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Risk Assessment for Obstructive Sleep Apnea in End Stage Renal Disease Patients Undergoing Maintenance Hemodialysis

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ABSTRACT

Background: Obstructive Sleep Apnea (OSA) is prevalent among patients with End Stage Renal Disease (ESRD) undergoing maintenance hemodialysis (MHD). OSA exacerbates cardiovascular risk and negatively impacts quality of life in these patients. This study aims to assess the prevalence and risk factors of OSA in ESRD patients undergoing MHD in a southern region of India. *Methods:* This exploratory observational cross-sectional study included 64 ESRD patients undergoing MHD. Participants were assessed using a customized case record form (CRF) collecting demographic data, medical history, presenting symptoms, and clinical examination findings. OSA risk was evaluated using the STOP-BANG questionnaire. Statistical analysis involved linear regression to explore associations between STOP-BANG scores and various patient parameters *Results:* Of the 64 patients (59.38% male, 40.63% female), 70.31% were over 40 years old. High OSA risk (STOP-BANG score ≥5) was identified in 17.19% of males and 3.13% of females. Common presenting symptoms included tiredness (56.25%), difficulty in falling asleep (54.68%), and frequent awakenings (46.87%). Hypertension (82.81%), diabetes mellitus (32.81%), and obesity (25.00%) were prevalent comorbidities. Linear regression revealed significant correlations between STOP-BANG scores and age, neck circumference, and height. *Conclusion:* The study highlights a substantial risk of OSA among ESRD patients on MHD, emphasizing the need for routine OSA screening and management in this population to mitigate cardiovascular risks and improve patient outcomes. Future research should focus on intervention strategies and longitudinal outcomes of OSA management in ESRD patients.

Index Terms **- ESRD, Hemodialysis, STOP-BANG, OSA, Screening**

INTRODUCTION

Sleep apnea occurs when the upper respiratory tract experiences interruptions lasting longer than 10 seconds during sleep. Obstructive Sleep Apnea (OSA) leads to recurrent arousals from sleep, oxygen desaturations, daytime sleepiness, fatigue, and cognitive impairment. This can have an adverse impact on quality of life. OSA is a common medical disorder affecting between 9% and 38% of the global adult population and from India, the prevalence of OSA in the general adult population ranges from 3.7% to 21%.[1] Accumulating data suggests a bidirectional relationship between OSA and CKD. That is, CKD likely confers an increased risk of OSA, and OSA may in turn increase the risk of renal injury.[2] According to studies, hemodialysis patients have a 10 times higher prevalence of sleep apnea than healthy individuals. According to estimates, sleep apnea is seen in 50–70% of maintenance hemodialysis (MHD) patients.[3] OSA disrupts sleep, leading to daytime symptoms, such as excessive daytime sleepiness. In the meantime, repeated oxygen saturation drops increase

oxidative stress and stimulate the sympathetic system, leading to hypertension and an increased cardiovascular risk. Diagnosing OSA is therefore important in the management of End Stage Renal Disease (ESRD) patients undergoing MHD with high cardiovascular morbidity and mortality since it is a treatable condition.[4]

NEED OF THE STUDY

Given the significance of sleep apnea and the high rates of cardiovascular disease and complications in ESRD patients, in addition to the limitations of prior studies on the prevalence of this disease and its risk factors in ESRD patients in India, the current study aimed to 'assess for the presence of risk factors of sleep apnea in ESRD patients undergoing hemodialysis.'

RESEARCH METHODOLOGY

The study was an exploratory, observational, cross-sectional study. After obtaining approval from the Institutional Ethics Committee (IEC approval number BMJH/DNB043/79/2016/02), the study was conducted from June 2015 to May 2016. All the adult patients above 18 years with ESRD undergoing MHD were considered for inclusion in the study. Patients who were critically ill, elderly, and not willing to give consent to participate in the study were excluded. The procedures were explained in simple terms and a consent form with details of procedure incorporated was given to the study participants. After obtaining consent, patients who presented to the study center for MHD and met the inclusion/exclusion criteria were subjected to history and examination as per a customized case record form (CRF) developed for the study.

In the present study, CRF had two parts for data collection. The first part included demographic parameters such as age, sex, weight in kilogram, height in centimeter, and body mass index (BMI). In addition, it included history of presenting complaints, most common habits before going to sleep, and relevant clinical examination findings. Presenting symptoms such as tiredness/easy fatigability, difficulty in falling asleep, frequent awakenings, problems in re-initiating sleep, early awakenings, impaired memory/concentration, loud snoring, excessive daytime sleepiness during reading/talking/watching television/driving/meetings, loss of libido, nightmares/panic attacks, un-refreshed sleep, morning headache, sleep walking/talk/eating, choking, sleep attacks (irresistible sleep), enuresis, sleep paralysis, abnormal leg movements, automatisms, and road traffic accident; Co-morbid conditions such as hypertension, diabetes mellitus, short neck, obesity, micrognathia, retrognathia, COPD, ischemic heart disease, hyperthyroidism, use of sleeping pills, cerebrovascular accidents, duration of ESRD in years, and frequency of dialysis per week.[5]

The second part of the questionnaire was a risk assessment of OSA using the STOP-BANG questionnaire. STOP-BANG questionnaire is a valid and effective screening tool for OSA in different populations and has a very strong identification ability. This questionnaire consists of eight items, including snoring, tiredness, observed apnea, hypertension, BMI ≥35 kg/m^2, age ≥50 years, neck circumference >40 cm, and male gender. Responses were graded as "Yes (Score 1)" for the presence of risk factors and "No (Score 0)" for absence. The patients were classified as those with STOP-BANG scores≥ 3 as being at risk for OSA. The results of STOP-BANG scoring and clinical examination that were performed were recorded in the study CRF and considered for analysis.[6] In addition, details of activities two hours before sleeping such as watching television, using mobile, coffee, smoking, computer, reading, and use of alcohol were also collected and presented in the form of a table along with other risk factors.

STATISTICAL ANALYSIS

The values were expressed in frequency, proportions, mean, and standard deviation (SD) as appropriate. Linear regression analysis of individual parameters with STOP-BANG score was done using Graph Pad InStat 3 statistical software. $p \leq 0.05$ at a 95% confidence interval was considered significant. Linear regression analysis output is presented as *R-value*, Slope, and 95% confidence interval from to values. The parameters such as Neck circumference, Age, Height, Weight, BMI, Sleep Latency, Duration of ESRD, Frequency of Hemodialysis, and Sleep duration in hours were considered for correlation analysis with STOP-BANG score and same is presented in the form of figures (Fig No. 01). MS Word and MS Excel were used to generate tables as necessary.

RESULTS AND DISCUSSION

DEMOGRAPHIC PARAMETERS

In the present study, sixty-four (64) ESRD patients who were on MHD were considered for analysis. Both male (N = 38, 59.37%) and female (N = 26, 40.63%) patients were included in the study. The majority (70.31%) of patients were aged more than 40 years. These patients underwent HD at least 1 time per week to a maximum of 3 times per week. The duration of ESRD ranged from 0.1 years to 22 years. Other demographic parameters details are given in **Table No. 1.**

Table No. 1: Demographic profile of ESRD patients on MHD

Parameter	Sub parameter	N=64 (%)	Mean ± SD	Comments/Inference
Age in Years and Gender	20-29 Yrs.	10 (15.63)	24.3±1.94	
	30-39 Yrs.	9 (14.06)	34.11±3.25	
	40-49 Yrs.	13 (20.31)	43.76±2.45	
	50-59 Yrs.	17 (26.56)	54.29±2.8	
	60-69 Yrs.	13 (20.31)	63.15±2.26	
	70-79 Yrs.	02 (03.13)	72±0	
	Male	38 (59.38)	46.02±15.88	Unpaired t-test. Comparison of age of Males Vs Females: p=0.5185 (not significant, t = 0.6494, df = 64)
	Female	26 (40.63)	48.38±11.46	
ESRD duration in years	-	64 (100.00)	5.56±4.47	Min=0.1, Max=22, Median=4
Hemodialysis frequency per week	-	64 (100.00)	2.29±0.49	Min=1, Max=3, Median=2
Body Metabolic Index	-	64 (100.00)	23.88±5.21	Min=15.8, Max=39.0, Median=23.4
Weight in Kg	-	64 (100.00)	60.87±13.81	Min=30, Max=103, Median=60.25
Height in cm	-	64 (100.00)	160.56±9.56	Min=138, Max=188, Median=161.5
STOP BANG Score: RISK OF OSA Low- 0 to 2 Intermediate- 3to4 High- >5	Male	≥5	11 (17.19%)	17.19% of male ESRD patients have the risk of OSA
		<5	27 (42.19%)	
	Female	≥5	02 (03.13)	03.13% of female ESRD patients have risk of OSA
		<5	24 (37.50)	

SYMPTOMS OF PATIENTS

The most common presenting symptoms were tiredness/fatigability (56.25%), difficulty in falling asleep (54.68%), frequent awakenings (46.87%), problems in re-initiation of sleep (45.31%), early awakenings (29.68%), etc. The frequency of presentation of other symptoms has been enumerated in **Table No. 2**.

Table No. 2: Symptoms at Presentation of ESRD and OSA patients undergoing MHD

Sl No.	Symptoms	No of ESRD patients N=64 (%)	At risk OSA patients, N=13 (%)
1.	Tiredness/fatigability	36 (56.25)	12 (92.30)
2.	Difficulty in falling asleep	35 (54.68)	10 (76.92)
3.	Frequent awakenings	30 (46.87)	13 (100.00)
4.	The problem in re-initiating sleep	29 (45.31)	13 (100.00)
5.	Early awakenings	25 (39.06)	09 (69.23)
6.	Impaired memory/concentration	19 (29.68)	07 (53.84)
7.	Loud snoring	17 (26.56)	07 (53.84)
8.	Excessive daytime sleepiness	12 (18.75)	06 (46.15)
9.	During reading/talking/watching tv/driving/meetings	11 (17.18)	04 (30.76)
10.	Loss of libido	08 (12.50)	04 (30.76)
11.	Nightmares/panic attacks	07 (10.93)	02 (15.38)
12.	Unrefreshed sleep	06 (09.37)	02 (15.38)
13.	Morning headache	04 (06.25)	00 (00.00)
14.	Sleep walking/talk/eating	03 (04.68)	00 (00.00)
15.	Choking	02 (03.12)	02 (15.38)
16.	Sleep attacks (irresistible sleep)	01 (01.56)	01 (7.69)
Note: None of the patients presented with enuresis, sleep paralysis, abnormal leg movements, automatisms, and road traffic accident.			

RISK FACTORS FOR OSA IN ESRD PATIENTS

A higher proportion of patients had hypertension (82.81%), diabetes mellitus (32.81%), Short neck (31.25%), Obesity (25.00%), Micrognathia (25.00%), and Retrognathia (25.00%) as co-morbid conditions. Watching television (42.19%), and use of Mobile (9.38%) were the most common activities that were prevalent two hours before sleep. Details of other risk factors and habits noted in the present study are listed in Table No. 3.

Table No. 3: Risk factors that were prevalent in ESRD patients undergoing MHD

Sl No.	Risk Factors		ESRD patients N=64 (%)	At risk OSA patients N=13 (%)
1.	**Co-morbid conditions**	Hypertension	53 (82.81%)	12 (92.30)
2.		Diabetes mellitus	21 (32.81%)	06 (46.15)
3.		Short neck	20 (31.25%)	05 (38.46)
4.		Obesity	16 (25.00%)	04 (30.76)
5.		Micrognathia	16 (25.00%)	05 (38.46)
6.		Retrognathia	16 (25.00%)	05 (38.46)
7.		COPD	4 (6.25%)	02 (15.38)
8.		Ischemic heart disease	3 (4.69%)	02 (15.38)
9.		Hyperthyroidism	3 (4.69%)	00 (00.00)
10.		Use of sleeping pills	1 (1.56%)	01 (7.69)
11.		Cerebro-vascular accidents	1 (1.56%)	01 (7.69)
12.	**Activities 2 hours before sleep**	Watching TV	27 (42.19%)	03 (23.07)
13.		Use of Mobile	6 (9.38%)	02 (15.38)
14.		Coffee	5 (7.81%)	01 (7.69)
15.		Smoking	3 (4.69%)	02 (15.38)
16.		Computer	3 (4.69%)	00 (00.00)
17.		Reading	2 (3.13%)	00 (00.00)
18.		Use of Alcohol	1 (1.56%)	01 (7.69)

Analysis of association of risk factors with ESRD using STOP BANG score:

Linear regression analysis of individual parameters (having continuous data) with STOP-BANG score suggested that: Considered significant and low positive correlation inferred with height (r=0.2681, Slope=1.782 (SE=0.8129, 95% CI is 0.1563 to 3.407), p=<0.0322) of patients; Considered not quite significant and very low correlation inferred with weight (r=0.2273, Slope=2.182 (SE=1.187, 95% CI is -0.1916 to 4.555), p=<0.0709); Considered not significant and very low correlation inferred with Sleep Latency (r=0.06007, Slope=1.710 (SE=3.608, 95% CI is -5.504 to 8.923), p=0.6373); Considered not significant and very low negative correlation inferred with duration of ESRD disease (r= - 0.1248, Slope= - 0.3880 (SE=0.3928, 95% CI is -1.171 to 0.3953), p=0.3259), frequency of hemodialysis (r= - 0.04398, slope= - 0.01509 (SE=0.04354, 95% CI is - 0.1021 to 0.07195), p=0.7300) and sleep duration in hours (r= - 0.1472, Slope= - 0.1610 (SE=0.1374, 95% CI is - 0.4357 to 0.1137), p=0.2457). (See Figure No. 1 A to I).

Figure No 1. Linear regression analysis of various parameters to find the association of risk factors with ESRD using STOP-BANG score analysis.

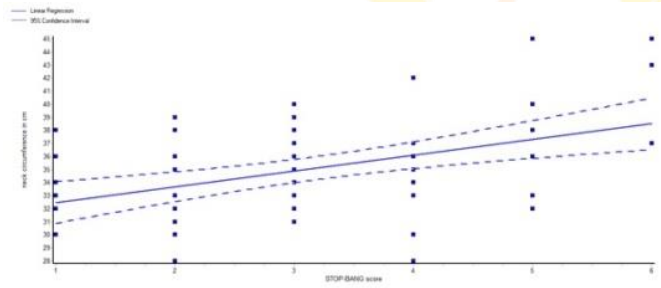


Fig 1A. STOP-BANG score vs. neck circumference. r=0.4428, Slope=1.205 (SE=0.3100, 95% CI is 0.2210 to 0.6210), p=0.0002**.

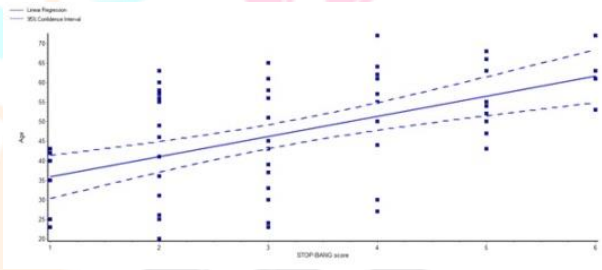


Fig 1B. STOP-BANG score Vs Age. r=0.5288, Slope=5.161 (SE=1.069, 95% CI is 3.024 to 7.297), p=<0.0001**.

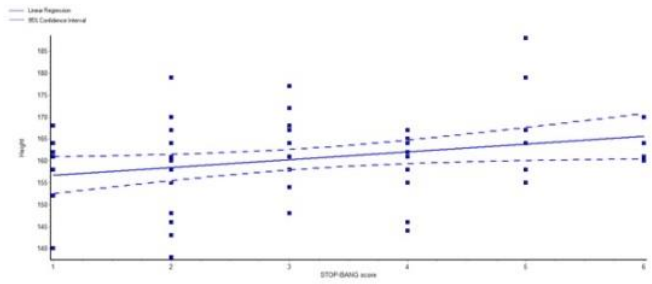


Fig 1C. STOP-BANG score Vs Height r=0.2681, Slope=1.782 (SE=0.8129, 95% CI is 0.1563 to 3.407), p=<0.0322*.

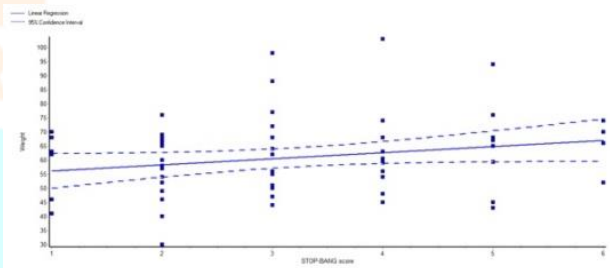


Fig 1D. STOP-BANG score Vs Weight r=0.2273, Slope=2.182 (SE=1.187, 95% CI is -0.1916 to 4.555), p=<0.0709$^{\#}$.

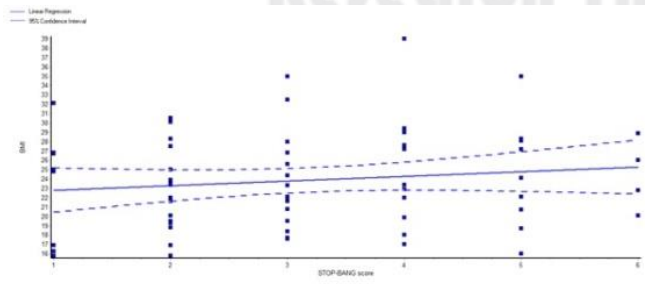


Fig 1E. STOP-BANG Score Vs BMI r=0.1366, Slope=0.4952 (SE=0.4560, 95% CI is -0.4165 to 1.407), p=0.2817$^{\$}$.

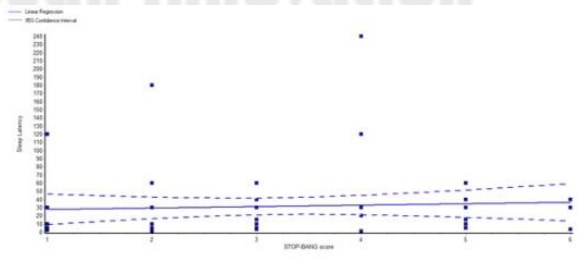


Fig 1F. STOP-BANG score Vs Sleep Latency r=0.06007, Slope=1.710 (SE=3.608, 95% CI is -5.504 to 8.923), p=0.6373$^{\$}$.

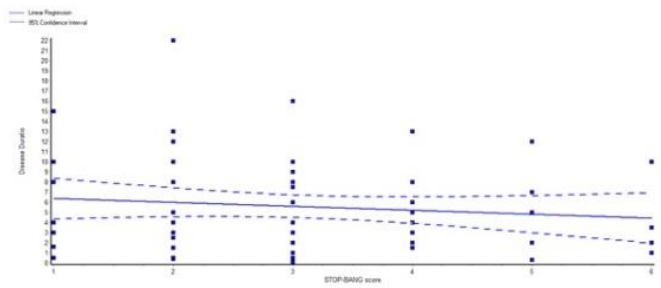


Fig 1G. STOP-BANG score Vs Duration of ESRD disease. r= - 0.1248, Slope= - 0.3880 (SE=0.3928, 95% CI is -1.171 to 0.3953), p=0.3259[@].

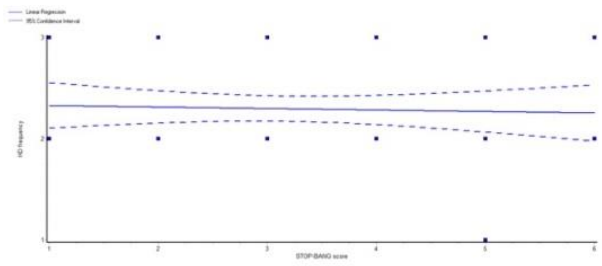
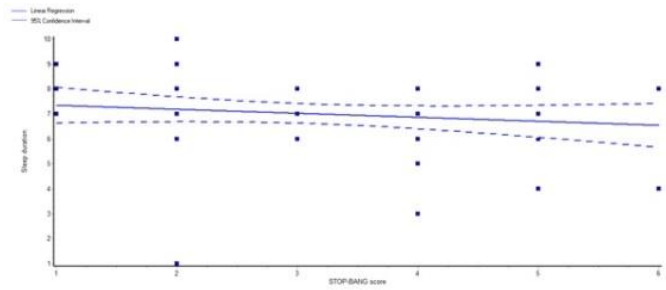


Fig 1H. STOP-BANG score Vs Frequency of Hemodialysis. r= - 0.04398, Slope= - 0.01509 (SE=0.04354, 95% CI is - 0.1021 to 0.07195), p=0.7300[@].



Note:
n=64, df=63, r = correlation coefficient
**considered extreemly significant and moderately positive correlation inferred.
*considered significant and low positive correlation inferred.
[#] considered not quite significant and very low correlation inferred.
[$]considered not significant and very low correlation inferred.
[@]considered not significant and very low negative correlation inferred.

End-stage renal disease (ESRD) patients have a higher risk of morbidity and require time-intensive care. It is an important chronic disease globally which can affect the quality of life and survival of the patient significantly. It affects a variety of populations throughout the world. Understanding the demographic factors, clinical features, and plausible risk factors can help us to identify the disease early and take preventive measures. Early detection and optimal management can improve patient outcomes. However, due to lower access to care, reactive treatment instead of proactive measures, can affect adversely. As reported by Gupta R et al [18] early detection, improved education level, and treatment of diabetes, hypertension, glomerulonephritis, and cystic kidney disease resulted in reduced ESRD. It was observed that Hypertension (N=53, 82.81%), Diabetes mellitus (N=21, 32.81%), Short neck (N=20, 31.25%), Obesity (N=16, 25.00%), and Micrognathia (N=16, 25.00%) were the common co-morbidities that were prevalent in the patients that were included in this study. These findings again recommend similar measures to detect and treat these diseases in early adulthood to prevent CKD and ESRD.

Similar data was provided by Singh P et al.[19] Causality of renal failure due to hypertension, diabetes mellitus, and renal calculi are explained by various authors. As per researchers, uncontrolled hypertension causes long-term damage to the blood vessels that supply the kidney. This affects the kidneys by reduction of oxygen and blood supply leading to failure of their function. Prolonged high serum glucose can result in damage and clogging of renal blood vessels affecting kidney function. Ureteral obstruction, hydronephrosis, and repeated infections due to renal calculi result in damage to the kidney. Prolonged obstruction in severe cases, can even lead to kidney failure. Therefore, chronic diseases were considered inconsequential as a causal factor for ESRD.

In our study, a good number of patients (N=36, 56.25%) were aged more than 45 years. In addition, there were a higher number of male patients (N=38, 59.37%) compared to female (N=26, 40.63%) patients suffering from ESRD. These findings were similar to the results published by Singh P et al[19]. As per their report, the most common age group for ESRD presentation was 46-60 years (52.1%). This may be due to the similar (Southeast Asian) populations were included in both studies. The results of the present study suggest the presence of sleep apnea in ESRD patients undergoing maintenance hemodialysis and investigate the effective factors in the occurrence of sleep apnea in these patients. The results showed that overall 20.31 % (n=13) of

patients had risk of obstructive sleep apnea (OSA). Out of which 17.19 % (n=11) was for males and 3.13% (n=2) for females.

A study by Forni Ogna et al., which aimed to determine the prevalence of sleep apnea and introduce a diagnostic approach for hemodialysis patients in Switzerland, showed that the prevalence of moderate to severe sleep apnea in ESRD patients was 56%.[4] Moreover, a study by Ghanei Geshlagh et al. showed that 41.7% of hemodialysis patients had sleep apnea in Iran.[7] Also, a study by Sabry et al. which aimed to determine the prevalence of sleep disorders in hemodialysis patients in Saudi Arabia showed that 31.8% of patients had these abnormalities.[8]

In contrast, some other studies reported a very high prevalence of sleep apnea in ESRD patients; a study by Huang et al. showed that 80% of ESRD patients had moderate or severe sleep apnea.[9] Also, another study investigated the prevalence of sleep disorders in hemodialysis patients in Iran and showed that the total prevalence of sleep disorders was 75% in these patients.[10] Overall, the prevalence of sleep apnea is high in ESRD patients, and the observed difference in the prevalence rates of different studies may be due to differences in the sample size, screening tools, diagnostic tools for measuring sleep apnea, and genetics.[11]
The main cause of the high prevalence of sleep apnea in ESRD patients is unknown. However, some studies have shown that uremic toxins, metabolic acidosis, chronic hypocapnia, amino-acid metabolism abnormalities, and hormone imbalance are associated with the occurrence of sleep apnea in ESRD patients. Given the high prevalence of sleep apnea in ESRD patients, its negative impact on the mental health and adaptability of patients, and its role in the increased cardiovascular morbidity and mortality of patients, it is essential to design and implement regular screening programs for the detection of sleep apnea in ESRD patients.[12,13]

Moreover, in the present study, the age of ESRD patients was showing a positive correlation. This finding is consistent with the results of previous studies, as they suggested older age as a risk factor for sleep apnea. This discrepancy may be attributed to the small sample size of our study. However, changes in the quantity and quality of sleep and the increased risk of sleep apnea in the elderly were observed, which may be due to the poor performance of muscles holding the open airway in the elderly.[14]

STOP-BANG scoring system is a widely accepted risk assessment method for OSA. It considers eight parameters such as snoring, tiredness, observed apnea, blood pressure, BMI, age, neck circumference, and gender. In our study, we observed a positive significant correlation with parameters such as age and neck circumference. In addition, a significant positive correlation was observed with height and weight parameters independently. However, BMI did not show any significant correlation with the STOP-BANG score. This may be attributed to lower mean BMI (23.88±5.21) noted in our population undergoing MHD. The findings of the present study showed that BMI had a very low correlation with the occurrence of sleep apnea in CKD patients, which is not in line with similar studies in this area. A study by Sadeghniiat-Haghighi et al., which aimed to determine the reliability and validity of the Persian version of the STOP-BANG questionnaire in a sleep clinic population (n=603), demonstrated a significant association between BMI and sleep apnea. Two other studies by Lurie and Moroni et al. showed a linear association between the increase in BMI and AHI. Also, previous studies have shown that a weight loss of 10% in obese patients could reduce AHI by 27%. Considering the important role of BMI and overweight in the development of sleep apnea, attention to this risk factor in the preventive and control programs of sleep apnea seems necessary.[15]

Sleep latency, duration of ESRD, and frequency of hemodialysis showed very low and insignificant correlation. Whereas sleep duration in hours showed a very low and insignificant negative correlation.[16] Consistent with previous studies,[8] our study found that only 23.19% of MHD patients met 5–7 ideal CVH metrics, less than half of the general Chinese population. Traditional risk factors for cardiovascular disease such as hypertension, diabetes, obesity, and lack of exercise are more common in MHD patients, while dialysis-related factors such as anemia, inflammation, oxidative stress, and fluid overload also increase the incidence of CVD events. However, the results of our study showed that despite regular visits to hospitals, MHD patients have a higher risk of cardiovascular disease than the general population and they are not well-controlled. Cardiovascular disease is the most common complication and the leading cause of death in MHD patients, so more attention should be paid to the prevention and control of CVD in HD patients.[17] One of the

limitations of this study is its cross-sectional design. Also, the small sample size (n=64) and the use of the STOP-BANG questionnaire rather than polysomnography, as the gold standard for OSA detection.

CONCLUSION

Poor sleep quality is common among dialysis patients and is associated with lower health-related quality of life. If OSA is one of the more prevalent sleep disorders within the dialysis patient population, perhaps screening for OSA ought to become a routine portion of case management of these patients. Early detection of sleep apnea in ESRD patients along with control of major risk factors associated with the disease prevents the occurrence of complications while undergoing maintenance hemodialysis allowing for better health-related outcomes in individual patients.

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