



# Relationship between restless leg syndrome and quality of life in uremic patients

## Üremik hastalarda huzursuz bacak sendromu ve yaşam kalitesi arasındaki ilişki

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### Summary

**Objectives:** Patients with RLS suffer nonrestorative sleep, daytime sleepiness, fatigue, and concentration problems. In addition, dialysis itself effects the psychological and social life of the patient negatively. The aim of this study was to determine the prevalence of RLS in patients on regular hemodialysis, and its relationship with patients' quality of life, socio-demographic and laboratory data.

**Methods:** One hundred and eighteen stable chronic hemodialysis (HD) patients referring to the hemodialysis unit of Turkish Kidney Foundation and 49 patients that met IRLSSG diagnostic criteria were included into the study. IRLSSG Diagnostic Criteria and International Restless Leg Syndrome rating scale were used as a guideline to diagnose and evaluate the severity of RLS. Short form-36 health survey was used to evaluate the quality of life. For statistical analysis, the "SPSS for Windows" package program was used.

**Results:** A total of forty-nine patients, of whom 26 were female and 23 were male, that met IRLSSG diagnostic criteria were included into the study. Mean age of the patients was  $61.35 \pm 13.17$  years. There was a negative correlation between the IRLSS score and SF36 Physical Score, Mental Score and Total Score, respectively ( $p=0.018$   $r=-0.351$ ,  $p=0.01$   $r=-0.380$ ,  $p=0.00$   $r=-0.499$ ). There was no significant correlation between the IRLSS score and dialysis duration, blood ferritin and parathyroid hormone and other comorbid diseases.

**Conclusion:** RLS is a common distressing problem in patients with ESRD, which negatively impacts functional health status. Clinicians should be aware of the symptoms of RLS to decrease morbidities related with quality of life.

Key words: Dialysis; restless leg syndrome; quality of life.

### Özet

**Amaç:** Huzursuz bacak sendromu (HBS) ağrı, dinlendirici olmayan uyku, gündüz uyku hali ve konsantrasyon bozuklukları yaratan bir hastalıktır. Düzenli hemodiyalize giren son dönem böbrek yetersizliği olan hastalarda huzursuz bacak sendromunun sıklığının artmış olabileceği düşünülmektedir. Bu çalışmada düzenli hemodiyalize giren hastalarda huzursuz bacak sendromu ve yaşam kalitesi arasındaki ilişkinin araştırılması amaçlandı.

**Gereç ve Yöntem:** Türk Böbrek Vakfı Diyaliz Ünitesi'ne ayaktan başvuran 118 kronik hemodiyaliz hastası değerlendirildi. Uluslararası Huzursuz Bacak Sendromu Çalışma Grubu'nun (IRLSSG) belirlediği tanı kriterlerine uyan 49 hasta çalışmaya dahil edildi. Huzursuz bacak sendromu semptomlarının şiddeti Uluslararası Huzursuz Bacak Sendromu Sınıflama Skalası (IRLS) kullanılarak değerlendirildi. Yaşam kalitesini değerlendirmek amacıyla KısaForm-36 (KF-36) ölçeği kullanıldı. Hastaların demografik özellikleri, komorbid hastalıkları ve laboratuvar verileri kaydedildi. İstatistiksel analizde SPSS paket programı kullanıldı.

**Bulgular:** Uluslararası Huzursuz Bacak Sendromu Çalışma Grubu tanı ölçütlerini karşılayan 26 kadın 23 erkek toplam 49 hasta çalışmaya dahil edildi. Hastaların yaş ortalaması  $61.35 \pm 13.17$  yıldır. IRLS skoru ile KF-36 Fiziksel, Zihinsel ve Toplam skorlar arasında istatistiksel açıdan anlamlı negatif korelasyon saptandı ( $p=0.018$   $r=-0.351$ ,  $p=0.01$   $r=-0.380$ ,  $p=0.00$   $r=-0.499$ ). IRLS skoru ile diyaliz süresi, yaş, serum ferritin, PTH ve komorbid hastalıklar ile anlamlı ilişki bulunmadı ( $p>0.05$ ).

**Sonuç:** Huzursuz bacak sendromu diyalize giren son dönem hastalarda sık rastlanan bir sorun olduğu düşünülmektedir. Huzursuz bacak sendromuna bağlı ağrı ve diğer semptomların son dönem böbrek yetersizlikli hastaların yaşam kalitesini kötü yönde etkileyebileceği düşünülerek bu yakınmalara yönelik tanı ve tedavi yaklaşımları bu hastaların yaşam kalitelerinin artırılmasına katkıda bulunacaktır.

Anahtar sözcükler: Diyaliz; huzursuz bacak sendromu; yaşam kalitesi.

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## Introduction

Restless-legs syndrome (RLS) is a sensorimotor problem characterized by uncomfortable and unpleasant sensations of the legs that are worse during periods of inactivity and usually causes a severe sleep disorder.<sup>[1,2]</sup>

The diagnosis of RLS is clinical and as several conditions like neuropathy, radiculopathy, depression, varicose disorders and akathisia may mimic RLS, its definition has been clarified and standardized by internationally recognized diagnostic criteria, published in 1995 by the International Restless Legs Syndrome Study Group (IRLSSG).<sup>[2,3]</sup> Some studies have indicated that 2-15% of the world's population may experience symptoms of RLS.<sup>[1]</sup> In most cases, RLS is idiopathic and is called primary RLS. It may also be secondary to iron deficiency, uremia, pregnancy, peripheral neuropathy and drugs, such as antipsychotics, antidepressants and dopamine antagonists.<sup>[4]</sup> RLS is common among patients on dialysis and the prevalence is estimated to be greater than in the general population.<sup>[4,5]</sup>

Patients with RLS suffer from disorders such as daytime sleepiness, tiredness and concentration problems. In addition, dialysis itself effects a patient's psychological and social life negatively. The experience of multiple losses, including kidney function, physical activity, sexual function, employment impact significantly on the lives of patients.<sup>[6]</sup> The aim of this study is to determine the prevalence of RLS in stable uremic patients and its relationship with patients' quality of life, sociodemographic and laboratory data.

## Materials and Methods

Between March 2012 and April 2012, 118 stable chronic hemodialysis (HD) patients recruited from hemodialysis unit of Turkish Kidney Foundation and 49 patients that met IRLSSG diagnostic criteria were included to the study. Patients with RLS were screened by the same neurologist. The patients underwent HD therapy three times per week which session lasting approximately 4 hours. An enoxaparin dose of 40-60 mg was administered intravenously before the beginning of each session and erythropoietin therapy was given after dialysis session to adjust hemoglobin levels. Patients who were in catabolic state that include malignancies, HIV and opportu-

nistic infections, who had neuropathies and received pharmacological treatment which could have effected quality of life were excluded from the study.

IRLSSG Diagnostic Criteria were used as a guideline to diagnose and evaluate severity of RLS. The four minimal criteria included: 1. urge to move the legs, usually accompanied or caused by uncomfortable leg sensations; 2. temporary relief with movement, partial or total relief from discomfort by walking or stretching; 3. onset or worsening of symptoms at rest or inactivity, such as when lying down or sitting; 4. an aggravation or onset of symptoms in the evening or at night.<sup>[3]</sup>

International Restless Leg Syndrome rating scale was developed as a tool for assessing the severity of RLS. The 10-item questionnaire asks respondents to use Likert-type ratings to indicate how acutely the disorder has affected them over the course of the past week. Questions can be divided into two categories: disorder symptoms (nature, intensity and frequency) and their impact (sleep issues, disturbances in daily functioning and resultant changes in mood).

Patients' rate each of ten questions on a scale from 0 to 4. Four representing the most severe and frequent symptoms, 0 representing the least. Total scores can range from 0 to 40.

### Short form 36 (SF-36) health survey

Health related quality of life (HRQoL) has increasingly been recognized as an important aspect of health care delivery in chronic medical conditions. SF-36 is a widely used and validated questionnaire for assessing HRQoL in populations including patients with ESRD.<sup>[7]</sup> Short form 36 health survey is a generic test that measures QoL through the perception of health by the patient. It contains 36 items in 8 subscales: physical functioning, emotional role, bodily pain, general health, vitality, social functioning and mental health. SF-36 total score lies between 0 and 100. Higher scores indicate better health. Validation study of the Turkish version of SF-36 has been performed.<sup>[8]</sup>

Patients' age, gender, dialysis duration, blood ferritin and parathyroid hormone (PTH) and other comorbid diseases were recorded. Comorbidities were obtained from medical records of the patients. Patients

**Table 1.** Clinical characteristics of the patients

	Minimum	Maximum	Mean	Std. Deviation
Age (years)	22	83	61.35	13.17
Dialysis duration (years)	1	24	9.52	6.971
Ferritin	14.0	3536,0	873.36	748.26
Parathyroid hormone	4.26	3332.00	580.34	588.103
IRLSSG Score	6	37	22.33	8.061

**Table 2.** IRLSSG scores and SF-36 Scores of the patients

	Minimum	Maximum	Mean	Std. Deviation
IRLSSG score	6	37	22.33	8.061
SF-36 PCS	10	62	35.96	11.429
SF-36 MCS	19.4	55.1	33.507	8.3824
SF-36 total score	18.1	62.7	39.787	11.5051

IRLSSG: International Restless Leg Syndrome Study Group; SF-36: Short Form-36. PCS physical component score, MCS mental component score.

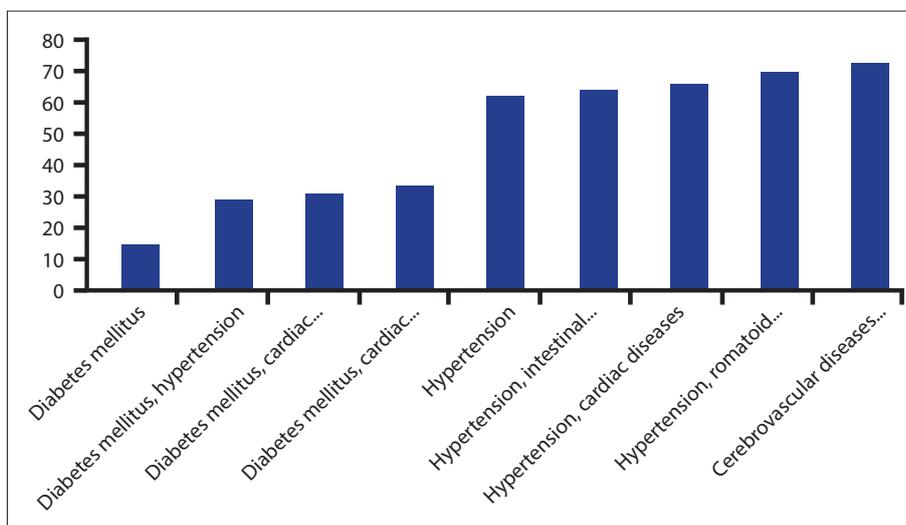
included in the study provided a written informed consent and an approval for the study was obtained from the Local Ethical Committee.

**Statistical analysis**

For the statistical analysis, the “SPSS for Windows” program was used to assess study data, together with the descriptive statistical methods (average, standard deviation). The Pearson Correlation Coefficient was used in the comparisons. Results were assessed in the 95% confidence range, with a significance level of  $p < 0.05$ .

**Results**

One hundred and eighteen stable chronic hemodialysis (HD) patients recruited from hemodialysis unit and 49 patients that met IRLSSG diagnostic criteria were included to the study. 26 patients were female and 23 patients were male. Mean age of patients was  $61.35 \pm 13.17$  years. Clinical characteristics and SF-36 scores of the patients are summarized in Table 1 and Table 2, respectively. Twenty three patients had severe-very severe symptoms and 26 patients had mild-moderate symptoms. There was no



**Figure 1.** Comorbidities of the patients.

significant difference between the patients with severe symptoms and the patients with mild to moderate symptoms in terms of clinical and laboratory parameters ( $p>0.05$ ). Comorbidities are shown in Figure 1. There was a negative correlation between IRLSSG score and SF-36 Physical Score, Mental Score and Total Score respectively ( $p=0.018$   $r=-0.351$ ,  $p=0.01$   $r=-0.380$ ,  $p=0.00$   $r=-0.499$ ). There was also significant negative correlation between IRLSSG score and SF-36 subscales (Table 3). No significant relation was found between SF-36 subscales and dialysis duration, ferritin and PTH values ( $p>0.05$ ).

There was no significant correlation between IRLSSG score and age, gender, dialysis duration, blood ferritin and parathyroid hormone and other comorbid diseases.

## Discussion

As a result of this study, 42% of the patients had

restless leg syndrome symptoms and there was a significant relationship between restless leg symptoms and quality of life.

The prevalence of restless leg syndrome among dialysis patients in different study populations is estimated to be between 6.6 and 80%.<sup>[5]</sup> This large interval may be explained with the heterogeneity of the study populations, like genetic differences and number of patients, and also with the different criteria used to diagnose the syndrome. Using the IRLSSG criteria, the prevalence of RLS in this study was in the range of values, 20-45%, reported by recent studies using the same criteria in Caucasians.<sup>[3,5]</sup>

Many studies have been conducted in dialysis clinics to clarify the risk factors for RLS, but the results have varied widely. We found no significant association between RLS and any of the following factors: age, gender, duration of dialysis and laboratory data including ferritin and parathyroid hormone. There

**Table 3.** Correlation between SF-36 subscales and IRLSSG, dialysis duration and ferritin and PTH

	IRLSSG scoring	Dialysis duration	Ferritin	PTH
Physical function				
Pearson correlation	-.311*	.437**	-.021	.127
P value	.037	.003	.894	.429
Role physical				
Pearson correlation	-.291	.060	.165	-.106
P value	.052	.698	.289	.509
General health				
Pearson correlation	-.524**	-.068	.108	-.119
P value	.000	.659	.491	.460
Vitality				
Pearson correlation	-.381**	-.193	.083	.024
P value	.010	.210	.595	.884
Social function				
Pearson correlation	-.463**	.035	.050	.010
P value	.001	.822	.750	.949
Role emotional				
Pearson correlation	-.490**	-.011	.213	.244
P value	.001	.944	.170	.124
Mental health				
Pearson correlation	-.435**	.007	.218	-.027
P value	.003	.964	.160	.867

SF: Social Function; IRLSSG: International Restless Legs Syndrome Study Group; PTH: Parathyroid hormone. \*Pearson correlation test was used.

was no association between SF-36 scores and that following factors either.

It is still not well defined what causes RLS in dialysis patients. Common complications of end stage renal disease, anemia, low serum ferritin levels and high serum levels of parathyroid hormone have been linked to RLS. A number of studies suggest that iron deficiency is the major problem since ferrous sulfate therapy, erythropoietin therapy and high-dose iron dextran infusion reduce RLS symptoms.<sup>[9-12]</sup> On the contrary, some recent studies do not support those findings.<sup>[13,14]</sup> Some researchers suggest that serum ferritin level is not a reliable parameter and according to the findings of low cerebrospinal fluid ferritin and low substantia nigra iron levels, RLS may be due to a problem about brain iron metabolism.<sup>[3,15]</sup> In this study, RLS was not associated with the presence of iron deficiency, assessed by serum ferritin, either. An association between RLS and parathyroid hormone has been suggested by a few studies in patients undergoing hemodialysis.<sup>[14]</sup> However, in this study, we determined no relationship between PTH concentrations and RLS as Miranda et al.<sup>[12]</sup> and Siddiqui et al.<sup>[16]</sup> There have been studies that measured the relationship between PTH and SF-36 scores in ESRD. Tanaka et al. found a relationship between mental health scores and high PTH levels, whereas Mingard and Klersy found no association.<sup>[17-19]</sup>

End stage renal disease itself is associated with decreased quality of life. Factors related with the kidney disease, such as medication side effects, psycho-social distress, anxiety, and sleep disorders like RLS have a negative impact on patients' quality of life. Duration of dialysis is estimated to be another reason for decreased life quality. Recent literature indicates the better HRQoL in kidney transplant recipients than patients treated with dialysis.<sup>[20]</sup> On the other hand, RLS is a chronic condition and people with RLS may have a distinctly impaired quality of life.<sup>[15,21]</sup>

In this study we found a significant correlation between mental, physical and total scores of SF-36 and RLS severity. A cross sectional study conducted on 894 dialysis patients investigated the relation between symptoms of restless legs, quality of life, and survival among incident hemodialysis and peritoneal dialysis patients. Symptoms of restless legs were

associated with lower physical and mental component scores of SF-36, vitality, bodily pain, and sleep quality.<sup>[13]</sup> In another study, the researchers found that RLS was associated with poor sleep, increased rates for insomnia and impaired quality of life in patients on maintenance dialysis.<sup>[3]</sup> Similar to those findings, Unruh et al. have reported the association between RLS and health related quality of life using SF-36 questionnaire.<sup>[13]</sup> These results suggest that RLS symptoms have a significant negative effect on already decreased health quality of patients with chronic renal failure.

There are some limitations in this study. First of all is the relatively small sample size. In addition, we did not consider the association between HRQoL and socio-demographic characteristics and comorbidities. Finally, we did not obtain data on electromyographic parameters because most of the patients did not agree to undergo such investigations. On the other hand, we tried to exclude other diseases that could mimic RLS by performing a detailed interview and neurological examination.

## Conclusions

RLS is a common distressing problem in patients with uremic patients and negatively impacts functional health status. The clinicians should be aware of symptoms of RLS to decrease morbidities related with quality of life. More studies with large number of patients are needed.

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