MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2023.11.115.119

OPEN ACCESS

Key Words
Chronic kidney disease, end-stage renal disease, renal replacement therapy, hemodialysis and kidney transplantation

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Received: 16 September 2023
Accepted: 11 October 2023
Published: 12 October 2023

Citation: Dinesh Kumar Saini, S.H.N. Murali Krishna, Deepak Kumar Garg, Col Saxena Sr and Col Mohan Mahale, 2023. A Study on Prevalence of Sleep Disorders in Chronic Kidney Disease on Renal Replacement Therapy (Hemodialysis /Continuous Ambulatory Peritoneal Dialysis. Res. J. Med. Sci., 17: 115-119, doi: 10.59218/makrjms. 2023.11. 115.119

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A Study on Prevalence of Sleep Disorders in Chronic Kidney Disease on Renal Replacement Therapy (Hemodialysis/Continuous Ambulatory Peritoneal Dialysis)

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ABSTRACT
The burden of sleep disorders is higher amongst patients with End-Stage Renal Disease (ESRD) on hemodialysis and continuous ambulatory peritoneal dialysis compared to the general population and is associated with increased morbidity and mortality. The actual burden of sleep disorders amongst Indian patients with ESRD on hemodialysis and CAPD is not known. The objective of the study was to assess the prevalence of sleep disorders e.g. Insomnia and Obstructive Sleep Apnea (OSA), restless leg syndrome (RLS), excessive daytime sleepiness (EDS), periodic limb movement disorders (PLMD) in patients with ESRD on renal replacement therapy and to determine the associated sociodemographic, clinical and biochemical parameters. The present study was a Observational and Cross Sectional based study. This Study was conducted January 2018 and June 2019 at Department of Medicine Command hospital (Eastern Command), Kolkata. Total 75 patients were included in this study. The study was conducted between jan 2018 to july 2019. Out of the 75 patients analysed, 74% were males, mean age was 44.7(±16.1) and mean BMI was 23.1(±5.1) kg m^{-2}. 62(69.6%) had sleep disorders, 50 (66.6%) had PLMD, 42 (56%) had insomnia, 39 (52%) had Obstructive Sleep Apnea, 31 (41.33%) had EDS and 26 (34.7%) had RLS. We obtained a high prevalence of sleep disorders, similar to that reported in other populations. Assessment for and management of sleep disorders in ESRD patients on hemodialysis and CAPD should be an important component of care.

INTRODUCTION

Sleep is a rapidly reversible state of reduced responsiveness, motor activity and metabolism[1].

Sleep quality is defined subjectively as one's perception of falling asleep easily, getting sufficient duration so as to wake up feeling rested and making it through their day without experiencing excessive daytime sleepiness[2].

The prevalence of sleep disorders is greater in ESRD than the general population. Poor quality of sleep contributes to poor health-related quality of life in hemodialysis and CAPD patients[3].

Sleep disorders are common in ESRD patients and insomnia is one of the most common symptoms with a prevalence of 79.5%[4]. Sleep disorders contribute to poor sleep quality in ESRD patients[5]. There are more than 70 sleep disorders that have been described and they can be managed effectively once a diagnosis is made. The most common sleep disorders in hemodialysis and CAPD patients are Insomnia, OSA, EDS and RLS[6].

The true burden of ESKD in India is not known, with few dedicated centers for care, lack of universal access to RRT and absence of a registry. With increasing life expectancy and the prevalence of lifestyle diseases. In western countries, hypertension and diabetes.

account for over 2/3rd of the cases of CKD. In India too, hypertension and diabetes today account for 40-60% cases of CKD. China, India and the USA are among the top three countries with a high number of diabetic populations.

However, sleep complaints are under-recognized by health care providers[7]. Improving the quality of sleep and treating sleep disorders may improve quality of life in these dialysis patients.

MATERIALS AND METHODS

Study design

Study area: Department of Medicine Command hospital (Eastern Command), Kolkata.

Study period: the study will be conducted between January 2018 and June 2019.

Study population: The study population will consist of outpatients with end stage renal disease on renal replacement therapy (HD/CAPD).

Sample size: Seventy five.

Study type: Observational.

Observational model: Cross sectional.

Case definition

ESRD (End stage renal disease): According to Kidney disease improving global outcomes (KGIDO) End stage renal disease is defined as kidney damage or decreased kidney function (estimated Glomerular filtration rate of <15 mL min^{-1}) for three or more months (to differentiate it from Acute Kidney Injury) or with on hemodialysis/CAPD.

For purposes of this study we defined ESRD patients as receiving hemodialysis/CAPD of a period of three months or more.

Inclusion criteria:

- All individuals above 18 years of age
- On hemodialysis/continuous ambulatory peritoneal dialysis secondary to ESRD (duration >3 months)
- All those who will consent to the study
- Able to read English and/or Bengali

Exclusion criteria:

- Individuals on supplemental oxygen use, CPAP therapy
- Individual with feature of fluid overload
- Any evidence of active infection such as pulmonary infection, severe anemia, cardiac disease
- Individual with known psychiatric conditions (psychosis, mania, bipolar disorders)
- Individuals on anxiolytics and hypnotics
- Individuals on night shift work

RESULTS

The mean age of patients on chronic hemodialysis and CAPD was 54.49 (±11.70) years. Age of these subjects ranged between 24 and 79yrs. Male outnumbered female (74.7% male vs. 25.4% female). The mean BMI was 21.92 (±2.99) kg m^{-2}. Seventy seven percent of patients had a normal BMI (18.5-24.9), twelve percent having an elevated BMI (>25 kg m^{-2}). Sixty seven patients (89.3%) were on hemodialysis. Among these 60 (89.5%) hemodialysis patients were on twice a week. Eight (10.7%) patients were on CAPD out of 75. A total of seventy patients (93.3%) had moderate to severe anemia. Sixty-six patients having Serum albumin range of 2.8-3.5 g dL^{-1} and rest nine patients less than 2.8 g dL^{-1}. Sixty three patient had hyperphosphatemia (>4.5 mg dL^{-1}) and only ten patients are having normal range serum phosphate (2.5-4.5 mg dL^{-1}). There were comparable parameters in patients with and without sleep disorders.

The prevalence of sleep disorders was 62 (82.66%) in this study. The most common sleep disorder was periodic limb movement disorder (66%), followed by

Table 1: Prevalence of various sleep disorders in ESRD patients on renal replacement therapy

	Male		Female		Total prevalence	
Variables	No.	Percentage	No.	Percentage	No.	Percentage
Sample size	56	74.00	19	26.00	75	100.00
Sleep disorders	45	80.00	17	89.00	62	82.66
Periodic limb movement disorders PLMD	39	69.00	11	57.00	50	66.60
Insomnia	29	51.75	13	68.33	42	56.00
Obstructive sleep apnea OSA	31	41.33	8	42.00	39	52.00
Excessive daytime sleepiness EDS	26	48.20	6	31.50	31	41.33
Restless leg syndrome RLS	21	37.50	5	26.00	26	34.70

Table 2: Distribution of according to AGE, BMI (kg m^{-2}), HB, Alb, PHOSP, PLMD (HR), ESS

	No.	Mean	SD	Minimum	Maximum	Median
AGE	75	54.4933	11.7028	24.0000	79.0000	58.0000
BMI (kg m^{-2})	75	21.9283	2.9905	15.9439	31.9350	21.7193
Hb	75	9.0267	1.1728	5.7000	13.0000	9.0000
Alb	75	2.9733	0.2002	2.4000	3.5000	3.0000
PHOSP	75	5.3853	1.1531	2.3000	9.0000	5.3000
PLMD (HR)	75	47.6676	48.7901	0.0000	259.2000	29.6500
ESS	75	14.8000	5.3474	0.0000	30.0000	14.0000

SD: Standard deviation

insomnia (56%), obstructive sleep apnea (54.7%), excessive daytime sleepiness (41.7%) and restless leg syndrome 34.7% (Table 1).

In this study found to that RLS correlated with insomnia ($p = 0.015$), OSA ($p = 0.01$) and PLMD ($p = 0.00004$), EDS correlated with insomnia ($p = 0.026$) and PLMD ($p = 0.0008$). Also correlated sleep disorders with demographic and lab parameters except frequency of dialysis with EDS ($p = 0.03$).

Insomnia: Using the insomnia severity index (ISI >15) to assess for insomnia, forty two patients (56%) had insomnia. In this study noted that insomnia was more prevalent in presence of severe anemia (<8 g dL^{-1}) 77%, low albumin (78%), high BMI (>25) 53%; dialysis HD 53%, CAPD 75%; hyperphosphatemia 54% patients.

Obstructive sleep apnea: Using the overnight polysomnography study (AHI >5) to diagnosed OSA, forty one (54.77%) had obstructive sleep apnea. In this study found to that an obstructive sleep apnea was present in severe anaemic (<8 g dL^{-1}) 54.5%, low albumin (<2.8 g dL^{-1}) 55.6%; high BMI (>25) 88.9%; HD 56.8%, CAPD 37.5%; high phosphate (>4.5 mg dL^{-1}) 58.7% (Table 2).

Restless leg syndrome: Using the IRLSSG diagnostic criteria for RLS. It is noted that twenty six 26 (34.7%) patients had RLS.

Periodic limb movement disorder: PLM counted by overnight polysomnography test and for diagnosis of PLMD, PLM was required >15 hrs^{-1}. The prevalence of PLMD was 51 (68%) of ESRD patient on renal replacement therapy.

Excessive daytime sleepiness (EDS): EDS was a clinical diagnosis, based on the questionnaire of Epworth sleepiness scale. We found that the prevalence of EDS was 31 (41.7%) patients out of seventy five ESRD patients on renal replacement therapy. In this study it was found prevalence of EDS in severe anemic (63%), albumin (<2.8 g dL^{-1}) 55.5% patients.

DISCUSSIONS

This study aimed to establish the prevalence of sleep disorders in ESRD patients on renal replacement therapy (hemodialysis/continuous ambulatory peritoneal dialysis) such as insomnia, excessive daytime sleepiness, obstructive sleep apnea, restless leg syndrome and periodic limb movement disorder at a tertiary care hospital in India, by using a cross- sectional observational study design. There is existing literature with a few numbers of studies assessing the prevalence of sleep disorders in ESRD patients on renal replacement therapy from other countries although these studies established that such patient has a high prevalence of sleep disorders.

There is a paucity of such data in India, on the prevalence of sleep disorders in ESRD patient on the hemodialysis and CAPD. Compared to the population studied in the previous studies, there are significant differences in the socio-economic and cultural background of our population.

Additional to that, country to country variability recently noted by elder for the prevalence of sleep disorders in dialysis patients and could be explained at least in part by the Unruh *et al*.[8] study suggested a racial influence on self-reported sleep quality. The present study was therefore undertaken to evaluate the actual prevalence of sleep disorders and factors associated among Indian ESRD patients on HD and CAPD.

Various previous studies suggested that Sleep disorders are common in dialysis patients[9]. One regional study done was by Rai, who assessed the prevalence of insomnia and increase risk of sleep apnea in ESRD patients on hemodialysis and found

a prevalence of 60.9 and 24.6%, respectively. Gupta *et al*.[10] studied on clinical practice guidelines for sleep disorders in general population in India. Gupta *et al*.[10] noted commonest sleep disorder is insomnia (10-15%), followed by OSA (14%). Others studies of Pai *et al*.[11] (38) noted that 49- 65% patients insomniac. Another Indian study, Ahmad found to have 35.5% insomnia among in maintenance hemodialysis population. In this study, the prevalence of sleep disorders was 82.6%.

Insomnia as defined by the Insomnia Severity Index (ISI>15) overall was 56%. There is an association with hyperphosphatemia 54%, severe anemia 73%, hypoalbumin 77%, which is not a statistically significant difference, which is comparable to other studied[12].

OSA is common and causes significant comorbidities in patients with end-stage renal disease who are on dialysis; the various studied Chen *et al*.[12] reported that prevalence ranges from 20-90%. The major reasons for this variation in prevalence are the method of the diagnosis selected (questionnaire or overnight Polysomnography) and the definition used to diagnose OSA. The reported prevalence for OSA is much higher than those for the general population (14%)[12]. However, in this study, the prevalence of OSA was 54.7%, as defined by the AHI (>5) on PSG test and an association with age, frequency of dialysis and obesity. Similar other studies, also noted that an association between OSA and older age, frequency of hemodialysis and obesity[13]. However, some other reported studies did not find any suchassociations.

In this study, note that the 88.9% prevalence of OSA in the BMI (>25 kg m^{-2}), which is not statistically significant, similar finding also note in other studies which is comparable to the studies. Previous studies have reported an almost equal prevalence of OSA in patients undergoing both hemodialysis and peritoneal dialysis[14]. However, in this study did not find such similarity in twice a week and CAPD. Addition to that an association between restless leg syndrome and OSA ($p = 0.009$).

In this study, EDS, as measured by the ESS, was reported 41.33% of the patients in ESRD on dialysis. Similar finding noted in sleep complaints are common in a dialysis unit noted prevalence of EDS 67%, another study Johns *et al*.[15] also noted the prevalence of EDS 50%, one more study noted less prevalence 31% by using Epworth sleepiness scale. There is no statistically significant an association between demographic, lab parameter and excessive day time sleepiness. Based on previous studies reported that, the prevalence of restless leg syndrome among ESRD patient on renal replacement therapy ranges from 14-57% compared with a prevalence of 5-15% in the general population. In this study prevalence was 34.7% by using IRLSSG diagnostic criteria. Periodic limb movement disorder (PLMD) defined by PLM >15 hrs^{-1} in PSG study was 68%, was associated with underdialysis, which is a statistically significant difference ($p = 0.03$). Similar finding was reported in previous studies[16].

Many studied reported including current study, anemia was associated with various sleep abnormalities e.g., RLS, insomnia and EDS. Bilgic *et al*.[17] noted that Hypoalbuminemia associated with insomnia, in this study, we also found the same but it is not statistically significant.

In this study, noted that low frequency of dialysis and hyperphosphatemia were highly correlated with sleep disorders. Some studies Chen *et al*.[18] and Perl *et al*.[18] suggested an association between under dialysis, higher serum phosphate and sleep abnormalities.

PLMD increased the odd for sleep disorders in our study population. Such observation is in agreement with that in other previous studies, Pai *et al*.[11] and Noda *et al*.[19].

Strengths and weaknesses: This study was the first of its kind studying sleep disorders in our dialysis cohort. This was a questionnaire based study however we used validated questionnaires translated to Bengali for ease of understanding. Despite this a few individuals had difficulty in understanding some of the questions, based on how they were framed.

There are a few weak points of this study. One is the fact that this is an observational rather than a prospective study, with the known limitations of observational studies. The other weak point that may be noted is the fact that the questionnaires were not validated; however, in this study we did not devise any of our own instruments for assessment of sleep disorders but, used questionnaires that were validated in the general population.

In this study did not included comorbidities like as diabetes, hypertension cardiovascular disease and obstructive airway disease.

The study was carried out in a public referral hospital. It was not a multicenter study and the data presented may not be generalizable to all patients with ESRD on chronic hemodialysis and CAPD in India

CONCLUSION

This study illustrates that patients on chronic hemodialysis and continuous ambulatory peritoneal dialysis have various sleep disorders. PLMD, insomnia and OSA are also very prevalent our dialysis cohort.

RECOMMENDATIONS

Due to the very high prevalence of sleep disorders obtained in this study, all patients undergoing chronic hemodialysis and CAPD should routinely be administered the validated questionnaire to assess

their sleep disorders. The dialysis unit team (nephrologists, internal medicine residents, renal nurses and dialysis technician) involved in the care of patients on chronic dialysis should enquire about sleep complaints in these patients and where appropriate screen patients for sleep disturbances (Insomnia, RLS and OSA), those at high risk may be referred for objective test like polysomnography studies and medications initiated where appropriate. Further studies are needed to further elucidate the relationship between comorbidity and sleep disorders.

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