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Original Research Article

Sleep Disorders; Severity and Factors Associated with it Among End Stage Renal Disease Patients Attending Al-Yarmook Dialysis Centre, Baghdad, Iraq

[1]Saad Ayid Jassam, *[2]Waqar Al Kubaisy and [3]Mazin Ghazi Alrubaey

[1]Third Year Student of the Iraqi Board for Medical Specialization in Family Medicine, Baghdad, Iraq

[2]CommunityMedicine and Public Health, Faculty of Medicine, Mutah University, Jordan

[3]Prof. Dr., Deputy Dean Faculty of Medicine AlMustansyria University, Baghdad, Iraq

***Corresponding Author's E-mail: waqar_abd@yahoo.co.uk**

Abstract

End stage renal disease (ESRD) could affect many aspects of patient's life including sleep quality. Severe sleep disorders if not detected and managed properly, may in turn exacerbate the patient's condition and increase the mortality rate. Determining the sleep disorders rate, and to assess the severity of sleepiness among ESRD patients is an important issue. A cross-sectional study was conducted in renal dialysis unit at Al-Yarmook Teaching Hospital, in Baghdad, during a five months period. A sample of 150 ESRD patients with undergoing haemodialysis (HD) was collected. Face to face interview was carried-out with each participant, using a reliable and validated questionnaire. This questionnaire containing a nine-item -specific for sleep disorder scale, and eight items that reflect the presence and severity of a sleep disorder using the 24-score Epworth sleepiness scale (ESS). Beside that the socio demographic information was included. The prevalence of sleep disorder was 78.66%. About 30% had moderate to severe sleep disorder, 46% had mild sleep disorders while 24% of patients were normal. Three factors were found to be significantly increasing the risk of sleep disorders. Those were: old age ≥ 50 years (OR = 2.24 95% CI 1.04-4.82), single marital status (OR= 2.81, 95% CI 1.08-7.31), and presence of comorbidity, represented by type 2 diabetes mellitus (DM) (OR= 4.04, 95% CI 1.06-15.35) or both DM, and hypertension (OR = 3.23, 95% CI 1.15-9.09). Sleep disorders are very common among patients with ESRD undergoing HD. Old ages (50 years or over) single patients, and the presence of chronic comorbidity, especially DM, are independent risk factors for developing sleep disorders among HD patients.

Keywords: End stage renal disease, Risk factors, Sleep disorders

INTRODUCTION

Sleep is a vital human biologic process that is essential for optimal health and life. Sleep plays a critical role in brain function including neurobehavioral, memory consolidation, cognitive and safety-related performance, mood regulation, and clearance of brain metabolites. Sleep is also critically involved in systemic physiology, including metabolism, cardiovascular systems immune and hormone function, and appetite regulation. Moreover, Sleep duration is associated with risk of mortality or risk of several health problems like cerebrovascular, cardiovascular diseases, cancer, obesity, diabetes, and depression (Watson et al (a) 2015). Adults should sleep 7 or more hours per night on a regular basis to promote optimal health. Sleeping less than 7 hours per night on a

regular basis is associated with adverse health outcomes. Normal healthy sleep is characterized by sufficient duration, good quality, appropriate timing and regularity, and the absence of sleep disturbances and disorders, (Watson et al (b) 2015)

Sleep disorders are defined as conditions characterized by disturbances of usual sleep patterns or behaviors that cause distress and impair daytime functioning. It has been estimated that the prevalence of sleep disorders in the general population could be as low as 10% and high as 37%, (Ram et al., 2010). This prevalence as reported by Harris, et al (2012) is much higher in patients with chronic kidney disease (CKD) particularly those with end stage renal disease (ESRD). Hui et al (2000) gave evidence that 80% of the ESRD patients receiving dialysis complaining of sleep disorders, with daytime sleepiness. Therefore, this is a very serious public health problems particularly if we know that currently, CKD is one of the most important health problems worldwide, approximately one million people with ESRD undergo replacement therapy worldwide (Harris et al., 2012).

Interestingly, Thorpy, (2012) stated that the International Classification of Sleep Disorders (ICSD3) have been categorized the sleep disorders into eight major categories, that include: insomnias, sleep-related breathing disorders, Central disorders of hypersomnolence, circadian rhythm sleep wake disorders, parasomnias sleep-related movement disorders. However, three are the most important sleep disorders that associated with CKD patients particularly those under haemodialysis (HD). First, Insomnia; which is define by Novak et al, (2006) as inability to fall asleep or stay asleep. It is characterized by poor sleep quality and poor quality of life. It is a common sleep disorder in the general population with a prevalence of 4% to 29%. Whereas in the ESRD population, as reported by Theofilou (2013) as 50%-75%. The risk of insomnia in ESRD patients is higher than the general population due to the physical stress of their condition, and chronic pain. Second is the sleep Apnea, which is a sleep-related breathing disorder which causes repeated cessation of breath while a person is sleeping. Characterising by loud snoring, breathlessness, waking up from sleep, and daytime sleepiness. The prevalence of the Sleep Apnea in general population is 2%-4% (Sim et al., 2010) while in ESRD patients it is 50%-80%, (Argekar et al., 2007). In the ESRD, Sim et al (2010), reported that the sleep apnea can cause excessive sleepiness and cognitive impairment, diminishing daytime functioning, depression, hypertension and increased cardiovascular morbidity and mortality.

The third category are the Parasomnias which are unwanted behaviours during sleep or during transitions between different stages of sleep or during sleep–wake transitions (Mahowald and Schenck, 2005). Parasomnias can be categorized as simple or complex. Simple parasomnias only involve one body area and are usually restricted to singular movements. Complex parasomnias are more bizarre behaviours, which can be disruptive of sleep and have the potential of harm to self or bed partner (Howell, 2012).

Several factors that may contribute in sleep disorders in ESRD patients who are undergoing dialysis. Sleep disorders may have direct effects on ESRD. It is evident that there is an alteration, in the activity of sympathetic nervous system, and in renin-angiotensin-aldosterone system (RAAS). Normally, there is an increase vagal tone and decreased sympathetic activity associated with nocturnal dipping of blood pressure. In CKD patients with sleep disorder, Somers et al (1995) stated that there is a sleep fragmentation accompanied by hyperactivation of the sympathetic nervous system and reduction in nocturnal dipping of blood pressure. Neumann, et al (2004), had been postulated that this may be a risk factor for CKD progression due to its effects on blood pressure and renal hemodynamies Hence further activation of the sympathetic nervous system due to sleep disorders can exacerbate this risk in patients with CKD. Moreover, Charloux et al. (2002) reported, that the nocturnal dropping of blood pressure is linked to elevation of nocturnal plasma renin activity. In fact, timing, quantity and quality of sleep affect both plasma renin and aldosterone levels. Both reduced sleep quality and sleep fragmentation reduces the nocturnal dipping of blood pressure and hence the sleep-related increases in renin and aldosterone levels are similarly affected. However, during recovery, sleep during daytime the plasma renin and aldosterone levels rise. This alteration in RAAS activity can have a role in CKD progression (Vejakama et al., 2017)

Thus, we can understand that, sleep disturbances play an important risk factor for the development and progression of CKD. Therefore, determining the occurrence and severity of sleep disorders in ESRD patients and treating, controlling or preventing this disorder, optimize duration and quality of a sleep which may reflected by a marked reduction in severity and progression of CKD. Therefore, our aims are to determine the prevalence of sleep disorders and to assess the severity of daytime sleeplessness among ESRD patients under HD

PATIENTS AND METHODS

A Pilot study was carried-out on ten uremic patients prior to embarking on the main project, for testing the reliability and validity of the questionnaire and to determine the difficulties that may arise during data collection and time that be needed to collect data. Ethical approval was obtained from the Ethical committee of the Iraqi board of medical specializations as well as from authorized person at Al-Yarmook Teaching Hospital. A

verbal consent from each participant was obtained after explaining the aim of study. The confidentiality of data throughout the study was guaranteed to each patient and he/she was given the complete unconditioned choice to withdraw anytime

A cross-sectional hospital based study was conducted at the renal unit of Al-Yarmook Teaching Hospital, Baghdad, Iraq during the period from 1st March to 1st September 2018. The renal unit of this hospital has 33 HD machines, and daily about 130 patients receive HD in four different shifts. Calculation of the estimated sample size was 131 patients, was done to be collected during the study period. Inclusion criteria; adult patients 18 years old or above, with ESRD for three months or more on HD. second to ESRD for at least one year. On the other hand we have excluded any patient with known psychiatric conditions and neurological disorders, patients who have medication with known effects on sleep-related measures (like melatonin, Methylpre-dnisolone) were excluded. Face to face direct interview was carried out with each participant, using a well-constructed, validated questionnaire. This questionnaire consist of three parts: Part I containing the socio demographic information of the participant including age, gender, marital status (single, married), educational level (primary, secondary and high), smoking status (never, ex/current smoker) and present of comorbidities (has no comorbidity, hypertension, diabetes). Part II, related to the Assessment of Sleep Disorders this part was already validated and reliable (Bastien al et., 2001). It consist of nine-items problem-specific sleep disorder scale was used to determine the patients' specific sleep disorders. This scale is based on the five-item Insomnia scale. Four items were further added to the scale through by different authors. These nine items are: 1. Frequent waking during nigh, 2. Morning headache 3. Loud snoring 4. Daytime dozing and lack of concentration, 5. Daytime sleepiness, 6. Having problems going to sleep while in bed, 7. Waking very early in the morning, 8. Night-time waking and having problems going to sleep again, 9. Nocturnal urine frequency. We considered patient as having a sleep disorder if at least one of the nine items was positive.

The presence and severity of a daytime sleepiness was determined using the 24-score Epworth sleepiness scale (ESS) which containing eight items reflecting information for the patients' likelihood to doze or fall asleep. Each item was scoring from 0 to 3. In which score 0 means no chance to doze, score 1, slight chance**,** score 2, moderate and score 3 means high (Johns 1993). These 8 items including: 1. Sitting and reading, 2. Watching TV, 3. Sitting inactive in a public place (e.g. theatre or meeting); 4. As a passenger in a car for an hour without a break, 5. Lying down to rest in the afternoon, 6. Sitting and talking to someone, 7. Sitting quite after a lunch without alcohol; 8. In a car while stopped for a few minutes in traffic. Based on the ESS, we have considered the total scores of :0 - 8 as normal, 9 - 12 as a mild sleep disorder, while a total score of 13 - 24 considered as moderate to severe state of sleep disorders.

All statistical analyses were performed using SPSS 13.0. Descriptive statistics (frequency, percentage, and means) was carried out. Chi square test x^2 was calculate as well as the odds ratio (OR) and their corresponding confidence interval (CI) in order to find out the association between each socio-demographic factor with the occurrence of sleep disorder. P value <0.05 was considered statistically significant

RESULTS

From this study, we detected that the prevalence of sleep disorder was 78.66%, where 118 out of 150 respondents reported at least one item out of nine. The mean age was 48.94±16.24 years (range 20-70 years). Patients ageing 59-70 years old, showed the (36%) highest proportion (Table 1). Males showed higher rate (61.33%) than females (38.67%). More than two-third (68.67%) of the participants were married, half of the patients (50%) had a secondary educational level, while the minority of them (9.33%) had a degree of higher education. Almost ¾ (71.33%) were never smoke, while 28.67% were considered as Ex/current. Comorbidity was reported by approximately two-third (64.75) of the patients including; DM (15.33%), HTN (24%) or both (25.33%).

According to the nine-item problem-specific sleep disorder scale, 118 out of 150 patients (78.66%) had some types of sleeping disorders, while the other 32 patients (21.33%) were free from any type of sleeping disorders. Studying the sleep disorders according to prevalent of each item of those nine-items Table 2 shows that, the majority of ESRD patients with sleeping disorders demonstrated a very high prevalence of three items. These items are; daytime sleepiness (96.6%), next to this, is frequent waking during night (94.9%) and daytime dozing and lack of concentration (91.5%). Night-time waking and having problems going to sleep again came next with (71.2%). On the other hand the sleeping disorder item with the lowest prevalence was (7.6%) the loud snoring, which was reported by nine patients only. (Table 2)

Regarding the Severity of daytime sleepiness. Depending upon the Epworth Sleepiness Scale which measures the severity of daytime sleepiness. Patients were categorized in to three categories: those who are normal (24%), those with mild severity (46%) and those with severe sleep disorder (30%) as shown in figure 1.

To investigate the relation of sleeping disorders with Socio-demographic characteristics of the patients. Our study detected that, those ESRD patients aging 50 years or above having significantly higher rate (58.78%) of sleeping disorder compared to the rate (41.23%) among

Table 1. Sociodemographic characteristics of 150ESRD patients under HD at Al Yarmook Teaching Hospital, Baghdad 2019

Socio demographic characteristics	No. (%)
Age, years	
20-32	39(26)
33-45	22(14.67)
46-58	35(23.33)
59-70	54(36)
Gender	
Male	92(61.33)
Female	58(38.67)
Marital status	
Married	103(68.67)
Single	47(31.33)
Educational status	
Primary	61(40.67)
Secondary	75(50)
Higher	14(9.33)
Smoking	
Never	107(71.33)
Ex/current	43(28.67)
Comorbidities	
No comorbidity	53(35.33)
Diabetes mellitus	23(15.33)
Hypertension	36(24)
Hypertension and diabetes mellitus	38(25.33)

Table 2. Frequency and Rate of sleeping disorder according to each item of the nine-item problem-specific scale among 150 ESRD patients under HD.

Items of Sleep Disorder	No &(%)
Frequent waking during night	112(94.9)
Morning headache	33(28)
Loud snoring	9(7.6)
Daytime dozing and lack of concentration	108(91.5)
Daytime sleepiness	114(96.6)
Having problems going to sleep while in bed	61(51.7)
Waking very early in the morning	75(63.6)
Night-time waking and having problems going to sleep again	84(71.2)
Nocturnal urine frequency	44(37.3.)

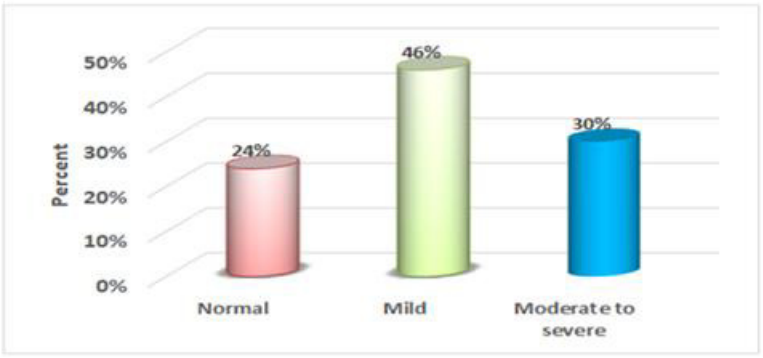

Figure 1. The rate of different degree of daytime sleepiness in 150 ESRD patients under HD.

Table 3. Socio-demographic factors with the occurrence of sleep disorders among ESRD patients at Al Yarmook Teaching Hospital

Variables	Without sleeping disorder (n=36)	With sleeping disorder (n=114)	X^2	P-value	OR (95%CI)
Age, years					
<50 (n=69)	22(61.11%)	47(41.23%)	4,35	0.037	2.24(1.04-4.82)
≥50 (n=81)	14(38.89%)	67(58.78%)			
Gender					
Male (n=92)	24(66.67%)	68(69.65%)	0.568	0.451	1.35(0.62-2.97)
Female (n=58)	12(33.33%)	46(40.35%)			
Marital status					
Married (n=103)	30(83.33%)	73(64.04%)	4.736	0.03	2.81(1.08-7.31)
Single (n=47)	6(16.67%)	41(35.96%)			
Educational status					
Primary (n=61)	14(38.89%)	47(41.23%)	0.015	0.923	1.14(0.52-2.51)
Secondary (n=75)	19(52.78%)	56(49.12%)	0.104	0.747	0.92(0.22-3.75)
Higher (n=14)	3(8.33%)	11(9.65%)	0.0969	0.902	
Smoking					
Never (n=107)	25(69.44%)	82(71.93%)	0.0826	0.774	0.89(0.39-2.01)
Ex/current (n=43)	11(30.56%)	32(28.07%)			
Comorbidities					
No comorbidity (n=53)	20(52.78%)	33(29.82%)	8.4778	0.039	
DM(n=23)	3(11.11%)	20(16.67%)	4.632	0.04	4.04(1.06-15.35)
Hypertension (n= 36)	7(19.44%)	29(25.44%)	3.394	0.07	2.51(0.93-6.79)
DM &hypertension (n= 38)	6(16.67%)	32(28.07%)	5.223	0.026	3.23(1.15-9.09)

those group at age ,<50 years, X^2 = 4,35, p=0.037. Moreover, patients at age 50 years or older, are at a significant risk of developing sleeping disorders more than two times than those younger than 50 years old. (OR= 2.24, 95%CI=1.04-4.82. The married ESRD patients showed significantly higher rate of sleep disorders (64.04%) comparing to (35.96%) those single patients (whether widow or never married), X^2 = 4.736, p = 0.003. Interestingly married ESRD patients were significantly almost three times more liable to develop sleeping disorders (OR= 2.81, 95%CI=1.08-7.31) than their counter group (Table 3).

About two-third of the ESRD patients were reported with comorbidity (represented by DM, HTN or both). Those patients showed significantly higher rate (29.82%) of sleeping disorders than those who are free from any comorbidity (X^2=8.4778, p=0.039). Interestingly, the presence of both DM and HTN seemed to be act as the highest risk factor (more than 3 times) for sleeping disorder among ESRD patients (OR=3.23, 95% CI =1.15-9.09), In addition strong significant association was detected between the two variables (presence of both DM and HTN with sleeping disorder) X^2=5,22, p=0.026). The diabetic ESRD patients showed significantly higher rate (16.67%) of sleeping disorders compared to those with no comorbidity. (X^2=4.632, p=0.04). .This study gave evidence that DM acts as a risk factor more than four times for exacerbating the development of sleep disorder among ESRD (OR=4.04, 95% CI =1.06-15.35).

Males showed higher rate (69.65%) of sleeping disorders than females (40.35%), but this difference was not significant. Level of education showed no significant association for the occurrence of sleep disorders among ESRD patients. Our study found no association between sleeping disorders and smoking status of the ESRD patients (Table 3)

DISCUSSION

This study gave evidence that HD patients having high prevalence (78.66%) of sleep disorders. This prevalence is almost similar to that (79.5%) of the study done in Egypt (Sabry et al., 2010). On the other hand it is much higher than the national rate (66%) reported by Al Ameedy (2016) in his study done in Babylon, Iraq. The prevalence of sleep disorders of current study is much higher than the prevalence reported at several countries. For example, a prevalence rates of, 74.4% and 66.6% found in Taiwan, (Pai et al., 2007; Chen et al., 2006 respectively), 57% in Brazilian (Araujo et al., 2011) and, 69% in Italy, (Merlino et al., 2006). On the other hands our study showed much lower prevalence of sleeping disorders than the rates from two studies done in Iran 86.6% and 95% (Masoumi et al., 2013 and Abassi et al., 2016 respectively). A variation can be notice in the prevalences of sleep disorders among different ESRD patients. However one evidence revealed from all these studies, that sleep disorders is a common health problem among ESRD. These variation could be attributed to several factors including sample size, age and sex of included patients, the duration and timing of dialysis, life style of the population like dietary habit and smoking all these can affect the results. Thus this high rate cannot

be attributed to single factor. It is multifactorial risk factors including sympathetic hyperactivity, decrease in vagal tone and in nocturnal secretion of melatonin, and may be other psychological factors (Neumann et al 2004; Mehta and Drawz, 2011).

Regarding the day time sleepiness, 76% of the ESRD suffering from this problem (46% mild and 30% moderate to severe), which was much higher than (63.63%) that found (59.09% and 4.54% respectively) in Iran (Abassi et al., 2016). This high prevalence could be attributed to the evidence that in CKD particularly with a sleep disorder, there is a hyper activation of the sympathetic nervous system and this may be a risk factor for CKD progression due to its effects on blood pressure and renal hemodynamies (Somers et al., 1995; Neumann et al., 2004). In addition, as Charloux et al. (2002), stated that, timing, quantity and quality of sleep affect both plasma renin and aldosterone levels. Both reduced sleep quality and sleep fragmentation reduces the nocturnal dipping of blood pressure and hence the sleep-related increases in renin and aldosterone levels are similarly affected. However, during recovery sleep during daytime the plasma renin and aldosterone levels rise. This alteration in RAAS activity can have a role in CKD progression (Vejakama et al., 2017).

However, these results in our study imply two important facts. The first one is the noticeable consistency between prevalence of (78.66%) sleep disorder using the nine-item scale and prevalence of (76%) day time sleepiness using Epworth Sleepiness Scale. The second fact is that a considerable number of patients on HD had severe sleep disorders which necessitate a particular treatment, otherwise the patient condition will be exacerbated.

In this study, it was detected that those who are 50 years old or older, were at 2.24-time higher risk of having sleep than younger age. Our finding supporting several studies done by, AL- Ameedy 2016;Chen et al 2006; Merlino et al., 2006; Masoumi et al., 2013; Sabbatini et al 2002. Many reasons are thought to be beyond this predilection, the most important of which is that older patients have less efficient renal function and physical activity and more exposure to comorbidities than younger patients, as well as the possible effect of nutritional status which is usually inadequate in elderly (Li et al., 2012; Burrowes et al., 2012; Sabbagh et al., 2008). The married ESRD patients are at almost 3 times risk of developing sleep disorders than single patients in our study, which is contradict the finding of Abassi et al (2016) and Chen et al,(2015) studies which reported no significant effect of spouse in the severity of sleep disorders. Our finding could be attributed that married patient are more under stress of life, particularly from socioeconomic, as well as his/her psychiatric status (Novak et al., 2006). The timing, and duration of dialysis could be differ, as the married patient have no time during the day for dialysis so using night shift dialysis, this will act as exacerbating factor for worsen sleep disorders. Moreover, genetic and familial condition could act as predisposing factors, in addition to the consanguinity marriages which is highly prevalent in our culture, particularly among old age group.

The presence of comorbidity, particularly DM with or without HTN showed significantly associated with sleep disorders in the current study. Such a result was supporting many studies (Araujo et al., 2011; Pai, et al., 2007; Unruh et al., 2006). While in contradict many other studies Chen, et al 2006; Sabry et al., 2010; Sabbatini et al., 2002. This discrepancy between the different studies can be attributed to several factors including the duration of the comorbidity and dialysis, age and gender of patients and type of treatment for the accompanied illness.

CONCLUSIONS AND RECOMMENDATIONS

Sleep disorders is a very common among patients with ESRD undergoing HD, Daytime sleep and frequent waking during night are the most common sleeping disorders symptoms, affecting more than half of the patients. A high rate of those patients had severe daytime sleepiness which warrants medical interventions. Old ages (50 years old or over), married patients, and the presence of chronic comorbidity, especially DM, are independent risk factors for developing sleep disorders among HD patients. Therefore our recommendations to the Nephrologists that they should increase their attention for sleep disorders among HD patients and use proper medications for severe cases. Chronic illnesses such as DM must be under control, with increase family support for those patients. Further assessment of sleep quality in HD patients is needed to include more risk factors such as duration and shift of HD and body mass index.

LIMITATION

The timing and duration of the dialysis, also duration of ESRD, family history and consanguinity of the patients were not recorded. However, one of this study's strengths that can be considered as the first study evaluating the sleeping disorders and factors related with. We have Identify the frequency and types of sleep disturbances, the risk factors and their possible consequences. Identify the need for treatment with general measures and drugs in the most severe cases which may have direct effects on ESRD

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COMPETING INTERESTS

The authors declare that they have no competing interests. Financial and non-financial competing interests.

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