

## Sleep Disorders in Hemodialysis Patients: Does RKF Matter?

Haitham Ezzat\*, Osama Mahmoud, Amr Mohab and Huseen Sayed

Nephrology Department, Ain Shams University, Cairo Governorate, Egypt

\*Corresponding author: Haitham Ezzat, Nephrology Department, Ain Shams University, Khalifa El-Maamon St El-Qobba Bridge, Cairo Governorate 11566, Egypt, Tel: +201006499550; E-mail: [haitham\\_ezzat@hotmail.com](mailto:haitham_ezzat@hotmail.com)

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### Abstract

**Background:** Sleep disorders are common in ESRD. Residual kidney function contributes significantly to the overall health and well-being of dialysis patients. The importance of RKF in patients on peritoneal dialysis is widely known, but only a few studies have examined RKF in patients on hemodialysis.

**Methods:** Our study aimed to evaluate sleep disorders in hemodialysis patients and the effect of residual renal function on them. A cross sectional study was conducted on 80 HD patients who were divided into 2 groups. Group I included 30 HD patients with RKF and group II included 50 HD patients without RKF. RKF (Kru) was calculated using the equation: Interdialytic urine volume x Urine urea concentration/Interdialytic period/Mean BUN. Where Mean BUN = (BUN 1 + BUN 2)/2. BUN 1 was measured after first dialysis of week and BUN 2 was measured prior to second dialysis of week. Routine laboratory investigations were done to all patients. We assessed the following sleep disorders in both group: insomnia through insomnia severity index, the restless leg syndrome through international restless leg syndrome study group (IRLSSG) and the excessive Daytime sleepiness through the Italian version of Epworth sleepiness scale.

**Results:** In group I, 43.3% were female and 56.7% were male with mean age  $40.47 \pm 13.96$  years and mean dialysis duration  $4.38 \pm 2.86$  years. In group II, 38% were female and 62% were male with mean age  $54.68 \pm 9.36$  years and mean dialysis duration  $6.90 \pm 3.82$  years. There was highly significant difference between both groups regarding age and dialysis duration ( $p=0.000$ ,  $0.002$  respectively). There was highly significant difference between the two groups regarding iPTH ( $106.71 \pm 57.34$  pg/ml,  $175.36 \pm 15.71$  pg/ml,  $p=0.000$ ). The prevalence of insomnia was 62% followed by IRLS 18.7% and EDS 12.5%. There was no statistically significant difference between group I and group II regarding insomnia severity index, while there was statistically significant difference between them regarding international restless limb syndrome and epworth sleepiness ( $p=0.040$ ,  $0.004$  respectively). There was no significant correlation between Kru and total score of insomnia severity index, total score of limb syndrome and total score of epworth sleepiness scale. In our study there was positive correlation between Phosph and total score of limb syndrome ( $p=0.010$ ). Also the level of iPTH was correlated with the total score of limbs syndrome and total score of Epworth sleepiness scale ( $p=0.027$ ,  $0.038$  respectively).

**Conclusion:** Sleep disorders are quite common in the HD patients. Patients with high level of iPTH and phosphorus are at major risk of sleep disorders. Residual kidney function is very important to control Ca, phosphorus and iPTH level but its effect on the sleep disorders is not obvious in our study.

**Keywords:** Residual kidney function; Hemodialysis; Sleep disorders

### Introduction

Sleep disorders are common among patients undergoing dialysis in end stage renal disease (ESRD). Although variable, their prevalence has been reported to be higher when compared to the general population. The most frequently reported complaints are insomnia, restless leg syndrome (RLS), sleep-disordered breathing and excessive daytime sleepiness (EDS) [1]. The prevalence of sleep apnea (SA) in ESRD and dialysis patients has been reported in (13-70%) which is much higher than the general population. This large variation in the prevalence of SA in dialysis patients is probably due to different populations being studied, the method of diagnosis (whether it is based on questionnaires or polysomnography (PSG)) and the definition used to diagnose SA [2]. Excessive daytime sleepiness (EDS), a major consequence of SA, is caused by sleep fragmentation that is triggered by repetitive episodes

of partial or complete upper airway obstruction. Sleep fragmentation may also contribute to impaired cognition and altered moods as well as subject the patient to increased risk of work- or driving-related accidents [3]. The incidence of sleep disorders and its causes in patients undergoing hemodialysis have attracted the attention of many researchers in the past 10 years [4]. On the other hand residual kidney function contributes significantly to the overall health and well-being of dialysis patients. It not only provides small solutes clearance but also plays an important role in maintaining fluid balance, phosphorus control and removal of middle molecular uremic toxins, decline of residual renal function also contributes significantly to anemia, inflammation and malnutrition in patients on dialysis [5]. The importance of RKF in patients on peritoneal dialysis is widely known, but only a few studies have examined RKF in patients on hemodialysis, despite the fact that up to 45% of patients in the United States initiate maintenance dialysis at eGFRs. 10 ml/min per 1.73 m<sup>2</sup>. Paucity of prior study in this area may, in part, be because of misconceptions that RKF

declines rapidly after starting maintenance hemodialysis, when, in fact, the rates of RKF decline in patients on hemodialysis may be similar to those in patients on peritoneal dialysis if the current standard biocompatible membranes and bicarbonate buffer are used. In addition, timed urine collections for patients undergoing maintenance hemodialysis are labor intensive, and hence, they are not performed routinely. This is likely another important reason for the paucity of studies of RKF in patients on hemodialysis [6].

## Methods

80 ESRD patients on regular haemodialysis, three times weekly for at least 6 month, were enrolled in our study. The exclusion criteria were: patients on medication with known effects on sleep related measure, patients with neurological disorders, patients with significant mental illness requiring psychiatric treatment (including those previously diagnosed with anxiety or depression and/or taking medication for those conditions), patient with co morbidities associated with nocturnal symptoms (congestive, heart failure, unstable angina, arthritis and chronic obstructive pulmonary disease and obese patient (BMI more than 35) and those with history of previously diagnosed and /or treated sleep disorders. Patients were given written fully informed consent for study participations. The study was approved by local ethical committee. Patients in our study were divided into 2 groups: Group I included 30 ESRD patients on regular hemodialysis three sessions per week with residual kidney function. Group II included 50 ESRD patients on regular hemodialysis three sessions per week without residual kidney function. Routine laboratory investigations were done to all patients who included serum urea, serum creatinine, Hb level, serum albumin, serum Ca<sup>+</sup>, P, iPTH. Dialysis efficacy was assessed by Urea reduction Ratio where  $URR = 100 \times 1 - (\text{postdialysis urea} / \text{predialysis urea})$ . RKF (Kru) was calculated using the equation:  $\text{Interdialytic urine volume} \times \text{Urine urea concentration} / \text{Interdialytic period} / \text{Mean BUN}$ . Where Mean BUN =  $(\text{BUN 1} + \text{BUN 2}) / 2$ . BUN 1 was measured after first dialysis of week and BUN 2 was measured prior to second dialysis of week [7]. We assessed the following sleep disorders in both group: Insomnia through insomnia severity index questionnaire, based on self-administrated questions. Subjects were asked to rate on a scale from 0 to 4. Score of >14 indicates clinically significant insomnia disorders and warrants further evaluation. We assessed the restless leg syndrome through the international restless leg syndrome rating scale (IRLS) based on self-administrated questions. Subjects Score of (1-10) considered mild, (11-20) considered moderate, (21-30) considered severe and >30 considered very severe. We assessed the excessive daytime sleepiness through the Italian version of Epworth sleepiness scale (ESS) based on questions referring to situation of everyday life. Subjects were asked to rate on a scale of 0-3 how likely they would be dose off or full a sleep in eight situations.

## Results

There was statistically highly significant difference between group I and group II regarding age and dialysis duration as shown in Table 1. There was statistically no significant difference between group 1 and group 2 regarding Hb, Albumin, urea, sodium creatinine and URR while there was statistically significant difference between them regarding iPTH, sodium calcite and phosphorus as shown in Table 2. The mean KrU was  $100.27 \pm 2.45$  ml/min. In our study we found that the prevalence of insomnia was 62% followed by IRLS 18.7% and EDS 12.5%. Our results showed that there was no statistically significant

difference between group 1 and group 2 regarding insomnia severity indexes, while there was statistically significant difference between them regarding international restless limb syndrome and epworth sleepiness as shown in Table 3. There was statistically significant positive correlation between total score of limb syndrome and both sodium phosphate and iPTH while there was highly significant negative correlation between urea post and total score of Epworth sleeping scale and significant positive correlation between URR and total score of Epworth sleeping scale, Table 4. No significant correlation was found between KrU and the examined sleep disorders.

		Group I	Group II	Independent t-test	
		N = 30	N = 50	t	p-value
Age	Mean $\pm$ SD	40.47 $\pm$ 13.96	54.68 $\pm$ 9.36	-5.451	0.000
	Range	15-63	33-76		
Sex	Female	13 (43.3%)	19 (38.0%)	0.222	0.637
	Male	17 (56.7%)	31 (62.0%)		
BMI	Mean $\pm$ SD	26.13 $\pm$ 3.44	26.92 $\pm$ 4.28	-0.854	0.396
	Range	18-33	19-35		
Duration of Dialysis (years)	Mean $\pm$ SD	4.38 $\pm$ 2.86	6.90 $\pm$ 3.82	3.129	0.002
	Range	1-13	2-18		

**Table 1:** Comparison between group I and group II regarding, Age, Sex, BMI and duration of dialysis.

		Group I	Group II	Independent t-test	
		N = 30	N = 50	t	p-value
Hb (mg/dl)	Mean $\pm$ SD	8.47 $\pm$ 0.98	8.50 $\pm$ 1.15	-0.098	0.922
	Range	6.8-10.2	4.1-10.5		
Alb.(g/dl)	Mean $\pm$ SD	3.83 $\pm$ 0.50	3.68 $\pm$ 0.75	0.939	0.351
	Range	2.4-4.5	2.4-4		
Ca (mg)	Mean $\pm$ SD	9.61 $\pm$ 1.71	8.73 $\pm$ 1.09	2.832	0.006
	Range	4.4-12.5	7-11		
Phosp. (mg)	Mean $\pm$ SD	3.87 $\pm$ 1.29	4.40 $\pm$ 0.95	-2.126	0.037
	Range	1.6-8.8	3.2-6.7		
iPTH (pg/ml)	Mean $\pm$ SD	106.71 $\pm$ 57.34	175.36 $\pm$ 15.71	8.010	0.000
	Range	14.3-193	150-210		
Urea (mg/dl)	Mean $\pm$ SD	162.67 $\pm$ 25.33	160.22 $\pm$ 34.92	0.335	0.739

	Range	110-213.7	8.6-204.1		
Creatinine (mg/dl)	Mean ± SD	8.40 ± 1.59	8.95 ± 1.74	-1.410	0.162
	Range	5.3-13.2	5.8-13.3		
URR	Mean ± SD	61.02 ± 8.11	63.96 ± 11.89	-1.199	0.234
	Range	43.77-78.44	0-79.12		

**Table 2:** Laboratory data of the studied groups.

		Group I N = 30	Group II N = 50	Independent t-test	
				t	p-value
Insomnia severity index Score	Mean ± SD	19.65 ± 1.41	18.76 ± 1.64	1.901	0.063
	Range	17-22	16-22		
The international restless limb syndrome (IRLS) rating scale	Mean ± SD	26.83 ± 4.49	30.33 ± 1.66	-2.160	0.040
	Range	19-31	28-32		
The epworth sleepiness scale	Mean ± SD	12.60 ± 1.67	16.40 ± 1.34	-3.962	0.004
	Range	11-15	15-18		

**Table 3:** Calculated scores for sleep disorders among the two studied groups.

	Total Score of Insomnia severity index		Total score of limb syndrome		Total score of epworth sleepiness scale	
	r	P-value	r	P-value	r	P-value
Hb	0.012	0.935	-0.449	0.093	0.280	0.434
Alb.	0.079	0.583	0.006	0.982	-0.003	0.993
Ca	0.191	0.184	-0.500	0.057	-0.379	0.280
Phosp.	-0.148	0.304	0.638	0.010	0.100	0.784
PTH	-0.200	0.165	0.569	0.027	0.661	0.038
Urea (pre)	-0.032	0.827	-0.352	0.198	-0.449	0.193
Urea (post)	0.047	0.748	-0.379	0.163	-0.814	0.004
URR	-0.010	0.943	0.266	0.337	0.665	0.036
Creat	-0.279	0.050	-0.288	0.299	0.287	0.422
KrU	-0.158	0.545	0.062	0.908	-0.556	0.331

**Table 4:** Correlations between studied sleep disorders and laboratory parameters in studied groups.

## Discussion

Our study aimed to evaluate sleep disorders in hemodialysis patients and the effect of residual renal function on them. The prevalence of sleep disorders observed in our patients was nearly similar to that reported with lesser or higher prevalence of insomnia, varied prevalence was also observed regarding RLS and sleep apnea. In a study conducted by Ezzat and Mohab [1], the percentage of sleep disorders in hemodialysis patients were as follow: insomnia (69%) followed by OSAS (24%), RLS and PLM (18%) and EDS (12%). Another study by Sabry et al. [8], it was found that the most common sleep abnormality was insomnia (65.9%), followed by RL S (42%), OSAS (31.8%) and EDS (27.3%). In Chen et al. (2) study, the percentage of sleep disorders were as follow; insomnia was (66.6%) followed by RLs (23%), Sleep apnea (20%) and EDS (16.8%). Our results were in agreement with most of other previous studies which demonstrated that the prevalence of Insomnia in HD patient is still very high. In our study there was positive correlation between sodium phosphate and total score of limb syndrome and this finding was in agreement with other studies [8,9], which demonstrated that hyperphosphataemia was associated with lower sleep quality in maintainence dialysis patients. In our study, the level of iPTH was highly correlated with the total score of limbs syndrome and total score of Epworth sleepiness scale. The same result was found by a study conducted by Sabbatini et al. [10]. In our study; we also found no statistically significant correlation between (Hb, s.Alb, S.ca and Kru) and sleep disorders. Sabbatini et al. [10] also found in his study that haemoglobin level and behavioural factors do not seem to play acritical rolein determining sleep disorders. On the other hand Sabry et al. [8] demonstrated that anemia was indicative of the most frequently reported sleep abnormalities, insomnia and RLS. Such observation was reported by many other investigators as Iliescu et al. and Pai et al. [11,12]. In our study there was statistically significant difference between the group I and groups II regarding s.Ca, s.phosphorus and iPTH. We also found statistically significant positive correlation between total score of limb syndrome and both iPTH and URR. These results were in agreement with the study of Wang et al. [4] which demonstrated that residual renal function contributed significantly to the overall health and well-being in dialysis patient as it plays an important role in maintaining fluid balance, phosphorus control and removal of middle molecular uremic toxins. In other study by Termorshuizen et al. [13], the investigators found that high rGFR was associated with better quality of life especially sleep disorders but in our study residual kidney function has no effect on sleep disorders.

## Conclusion

Sleep disorders are quite common in HD patients. Patients with high level of iPTH and phosphorus are at major risk of sleep disorders. Residual kidney function is very important to control Ca, phosphorus and iPTH levels but its effect on the sleep disorders is not obvious in our study. Of course further studies with more patient numbers with RKF are required to investigate its effect on sleep disorders.

## Declarations

The authors declare that they have no competing interests.

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