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RESEARCH ARTICLE

STUDY OF SLEEP DISORDERS IN PATIENTS WITH END STAGE RENAL DISEASE ON HAEMODIALYSIS: A HOSPITAL BASED CROSS SECTIONAL STUDY

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Abstract

Background: Sleep disorders are prevalent but underrecognized in patients with chronic kidney disease (CKD) in particular those with end stage renal disease (ESRD) undergoing dialysis therapy.⁹ Although variable, their prevalence has been reported to be much higher than in the general population

Aim: To study the pattern of sleep disorder in patients with end stage renal disease on haemodialysis and their association with comorbidities.

Material

and

Methods: This was a cross-sectional study on 100 patients attending the dialysis centre of Chalmeda Anand Rao Institute of Medical Sciences. Patient data was collected using a self-administered questionnaire.

Results: Of the 100 patients of end stage renal disease (ESRD) on haemodialysis, 76 (76%) had some form of sleep disorder. The pattern of sleep disorders was: 64 (84.21%) had insomnia, 25 (32.89%) had excessive daytime sleepiness (EDS), 20 (26.32%) had obstructive sleep apnoea (OSA), 7 (9.21%) had restless legs syndrome (RLS), 2 (2.63%) had nightmares and 2 (2.63%) had sleep-walking.

Patients with history of smoking ($p=0.034$) and history of alcohol consumption ($p=0.010$) or treatment with benzodiazepines ($p=.002$) were more prone to sleep disorders. Patients with sleep disorders were found to have lower hemoglobin and iron stores. An association was specially noticed between RLS and low iron status.

Conclusion: Three out of four of patients with ESRD on haemodialysis have sleep disorders. Insomnia was noted to be the commonest sleep disorder followed by EDS.

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Introduction:-

The human body has adapted to daily changes in dark and light such that it anticipates periods of sleep and activity¹⁻⁷. Deviations from this circadian rhythm come with functional consequences like sleep problems, which are common.

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Population studies show that sleep deprivation and disorders affect many more people worldwide than had been previously thought.

Sleep problems are associated with short and long-term effects on health and well-being. Immediate effects at the individual level relate to well-being, performance, daytime sleepiness and fatigue.

Longer term, evidence has accumulated of associations between sleep deprivation and sleep disorders and numerous health outcomes including premature mortality, cardiovascular disease, hypertension, inflammation, obesity, diabetes or impaired glucose tolerance, and psychiatric disorders, such as anxiety and depression.⁸

Sleep disorders are prevalent but underrecognized in patients with chronic kidney disease (CKD) in particular those with end stage renal disease (ESRD) undergoing dialysis therapy.⁹ Although variable, their prevalence has been reported to be much higher than in the general population. The most frequently reported complaints are insomnia, restless leg syndrome (RLS), sleep-disordered breathing and excessive daytime sleepiness (EDS).¹⁰ It has been reported that 80% of ESRD patients receiving dialysis have sleep complaints, with daytime sleepiness as the most common reported symptom.¹¹⁻¹³ They have a myriad of other problems including RLS and OSA.^{14,15} In addition, non-CKD-related renal disorders could be associated with some sleep disorders.

A number of studies⁹⁻¹² have been carried out recently to understand the real impact of sleep disorders on dialysis patients and identify whether these complaints are correlated with clinical and/or demographic data. However, to date, limited number of studies¹⁵⁻¹⁶ have been published on the epidemiology of sleep disorders in Indian settings.

Hence the Purpose of the present study was an attempt to find the prevalence and pattern of sleep disorders in such patients, from the south part of India.

Methods:-

1. Study Design: A Hospital Based Cross Sectional Study
2. Total Number of Sampling: 100
3. Study Center: Chalmeda Anand Rao Institute of Medical Sciences, Bommakal, Karimnagar
4. Study Duration: From January 2022 to December 2022 (1 year)
5. Inclusion Criteria: Participants were consecutive adult patients (≥ 18 years), men or women with ESRD on haemodialysis for at least 3 months.
6. Exclusion Criteria: Patients who developed acute kidney injury (AKI) or rejection in previously renal transplant patients where required dialysis were excluded from the study.

Data Collection:

Patients were interviewed and information regarding demographic data such as age and sex along with history of other co-morbid conditions such as, hypertension, diabetes mellitus, hypothyroidism, ischemic heart disease, cerebrovascular disease/neurological disorders, lung related complications were obtained. Also patients were asked about the personal history such as smoking, alcohol consumption, chewing tobacco, consumption of coffee multiple times a day. The dialysis history, duration of dialysis, frequency of dialysis, shift of dialysis, were collated. History of consumption of medications like benzodiazepine, antidepressant, CNS stimulants, theophylline, steroids and recent withdrawal of narcotics/benzodiazepine, which might impact sleep pattern was looked for.

A thorough physical examination was conducted for anthropometry followed by systemic examination.

Outcome variables:

Patients were evaluated for sleep disorders by interviewing them with a questionnaire¹⁻⁷, by the principal investigator. Using the questionnaire¹⁻⁷ following sleep disorders was identified.

1. Insomnia¹⁻²
2. Restless legs syndrome³
3. Obstructive sleep apnea syndrome (OSAS)⁴
4. Excessive daytime sleepiness (EDS)⁵
5. Possible narcolepsy⁶
6. Sleepwalking and Nightmares⁷

IEC Approval:

This study was approved by Institutional Ethics Committee (IEC) and Scientific Research Committee (SRC). Informed consent was taken from each patient, before collecting the data.

Statistical Analysis:

The data obtained was coded and entered into Microsoft Excel Worksheet. The data was analyzed using statistical software SPSS version 20.0. Continuous variables analyzed for normality by the Shapiro-Wilk test and those with normal distribution were presented as mean \pm standard deviation (SD) and those did not follow normal distribution were expressed in terms of median and interquartile range (IQR). Categorical variables were compared using the Chi-square or Fisher's exact test while continuous variables with normal distribution were compared using Independent t-test and those did not follow normal distribution were tested using Mann-Whitney U test. At 95% confidence interval (CI), a probability value ('p' value) of less than or equal to 0.05 was considered to be statistically significant.

Results:-

Of the 100 patients studied, 76 (76%) had some form of sleep disorder. Further, the pattern of sleep disorder: 64 (84.21%) had insomnia, 25 (32.89%) had excessive daytime sleepiness, 20 (26.32%) had OSA, 7 (9.21%) had RLS, 2 (2.63%) had nightmares and 2 (2.63%) had sleep-walking.

The mean age of the study population was 61.36 ± 13.0 . Of the patients, 39% were aged between 61 to 70 years. The maximum prevalence i.e. 43.42% of the sleep disorders, was in patients aged between 61 to 70 years. But no linear association was found between sleep disorders and age ($p=0.086$). The number of patients in the 71-90 age group were too few to derive any conclusion.

In the present study, 64% of the patients were males and the male to female ratio was 1.77:1. Further, 61.84% of the males had sleep disorders compared to 38.16% of the females. However, this difference was statistically not significant ($p=0.474$).

Hypertension was noted in 97%, diabetes mellitus in 60%, hypothyroidism in 37% and lung related complications in 27% of the patients. However, no association was found between sleep disorders with hypertension ($p=0.435$), diabetes mellitus ($p=0.516$), hypothyroidism ($p=1.000$), obesity ($p=0.576$) or psychiatric disorders ($p=0.576$). The number of patients with co morbidities like psychiatric disorders were too small to derive any conclusion.

The frequency of dialysis was three times per week in 84% of the patients. Further, 84.21% of the patients with three times per week dialysis, had sleep disorders. But, no association was found between sleep disorders and the frequency of dialysis ($p=0.571$). The number of patients with frequency of dialysis as two times per week was relatively small, to make any conclusions.

In this study, 34% of the patients were scheduled for dialysis in the evening and 32% in the morning. However, the frequency of sleep disorders was comparable among the patients who were undergoing dialysis in different shifts ($p=0.553$). The subset of patients with dialysis during night shift was inadequate to derive any conclusion.

History of smoking and alcohol consumption was noted in 45% and 44% of the patients respectively, while history of chewing tobacco and consumption of coffee multiple times a day was noted in 4% and 2% respectively. Significantly higher number of patients with history of smoking (51.32%; $p=0.034$) and history of alcohol consumption (51.32%; $p=0.010$) had history of sleep disorders.

However, no association was found between sleep disorders and chewing tobacco (3.95%; $p=0.673$), and consumption of coffee multiple times a day (2.63%; $p=0.576$), maybe due to the smaller subset of patients with consumption of coffee multiple times a day.

Treatment history of Benzodiazepines and CNS stimulant was noted in 20% and 1% of the patients respectively. Sleep disorders were significantly high in patients with treatment history of benzodiazepines (26.32%; $p=0.002$). However, no association was found between sleep disorders and treatment history with CNS stimulant (1.32%; $p=0.760$). Since none of the patient had treatment history of antidepressant, theophylline steroids and recent withdrawal of narcotics/benzodiazepines and only a handful of patients were on CNS stimulant no firm conclusion could be made regarding their contribution.

The serum haemoglobin and iron profile seemed to have an impact on sleep disorders. In this study, the median haemoglobin levels were found to be significantly lower in patients with sleep disorders (8.60 gm%) compared to those who did not have sleep disorders (9.90 gm%) ($p = 0.002$). Low levels of iron (iron = 30 mcg/dl) ($p = <0.001$) and ferritin (205.75 ng/ml) ($p = 0.001$), were more prevalent in those with sleep disorders.

In this study, about 9 % i.e. 7 patients had restless leg syndrome ($N = 7$). Almost all the patients with restless leg syndrome had low iron (iron = 30 mcg/dl) and relatively low ferritin (205.75 ng/ml) when compared to patients with other sleep disorders.

Table 1:- Comparison of Clinical profile of the patients:

Sleep disorders					
Parameters	Absent (n=24)		Present (n=76)		pvalue
	Median	IQR	Median	IQR	
Hemoglobin (gm%)	9.90	1.08	8.60	1.70	0.002
Iron (mcg/dL)	64.00	18.75	38.00	30.00	0.001
Ferritin (ng/mL)	350.00	45.00	220.00	205.75	0.001

Discussion:-

Sleep disorders are common in patients with ESRD undergoing dialysis. They typically exhibit poor sleep architecture as measured objectively on polysomnographic studies. The most frequently reported complaints are insomnia, RLS, sleep-disordered breathing and EDS. These lead to a significant negative impact on functional health status in uremic patients, hence recognition and effective treatment of these conditions may help in restoring their quality of life.¹⁷

However, limited studies^{10,17,18} have been done in Indian settings in this regard and no such study has been undertaken from Eastern part of India. Hence the present study was an attempt to delineate the prevalence and pattern of sleep disorders in such a study population.

In the present study, 76% of the patients were diagnosed to have sleep disorders. These observations were consistent with several other previous studies. Sabry et al.¹⁸ reported sleep disorders in 79.5% in a haemodialysis population from Egypt and Merlino et al.¹⁷ reported them in 80.2% of the patients in Italy. Similarly in a study by Walker et al.¹², 83.3% of the patients were seen to have sleep-wake complaints in Canada. In contrast to the observations from the present study, some earlier studies reported lesser prevalence of sleep disorders. Friedrich RM.²⁰ noted in 1980, that only 42.7% of patients on dialysis had sleep disorders and Strub et al.¹⁹ noted them in 63% in 1982.

The variation in the prevalence of sleep disorders noted in the present study and those of Strub and Friedrich may be explained by the country to country and ethnic variability on self-reported sleep quality. On the other hand, the studies by Strub et al.¹⁹ and Friedrich et al.²⁰ were done earlier, about 30 years ago. The life stresses may have increased since then, with the changing global socio-economic condition.

In the Indian setting, Pai et al.¹⁰ conducted a study in Yenepoya Medical College, Mangalore, regarding the quality of sleep and sleep abnormalities in patients with ESRD. Patient data were collected using Pittsburgh Sleep Quality Index (PSQI). Scoring of seven components answers was based on a 0 to 3 scale which reflects the various states of sleeping disorders. Study showed that during the earlier stage of haemodialysis patients may have a high PSQI test score. In the period of 3-12-month patients were facing poor sleep quality; indicating that in the earlier period of treatment patients may have taken more stress and conscious to adjust with haemodialysis as a routine treatment procedure for the rest of the life. This may have caused a high score in PSQI test. The study concluded that RLS, poor quality sleep, and EDS are common in ESRD patients on HD.

Now looking at the pattern of sleep disorders, in this study the pattern insomnia (84.21%), EDS (32.89%), OSA (26.32%), RLS (9.21%), nightmares (2.63%) and sleep walking (2.63%), was somewhat similar to the findings from the study by Merlino et al.¹⁷ who reported insomnia (69.1%), OSA (23.6%), RLS (18.4%), EDS (11.8%), narcolepsy (1.4%), sleepwalking (2.1%), nightmares (13.3%) and rapid eye movement disorders (2.3%).

As in this study, a number of others have identified insomnia as the commonest sleep disorder in dialysis patients. In addition to Merlino, Sabri et al.¹⁸ reported insomnia in 65.9% and Sabbatini et al.²¹ in 45% of patients.

In the present study, the second most frequent sleep disorder was EDS which was present among nearly one third (32.89%) of the patients. This was comparable with the study by Sabri et al.¹⁸, where EDS was noted in 27.3%. However, Merlino et al.¹⁷ reported EDS in 11.80% of the patients.

OSA is a frequent disorder in patients with ESRD on dialysis.¹⁷ In the present study, the third most common sleep disorder was OSA which was present among 20 (26.32%) patients. Among them, nine (45%) had OSA I, three (15%) had OSA II and eight (40%) had OSA III sleep disorders. The prevalence of OSA noted in the present study was comparable with the previous studies by Merlino et al.¹⁷ and Sabri et al.¹⁸ where OSA was noted in 23.6% and 31.8% of the patients.

In the present study RLS was noted in a few patients (9.21%), in contrast to studies by Sabri et al.¹⁸, who reported RLS in 42% of the patients.

In the present study few patients had nightmares and sleep walking, (2.63%) each. Merlino et al.¹⁷, reported sleep walking in 2.1% of the patients, which was similar to the present study but reported nightmares in 13.3%. On the other hand, none of the patients had nightmares in the study by Sabri et al.¹⁸, while sleep walking was evident in 3.4% of the patients.

In the present study 64% of patients were male and most of the patients (39%) were aged between 61 to 70 years. No association was found between sleep disorders with age or gender. Sabri et al.¹⁸ also did not detect any significant correlation between sleep disruption and age or gender. In contrast, Merlino et al.¹⁷ reported that increasing age was a predictor of sleep disorders.

With regard to comorbidities, in the present study, hypertension was noted in majority of the patients (97%) followed by diabetes mellitus (60%), hypothyroidism (37%), coronary artery disease (CAD) (35%), lung related complications (27%) and cerebrovascular accident (CVA)/Neurological disorder (14%) but, no association was found between sleep disorders and these comorbidities. The study by Sabri et al.¹⁸ found a correlation of psychological factors such as depression, anxiety, and social worry with the impairment of sleep quality in chronic dialysis patients which was similar to the present study. Unruh et al.²⁰⁻²² noted that sleep-disordered breathing (SDB) was more common in diabetic patients on HD.

In this study, history of smoking (45%) and alcohol consumption (44%) were noted in nearly half of the study population. Significantly higher number of patients with history of smoking (51.32%; $p=0.034$) and history of alcohol consumption (51.32%; $p=0.010$) had sleep disorders. No association was found between sleep disorders and chewing tobacco. Merlino et al.¹⁷ also highlighted the fact that excessive alcohol intake and cigarette smoking are independent predictors of sleep disorders.

In the present study, the frequency of dialysis was three times per week in majority (84%) of the patients. No association was found between sleep disorders and the frequency of dialysis. In contrast, under dialysis was considered by Chen WC. et al.²⁴⁻²⁵ as a factor that increased the likelihood of sleep disruption in hemodialysis patients, and Perl J. et al.²³ regarded the sleep abnormality as a marker of inadequate dialysis. In this study, since the number of patients with twice a week dialysis were relatively small, we may not have found any correlation, with frequency.

In this study, 32% of patients were scheduled for dialysis in the morning, 21% in the afternoon, 34% in the evening and 13% in the night. However, the frequency of sleep disorders was comparable among the patients who were undergoing dialysis in different shifts. In contrast, Merlino et al.¹⁷ observed that, dialysis shift was associated with sleep disorders and reported that this association is due to the link between the morning shift and insomnia.

In this study, 20% of the patients had been treated with benzodiazepines and 1% reported taking CNS stimulants. Intake of benzodiazepines was definitely associated with sleep disorders.

The median hemoglobin levels were found to be significantly lower in patients with sleep disorders (8.60 gm%) compared to those who did not have sleep disorders (9.90 gm%). Same observations were noted with respect to iron

and ferritin levels. Similar findings were reported by Sabri et al.¹⁸ who observed that anemia correlated with the most frequently reported sleep abnormalities, insomnia and RLS.

Low levels of iron have been implicated as the primary cause of RLS and this is directly linked to CKD and dialysis.¹⁵ Maunget al.¹³ hypothesized that, brain iron dysregulation plays a role in RLS,²⁶ possibly during transport across the blood brain barrier. Since iron is an essential cofactor in the production of dopamine, low iron levels could explain the changes in dopamine metabolism that occur in RLS. The syndrome is worsened by iron deficiency and symptoms are improved by iron supplementation. RLS sufferers show a drop in CSF ferritin levels throughout the night, while healthy controls do not. Circadian changes in brain iron status are what make this a circadian disease.¹³

The limitations of the study were that, the data was collected from a relatively small sample size of patients from a single center. Secondly, owing to the smaller subset of patients with different sleep disorders and in the night shift, small number of patients having twice weekly dialysis and in the 70-90 year group, all the variables responsible for sleep disorders could not be analyzed adequately.

Finally, long term outcome was not considered as it was beyond the scope of this study period.

Sleep disorders are common in patients with ESRD undergoing dialysis and one must realize a need for a team approach involving nephrologists and a neurologist/sleep specialist to recognize and treat the complaints regarding sleep, in order to improve the quality of life, reduce health related risks,²⁷ and mortality in these patients.

Conclusion:-

A substantial number of patients with ESRD on hemodialysis have sleep disorders. Insomnia followed by EDS are the most common maladies. Patients with history of smoking, alcohol consumption or treatment with benzodiazepines are more prone. Anemia, especially iron deficiency, has a correlation with disordered sleep. Low iron status was more prevalent in patients with RLS.

Conflict of Interest:

Nil.

Funding:

Nil.

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