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## Sleep disorders with biochemical parameters in hemodialysis patients

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### ABSTRACT

One of the major problems in patients undergoing chronic hemodialysis is sleep disorders, and potentially predictor of mortality and quality of life in these patients. Therefore, this study is evaluated sleep disorders in the city of Zabol in hemodialysis patients. This is a cross-sectional study on 37 patients with chronic hemodialysis in Zabol University of Medical Sciences at least six months passed of their hemodialysis treatment and did hemodialysis 3 times a week between three and four hours. Data collection tool in this study was a questionnaire based on the Epworth Sleepiness Scale drowsiness, insomnia Sleepiness Scale Pittsburgh and standard interview form was prepared and also valid questionnaires Post Sleep Inventory Modified (PSI) to coincide with the completion of questionnaires from patients to measure blood levels of uric acid, creatinine, calcium, thyroid hormones, CRP and PTH. Collected data was analyzed by SPSS software. The results showed that in general, 99.4% of subjects had sleep disorder, meaning that 72.9 % had delay in falling asleep, 66.3% had frequent awakening during sleep, 43.2% had waking up early in the morning, 43.2% feel sleepy during the day and 4.48% of patients had fatigue during the day. According to the findings of this study, hemoglobin, iron, calcium, CRP, urea, creatinine, TSH, T4, phosphorus, and PTH albumin had no significant correlation with sleep disorders; while uric acid and T3 had inverse correlation with sleep disorders. ( $p=0.01$  and  $0.012$ ). Sleep disorders are a common phenomenon in hemodialysis patients. It can affect patients' psychological and social performance. It seems that according to the results, it is suggested to focus attention on the treatment and care of patients undergoing chronic hemodialysis for sleep disturbances by nursing.

**Keywords:** Sleep Disorders, Biochemical Parameters, Hemodialysis

### INTRODUCTION

Chronic kidney disease (CKD) is one of the major health problems (1) and the annual growth rate of the disease in Iran is about 11% according to the management of specific diseases and the Ministry of Health. It has reached to about 40 thousands people in 2009. Amount of annual incidence of the disease is 53 people per one million people and the prevalence of 250 cases per one million people in Iran. These figures are respectively 200 and 975 people in America per million people (2). Currently, the most common treatment for advanced kidney failure is hemodialysis (3). According to the Society for the Protection of kidney patients out of 15 million people, 40 thousand needed dialysis and about 1,500 of them lose their lives because of complications of the disease annually (4). In Maslow's human needs theory, sleep is one of the physiologic needs, if the patients are sleeping well, their strengths and health maintain which in addition to maintaining physical and mental health, reduce stress, and strengthen the power of compromise and focus on everyday activities (5). Different factors such as age, physical activity, alcohol and drinks containing caffeine, diet and some specific diseases such as chronic renal failure can affect sleep quality and quantity (6). Sleep disturbance is a common phenomenon among chronic hemodialysis patients and cause of death is high (7) and in 80% of patients with chronic renal failure have been reported (8). Also according to Merlino results

(2006), more than 50% of patients with kidney failure have sleep disorders (9). Sleep disorder is a condition that disrupts the sleep pattern or behavior (10).

Several studies have shown that sleep apnea, restless legs syndrome, periodic limb movement disorder (PLMD) and daytime sleepiness is the most common sleep problems in these patients, (6) and complaints of the patients in the sleeping include items such as difficulty in falling asleep and frequent waking, unwanted nap and restless legs (11). In a study by Holley et al. (1999) to evaluate the characteristics of sleep disturbance in chronic hemodialysis patients; it was found 52% of these patients have sleep problems and sleep problems and variables between smoking and bone pain was correlated. Also restless legs syndrome (84%) and primary insomnia (76%) were features of sleep disturbance in these patients (12). Various factors in patients with chronic renal failure undergoing hemodialysis lead to sleep disorders including blood urea and creatinine levels, systolic and diastolic blood pressure, comorbidities, parathyroid and thyroid hormones. (15-13). On the other hand inflammatory processes also play an important role in the development of signs and symptoms in patients on hemodialysis. In these patients, the body's homeostasis natural mechanisms to achieve new levels of of metabolic interactions is specific to dialysis patients are changes and these changes are associated by creating a series of factors, including the production of acute phase proteins and the most important is C- Reactive Protein( CRP) (20-16). According to the results of various studies, sleep disorders in hemodialysis patients can affect their quality of life and lead to impaired mental functioning and social and interpersonal relationships. (23-21) According to the principle of "prevention is better than cure", identifying the effective factors in disease processes in explaining the treatment process is the most basic measures and on the other hand, extensive search of electronic resources are few studies on the factors associated with sleep disorders in hemodialysis patients was conducted. Therefore since the different studies has been proved impact of sleep disorders on general health conditions, life satisfaction, work ethics and the quality of individual tasks, also, given the high prevalence of sleep disorders in patients on chronic hemodialysis is growing interest in the study of sleep disorders, causes and factors associated with it during the past 10 years has been focused, (21,25-24) Therefore this study is evaluated sleep disorders in patients with hemodialysis.

## MATERIALS AND METHODS

This is cross-sectional study, the prevalence of sleep disorders has investigated in hemodialysis patients referred to hospitals in 2010-2012. The samples were 37 patients who received hemodialysis three times weekly. Profile subjects for inclusion were:

1. Willingness to participate in research
2. At least 18 years of age and at least one year of dialysis
3. A case study sites in hemodialysis hospitals (Hospital Amiral momenin and Seyyes Al-Shohada)
4. Being on the list of weekly dialysis do it 2 or 3 times a week and every 3 to 4 hours.
5. Lack of mental and physical disabilities.
6. Have a complete alertness, ability to answer questions Listening and Speaking acceptable.
7. No smoking, No sedatives, No hypnotics or narcotic. At the same time, patients despite the gender, education, and marital status could participate.

**Table 1: International questionnaire Modified post sleep inventory**

Sleep in patients problems separately
<b>A. time to sleep onset (PSI<sub>1</sub>)</b>
1- Quickly fall asleep
2. Sense of calm when entering the bed
3. Feel sleepy when entering the bed
4. Feel tired when entering the bed
<b>B. during sleep (PSI<sub>2</sub>)</b>
1. Frequent waking during sleep
2. Move the bed while sleeping
3. Quickly fall asleep after waking up
4. Feel the need for sleep
<b>C: When waking up from sleep (PSI<sub>3</sub>)</b>
1. Waking time set
2. When you wake up feeling tired
3. Feel extreme sleepiness during waking
4. Body soreness felt when waking up

Data gathered tool was a questionnaire based on the Epworth Sleepiness Scale drowsiness, insomnia Sleepiness Scale Pittsburgh and standard interview form was prepared. The first part of the questionnaire related to the demographic characteristics of the participants, including age, gender, marital status, family size, education level, physical activity, income, history of kidney disease, duration of hemodialysis and history of the underlying disease. The second part of the questionnaire related to sleep disorders and determine its severity, so that every question had

four options were considered of little value 0 to 3. The scientific validity of research instrument was assessed using content validity. Test-retest was used for reliability and calculated 95%. After determining the validity and reliability, data were collected through interviews through this prepared questionnaire by the researcher. In this study, if the study subjects' responses to questions related to sleep occasionally, often or always they were in patients with sleep disorders. In order to determine the severity of sleep disorders in their four point Likert scale (zero = never, 1 = rarely, 2 = sometimes, and 3 = always) was used and patients were placed in three groups with sleep disorders, mild, moderate, or severe respectively. During dialysis, for all patients with sleep disorders in accordance with the valid PSI (Modified post sleep inventory) were completed. (26) In this questionnaire, items about sleep disorders at the beginning of the three forms of sleep disorder (PSI1), during sleep (PSI2) and when waking up (PSI3) was expressed in the resolution (Table 1).

In addition, before the start of dialysis, 5 ml blood was taken from the patient from peripheral vein of the upper limb and was sent to the laboratory in less than an hour. Then test results were followed and attach a file. Abnormal cases were noticed to nurse in charge.

## RESULTS

The results showed that the majority of the subjects were male 62.2 % and 73 % were married. The average age of the patients was  $18.1 \pm 45.1$ . Most of the samples had 37.8% of secondary school education and then 32.4 % had highschool education. . In terms of location 62.2 % were from rural areas. Most of samples (56.8%) had income between 200000 - 400000 Toman per month. About 67.6 % of them also did not exercise. The majority of them received hemodialysis at the morning shift (45.9%). The findings showed that majority of samples (94.6%) had not smoking, not used hookah (100%) and not used opium (86.5 %). About medicine taking, 59.5% did not take anti-hypertensive drugs, 94.6% did not take narcotic drugs, and 100% did not take antidepressants. Based on the findings, 48.6% of the samples, most often during sleep, they wake up frequently (Table 1). The findings also showed that levels of uric acid and T3 are negatively correlated with sleep disorders (Table 3 and 4).

Table 1: Distribution of absolute and relative frequency of subjects in terms of incidence of sleep disorders

Always		Often		Rarely		Never		Sleep disorder	Row
Percent	Number	Percent	Number	Percent	Number	Percent	Number		
13.5	5	13.5	5	32.4	12	40.5	15	At the time of feeling sleep goes to sleep quickly.	1
2.7	1	13.5	5	40.5	15	43.2	16	Sometimes drink hot drinks to sleep.	2
27.0	10	27.0	10	29.7	11	16.2	6	More than half the time it takes to go to sleep.	3
16.2	6	18.9	7	40.5	15	24.3	9	Trying to go to sleep disturbed thoughts come to me.	4
18.9	7	40.5	15	24.3	9	16.2	6	When entering into bed, I feel relieved.	5
5.4	2	27.0	10	43.2	16	24.3	9	On arrival bed gives me sleepy.	6
10.8	4	32.4	12	29.7	11	27.0	10	On arrival bed I feel tired.	7
24.3	9	48.6	18	16.2	6	10.8	4	I wake up frequently during the night.	8
29.7	11	27.0	10	10.8	4	32.4	12	Tingling in the legs, feet and other extremities during sleep.	9
10.8	4	24.3	9	24.3	9	40.5	15	I move a lot while sleeping in bed.	10
21.6	8	10.8	4	29.7	11	37.8	14	Irresistible desire to move the legs during sleep much.	11
16.2	6	32.4	12	29.7	11	21.6	8	After waking up late at night to sleep.	12
5.4	2	24.3	9	40.5	15	29.7	11	I wake up with nightmares.	13
5.4	2	18.9	7	27.0	10	48.6	18	I feel short of breath during sleep.	14
35.1	13	35.1	13	13.5	5	16.2	6	I woke up with a minimum of fuss.	15
5.4	2	10.8	4	21.6	8	62.2	23	I snore during sleep.	16
8.1	3	21.6	8	35.1	13	35.1	13	I wake up with a sudden jump muscle.	17
10.8	4	32.4	12	37.8	14	18.9	7	About 3-2 hours I wake up early.	18
10.8	4	18.9	7	39.7	11	40.5	15	After waking up from sleep, feeling enough for me to sleep.	19
21.6	8	35.1	13	35.1	13	8.1	3	I wake up early.	20
16.2	6	40.5	15	18.9	7	24.3	9	Feeling tired or feeling fatigue during waking up from sleep my body.	21
13.5	5	29.7	11	21.6	8	35.1	13	I felt extreme drowsiness after waking up from sleep.	22
13.5	5	24.3	9	21.6	8	40.5	15	When waking up from sleep angry.	23
8.1	3	40.5	15	29.7	11	21.6	8	Do you feel tired during the day?	24
5.4	2	27.0	10	40.5	15	27.0	10	Do you have trouble focusing during the day?	25
8.1	3	35.1	13	27.0	10	29.7	11	You feel sleepy during the day.	26

**Table 2: Mean and standard deviation of sleep disorders in these patients**

average $\pm$ Standard deviance	Sleep disorders
0.43 $\pm$ 2.24	Disorder began to fall asleep
0.56 $\pm$ 2.21	During sleep disorder
0.51 $\pm$ 2.29	When waking up in disorder

**Table 3: biochemical parameters associated with sleep disorder**

P-value	average $\pm$ Standard deviance	Variables
0.415	1.5 $\pm$ 9.9	Hemoglobin
0.776	311.3 $\pm$ 562.9	Iron
0.640	1.3 $\pm$ 8.5	Calcium
0.172	0.7 $\pm$ 1.0	CRP
0.254	31.9 $\pm$ 46.8	Urea
0.134	4.0 $\pm$ 8.7	Cratinin
<u>0.010</u>	2.4 $\pm$ 5.8	uric acid
0.052	1.2 $\pm$ 3.1	TSH
0.782	26.2 $\pm$ 13.0	T4
<u>0.012</u>	63.1 $\pm$ 99.1	T3
0.274	2.2 $\pm$ 6.0	Phosphor
0.168	1.0 $\pm$ 4.7	Albumin
0.083	234.3 $\pm$ 459.8	Paratormon

The table 3 shows that the levels of uric acid and T3 there were a significant association with sleep disorders.

**Table 4: The relationship between uric acid and T3 with sleep disorder**

P valu	r	Variable
0.01	-0.422	uric acid
0.012	-0.204	T3

The table 4 represents the amount of uric acid and T3 is negatively correlated with sleep disorders.

## DISCUSSION AND CONCLUSION

Based on the findings of this study, the majority of patients (99.4%) had sleep disorder. Between uric acid levels and hormone Triiodothyronine (T3) and a statistically significant inverse relationship between sleep disturbances are correlated. One of the major problems in chronic hemodialysis patients is sleep disorder. In recent years researchers have studied the relationship between sleep disturbance in patients with increasing age, female gender, duration of morning shift will start hemodialysis and hemodialysis has been proven and also sleep disorders and CRP, iron, creatinine, uric acid and communication is shown. In this study, we discuss various aspects of sleep disorders. The study of Mollahoseini (2005) and Cengiç (2012) results showed that 73% -94% of kidney failure patients had sleep disorders. (28-27) According to results Mollahoseini between sleep disorders and demographic characteristics of the subjects, there was no significant relationship. 58.9% had sleep disorders on average, 39.9 percent had mild sleep disorder and only 1.2% had suffered severe sleep disturbances (27). In a study conducted in 2002 by Hui and colleagues the prevalence of sleep disorders in patients with chronic renal failure undergoing hemodialysis Chinese, was carried out showed that 79 percent of frequent awakenings, 64% of insomnia, 74 % complained of daytime sleepiness (29). In a study which by Iliescu et al. (2003) in Canada about the sleep quality of hemodialysis patients concluded that 71% of patients were suffering from sleep disorders (30).

In the present study, 72.9 % of patients had delay sleeping, 66.3% had frequent awakening during sleep, 43.2% had waking up early in the morning, 43.2 percent feel sleepy during the day and 48.6% of people who feel tired during the day. In this regard, Shiri et al (2006) investigated the amount and type of sleep disorders and sleep hygiene in hemodialysis patients reported that, in general, 34.7% of research had sleep disorder. Their results also showed that at least three days a week, 42.1% of patients delay in falling asleep, 63.2% of patients waking up frequently during the night, 17.6% of patients waking up early in the morning and 25.1 percent had a nap during the day. As well as patient discomfort (including pain, shortness of breath, muscle cramps, itching, cough, and thirst) had a significant relationship with the percentage of sleep disorders. (31) The findings of the present study also showed that, respectively, frequent waking during sleep and fall asleep latency (in line with other studies) were most common. Also in this study, waking up early in the morning was relatively low compared to other studies.

In the study of Mollahoseini et al. (2005) studied the majority of married men aged 55-64 years old were in line with the results of the present study (27). Iitaka et al (1998) in their study reported the majority of the participants were men over 54 years (32). Based on the results of this study, the hemoglobin, Fe, calcium, CRP, urea, creatinine,

TSH, T4, phosphorus and PTH albumin statistically significant relationship was observed with sleep disorders. Unlike the present study, in the study Ebrahimi *et al.* (2015) was a significant relationship between the amount of albumin, hemoglobin, calcium, phosphorus, creatinine were observed and the quality of life for dialysis patients. (33) The quantity and quality of sleep affects the quality of life of the individual, (34) and in different studies on the relationship between quality of life with sleep quality is emphasized (36-35).

According to the results of Baraz (2008) between sleep quality score hemoglobin and albumin dialysis patients; there was an inverse relationship (37) which is incompatible with the results. Also according to the study Benz (1999) and Morton (1996) after the treatment of anemia in hemodialysis patients' sleep quality, improved. (39-38). In the present study, based on results Al- jahdali (2010) between sleep disorders and laboratory markers such as hemoglobin, ferritin and phosphorus statistically significant relationship was observed. (24) Also in the a study by Ein ollahi and colleagues (2015) on sleep quality hemodialysis patients in Iran, the results showed no statistically significant association between hemoglobin, iron, PTH, phosphorus, calcium and serum albumin with sleep quality (40) which is in line with the results of this study; In this study unlike the study of blood uric acid in patients with sleep disorders Einollahi significant relationship was observed. Ezzat and Mahab (2015) in the study of sleep disorders and hemoglobin, albumin and creatinine negative correlation with P reported a positive relationship, According to the results Ezzat study, treatment of anemia, hyperphosphatemia and hypoalbuminemia can be effective in improving sleep quality dialysis patients(25). Bornivelli (2008) in his study showed sleep disorders associated with biochemical parameters in chronic hemodialysis patients; there is significant relationship between CRP and serum albumin in hemodialysis patients with insomnia; so that patients with sleep disorders had lower CRP and albumin (41).

In the study Jenabi *et al.* showed that a statistically significant relationship between serum levels of CRP and sleep disorders in general is established, ( $P=0.016$  and  $R=0.191$ ) with female sexual differentiation, the relationship than men was more significant(26). Also serum levels of CRP in people who lived for more than 48 months of hemodialysis was correlated with sleep disorders, ( $P=0.001$  and  $R= 0.364$  ) and a form of sleep disorder during sleep (PSI2) of these patients, establish a significant relationship, ( $P=0.02$  and  $R= 0.249$ ) While age categories and other forms of sleep disorders, no significant correlation with CRP (26) In the present study, unlike Jenabi study, CRP levels were not significantly associated with sleep disturbance ( $P=0.172$ ). Chiu *et al.* (2009) also stated that there was a relationship between high CRP and sleep disorders in hemodialysis patients (42).

Based on the results of this study, there was no significant relationship between levels of PTH and sleep disorders; but in study Veiga (1997) a significant relationship was observed between PTH and sleep disorders, so that patients with high PTH compared to more patients suffering from sleep disorders. (43) In this study, De Santo (2008) showed significant relationship between the sleep disorder with PTH, anemia, creatinine, plasma urea and uric acid (15) while in the present study found an inverse relationship between uric acid and sleep disorders. Although the evidence is conflicting evidence on the role of PTH in hemodialysis patients are sleep disorders, results De Santo showed that in patients undergoing parathyroidectomy surgery, were more common sleep disorders (15). Also Esposito (2008) in his study of the impact of parathyroidectomy on improving sleep quality in hemodialysis patients with hyperparathyroidism cleared that parathyroidectomy surgery, improve the sleep quality of patients (44). Sarookhani study showed that thyroid function very common in hemodialysis patients showed that the decrease in T4, FTI was the least disturbance. Among the abnormal, a significant number of patients decreases in T3 and FTI but most of them T3RU and TSH were increased. In all cases the disorder, 22 patients with hypothyroidism and hyperthyroidism patients were 1. Other patient's lack the full criteria were hypo- or hyperthyroidism (45). Research findings showed that T3 is negatively correlated with sleep disorders, ( $p = 0.012$ ), but the levels of TSH, T4 significant difference was observed in subjects. Also in the Shamsoddini and his colleagues as study of chronic renal failure (CRF) and hemodialysis on serum levels of thyroid hormones, the results showed that lower hormone levels in dialysis patients than in healthy controls and after hemodialysis and hemodialysis patients are not more than that these findings could represent a reduction of thyroid function after dialysis patients is the accumulation of waste in the body that after every dialysis session, the thyroid gland in the absence of this waste could provide more activities (46). Halicevic *et al.*(2015) in their study suggested that in patients with kidney failure, the amount of T3 is less(47). Recent studies have indicated the existence of a potential link between lacks of sleep, poor quality of sleep disorders with increased mortality in these patients (43, 48). Sleep quality can demonstrate sleepness and it may affect people physically and mentally, in turn, it can influence the quality of life (QOL) and ultimately it can lead in depression. In order to keep mental balance, persons and patients need sleeping and rest (49). Arbabisarjou *et al.*(2016) concluded that social intimacy and sleep quality were recognized as the effective factors in burnout. Also, they found that if the academic performance improves more, the sleep quality will be more (50). Hence seems to be trying to find factors and factors related to sleep disorders in hemodialysis patients may be beneficial to have beneficial results. Therefore, given that the studies produced conflicting results on blood biochemical factors and sleep disorders have suggested further studies with larger sample size.

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