not been reported again in the past. This fact proves that the specific field of RLS in patients with ESRD remains partially unexplained and further studies are needed to illuminate this multi-faceted syndrome in this particular population group.

ΠΕΡΙΛΗΨΗ

Η ποιότητα του ύπνου σε ασθενείς με τελικού σταδίου νεφρική ανεπάρκεια

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Το σύνδρομο ανήσυχων ποδιών (RLS) είναι μια κοινή διαταραχή των κάτω άκρων, που χαρακτηρίζεται από έντονη ανάγκη για συνεχή κίνηση τους και συνήθως συνοδεύεται από δυσαισθησία. Σε ασθενείς με χρόνια νεφρική ανεπάρκεια υπό αιμοκάθαρση και υπό περιτοναϊκή κάθαρση, το σύνδρομο δεν έχει μελετηθεί διεξοδικά, ιδιαίτερα στον ελληνικό πληθυσμό. Σκοπός της μελέτης ήταν η επιδημιολογική μελέτη του RLS σε νεφρική νόσο τελικού σταδίου. Οι ασθενείς με νεφρική νόσο τελικού σταδίου υποβλήθηκαν σε εργαστηριακές εξετάσεις και συμπλήρωσαν το ερωτηματολόγιο ποιότητας ύπνου του Pittsburgh (PSQI). Η τρέχουσα επιδημιολογική μελέτη διαπίστωσε ότι 3 από τους 10 νεφροπαθείς υπό θεραπεία αποκατάστασης πάσχουν από RLS, με τον σχετικό κίνδυνο να είναι αυξημένος σε ασθενείς με υψηλά επίπεδα παραθυρεοειδούς ορμόνης. Αντίθετα, δεν βρέθηκε συσχέτιση μεταξύ των επιπέδων αιματοκρίτη και των χαρακτηριστικών αιμοκάθαρσης. Η τιμή της ουρίας, της β2-μικροσφαιρίνης και της παραθυρεοειδούς ορμόνης σχετίστηκε με τις επιμέρους βαθμολογίες του ερωτηματολογίου ποιότητας ύπνου του Pittsburgh (PSQI).

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Λέξεις - Κλειδιά: *Σύνδρομο ανήσυχων ποδιών, Νεφρική ανεπάρκεια, Ποιότητα ύπνου*

REFERENCES

1. American Academy of Sleep Medicine. International Classification of Sleep Disorders. 3rd ed. 2004.
2. Garcia-Borreguero D, Larrosa D, Granizo JJ et al. Circadian variation in neuroendocrine response to L-dopa in patients with restless legs syndrome. Sleep 2004; 27:669.
3. Allen R. Dopamine and iron in the pathophysiology of restless legs syndrome. Sleep Med 2004; 5:385–91.
4. Hadjigeorgiou GM, Stefanidis I, Dardiotis E, et al. Low RLS prevalence and awareness in central Greece: an epidemiological survey. Eur J Neurol 2007;14:1275-80.
5. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification and stratification. Am J Kidney Dis 2002; 39(Suppl. 1):S1-266.
6. Cheema B, Abas H, Smith B, et al. Progressive exercise for anabolism in kidney disease (PEAK): A randomized, controlled trial of resistance training during hemodialysis. Journal of American Society of Nephrology JASN 2007; 18:1594-1601; DOI: https://

doi.org/10.1681/ASN.2006121329.
7. Winkelman JW, Chertow GM, Lazarus JM. Restless legs syndrome in end-stage renal disease. Am J Kidney Dis 1996;28:372–8.
8. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index (PSQI): A new instrument for psychiatric research and practice. Psychiatry Research 1998; 28:193-213.
9. Vainas A. Epidemiological study of restless legs syndrome (RLS) in patients with end stage renal disease (ESRD) 2013.
10. Monk TH, Folkard S. Introduction. Making shift work tolerable. London: Francis & Taylor 1992.
11. Araujo SM, de Bruin VM, Nepomuceno LA, et al. Restless legs syndrome in end-stage renal disease: Clinical characteristics and associated comorbidities. Sleep Med 2010; 11:785-90. doi: 10.1016/j.sleep.2010.02.011. Epub 2010 Jul 27.
12. Gade K, Blaschke S, Rodenbeck A, Becker A, Anderson-Schmidt H, Cohrs S. Uremic restless legs syndrome (RLS) and sleep quality in patients with end-stage renal disease on hemodialysis: potential role of homocysteine and parathyroid hormone. Kidney Blood Press Res 2013; 37:458-63. doi: 10.1159/000355727. Epub 2013 Oct 25.
13. Santos RS, Coelho FM, Silva BC, et al. Parathyroidectomy improves restless leg syndrome in patients on hemodialysis. PLoS One 2016; 11:e0155835. doi: 10.1371/ journal.pone.0155835. eCollection 2016.
14. Molnar MZ, Novak M, Ambrus C, et al. Restless Leg Syndrome in patients after renal transplantation. Am J Kidney Dis 2005; 45:388-96.
15. Winkelmann J, Stautner A, Samtleben W, Trenkwalder C. Long-term course of restless leg syndrome in dialysis patients after kidney transplantation. Mov Disord 2002;17:1072-6.
16. Al-Jahdali HH, Al-Qadhi WA, Khogeer HA, Al-Hejaili FF, Al-Ghamdi SM, Al Sayyari AA. Restless legs syndrome in patients on dialysis. Saudi J Kidney Dis Transpl 2009;20:378-85.
17. Gigli GL, Adorati M, Dolso P, et al. Restless legs syndrome in end-stage renal disease. Sleep Med 2004; 5:309-15.
18. La Manna G, Pizza F, Persici E, et al. Restless legs syndrome enhances cardiovascular risk and mortality in patients with end-stage kidney disease undergoing long-term haemodialysis treatment. Nephrol Dial Transplant 2011;26:1976-83. doi: 10.1093/ndt/gfq681. Epub 2010 Nov 5. PMID: 21056943.
19. Siddiqui S, Kavanagh D, Traynor J, Mak M, Deighan C, Geddes C. Risk factors for restless legs syndrome in dialysis patients. Nephron Clin Pract 2005;101:c155-60. Epub 2005 Jul 14. PMID: 16020954
20. Cengić B, Resić H, Spasovski G, Avdić E, Alajbegović A. Quality of sleep in patients undergoing hemodialysis. Int Urol Nephrol 2012;44:557-67. doi: 10.1007/s11255-010-9881-x. Epub 2010 Dec 9.
21. Takaki J, Nishi T, Nangaku M, et al. Clinical and psychological aspects of restless legs syndrome in uremic patients on hemodialysis. Am J Kidney Dis 2003;41:833-9.
22. Losso RL, Minhoto GR, Riella MC. Sleep disorders in patients with end-stage renal disease undergoing dialysis: comparison between hemodialysis, continuous ambulatory peritoneal dialysis and automated peritoneal dialysis. Int Urol Nephrol 2015;47:369-75. doi: 10.1007/s11255-014-0860-5. Epub 2014 Oct 31.
23. Siraj Omar Wali, Abeer Alkhouli, Mohannad Howladar, Ibrahim Ahmad, Saeed Al-Ghamdi, Ayman Krayem. Risk of obstructive sleep apnea among Saudis with chronic renal failure on hemodialysis. Ann Thorac Med 2015; 10:263–8. doi: 10.4103/1817-1737.164300.
24. Merlino G, Piani A, Dolso P, et al. Sleep disorders in patients with end-stage renal disease undergoing dialysis therapy. Nephrol Dial Transplant 2006;21:184–90.
25. Roumelioti ME, Buysse DJ, Sanders MH, Strollo P, Newman AB, Unruh ML. Sleep-disordered breathing and excessive daytime sleepiness in chronic kidney disease and hemodialysis. Clin J Am Soc Nephrol 2011;6:986–94.
26. Nicholl DD, Ahmed SB, Loewen AH, et al. Declining kidney function increases the prevalence of sleep apnea and nocturnal hypoxia. Chest 2012;141:1422–30.
27. Lee J, Nicholl DD, Ahmed SB, et al. The prevalence of restless legs syndrome across the full spectrum of kidney disease. J Clin Sleep Med 2013;9:455–9.