ORIGINAL ARTICLE

Prevalence and Clinical Features of Rapid Eye Movement-related Obstructive Sleep Apnea: A Cross-sectional Analysis of Clinical Population from South India

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Abstract

Introduction: Rapid eye movement (REM)-related obstructive sleep apnea (OSA) is a condition where apneas and hypopneas occur predominately during REM sleep. There is limited data on the prevalence of REM-related breathing disorders in the Indian population.

Aim of the study: To estimate the prevalence of REM-related OSA in a clinic-based population in South India.

Methodology: This cross-sectional observational study was done in a tertiary care center in South India from January 2017 to December 2019. Consecutive adult patients who underwent level-I polysomnography were enrolled. Apnea–Hypopnea Index (AHI) was computed as the total number of apneas and hypopneas per hour of total sleep time. Sleep-state-dependent indices were also determined by dividing the number of events in nonrapid eye movement (NREM) and REM sleep by the amount of NREM and REM time, respectively. Patients with an AHI greater than five were diagnosed with OSA and included in this study.

Rapid eye movement-related obstructive sleep apnea was defined as overall AHI ≥5 and AHI REM/AHI NREM ≥2.

Nonrapid eye movement-related OSA was defined as overall AHI ≥5 and AHI REM/AHI NREM ≥2.

Statistical analysis was performed using IBM SPSS version 21.0.

Results: One hundred ninety-nine patients diagnosed with OSA were included in the study. Rapid eye movement OSA has a prevalence of 24.12% in this population. Age >50 years and female sex were the factors associated with REM-predominant OSA, while T88% >20% was associated with NREM OSA.

Conclusion: Rapid eye movement-related OSA is prevalent in South Indian patients referred for evaluation of sleepiness.

Keywords: Gender, Obstructive sleep apnea, Rapid eye movement.

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Introduction

Obstructive sleep apnea (OSA), which denotes an intermittent mechanical obstruction of the upper airway during sleep and results in decreased airflow to the lungs, is one of an array of disorders that make up the sleep-disordered breathing (SDB) spectrum.[1]

Obstructive sleep apnea episodes may occur both during rapid eye movement (REM) and nonrapid eye movement (NREM) sleep in SDB patients. Apneas and hypopneas predominantly happen during REM sleep in REM-related SDB. Few studies from the Western world show a prevalence ranging from 13.5 to 36%.[2] The pathophysiology of REM-related OSA is under research. Hypotonia of the upper airway muscles raises the probability of obstruction of upper airways during REM sleep.[3] A cohort study shows an independent association of REM-related OSA with significant metabolic and cardiovascular risk factors such as hypertension, metabolic syndrome, and diabetes.[4] Determining the prevalence of this phenotype of OSA in the Indian population will help in identifying and correcting the risk factor for these metabolic complications. Data on the prevalence of REM-related respiratory issues in the Indian population are limited. The purpose of this study is to provide insight into the prevalence and clinical characteristics of REM-related OSA in the Indian population.

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Study Objectives

Primary

To determine the prevalence of REM-related OSA in a south Indian clinic-based population.

Secondary

- To compare the demographic and polysomnographic characteristics in patients with REM- and NREM-related OSA patients.
- To find the factors associated with NREM- and REM-related OSA.
- To determine the continuous positive airway pressure (CPAP) prescription trends among individuals with OSA related to REM.

Study Design

A cross-sectional observation (retrospective evaluation of prospectively collected data).

Study Setting

Department of Respiratory Medicine, AIMS, Kochi.

Methodology

The study was done after the hospital's Institutional Review Board (IRB) approval.

Consecutive adult patients who underwent level-I polysomnography from January 2017 to December 2019 were included in the study at the Department of Respiratory Medicine. Using the 2.4 edition of the American Academy of Sleep Medicine's (AASM) Manual for the Scoring of Sleep and Associated Events, biophysiological changes in the polysomnography (PSG) equipment were assessed.[5]

Apnea is defined as a larger than 90% reduction in airflow that lasts for at least 10 seconds and has a persistent respiratory effect. Hypopnea is defined as a decrease in airflow of more than 30% accompanied by electroencephalographic arousal or a 3% drop in SaO_2.

The number of apneas and hypopneas experienced during a given hour of sleep was used to compute the Apnea–Hypopnea Index (AHI). By dividing the total number of events during NREM and REM sleep by the corresponding NREM and REM duration, the sleep-state-dependent indices (i.e., NREM–AHI and REM–AHI) were also calculated. Patients having an OSA diagnosis with an AHI of five or higher were included in this study.

Definitions

Rapid eye movement -related OSA was defined as AHI ≥ 5 and AHI REM/AHI NREM ≥2.

Nonrapid eye movement-related OSA is defined as overall AHI REM / AHI NREM ≥2 and AHI ≥5.

In addition to an AHI of less than 5 events/hour in a nonsupine posture, supine-isolated OSA is defined as a doubling of AHI in a supine position.

Apnea–Hypopnea Index nonsupine >2 events/hour, and AHI nonsupine <5 events/hour.

Supine-predominant OSA was defined as a doubling of AHI in the supine position versus the nonsupine position, where the nonsupine AHI may remain >5 events/hour.

AHI supine: AHI nonsupine >2 events/hour and AHI nonsupine ≥5 events/hour.

Patients not meeting the above criteria (i.e., events are scattered throughout nonsupine and supine position) were classified as position-independent OSA.

Demographic information included gender, age, and body mass index (BMI). We compared the patient characteristics between REM-related OSA and NREM-related OSA done. Patient's medical records were checked for positive airway pressure (PAP) prescription data.

Statistical Analysis

In order to perform the statistical analysis, IBM SPSS version 21.0 (Chicago, USA) was used. In order to express categorical variables, frequency and percentage are used. Mean, standard deviation (SD), and range are used to express continuous variables, whereas standard deviation and median with interquartile range. The Chi-square test was performed to see whether there was any difference in the proportion of age between the two groups. For testing the statistical significance of the difference in the mean and median continuous variables between the two groups, Mann–Whitney *U* test for skewed data and Student's *t*-test for normal data were employed. Then, to determine the odds ratio (OR) and the 95% confidence interval (CI), a multivariate logistic regression analysis was carried out to find variables independently linked with REM OSA. A *p*-value of less than 0.05 was taken as significant.

Results

From January 2017 to December 2019, 386 patients got referred to a sleep lab at the Department of Respiratory Medicine. Clinical suspicion of OSA, which was supported by symptoms, including snoring, increasing daytime sleepiness, witnessed apnea, and morning headache, was the reason for their referral. Obstructive sleep apnea was diagnosed based on an AHI value of >5. Consequently, these patients were included in the study. Accordingly, 199 patients were included.

The baseline demographic and polysomnographic features of the study population are depicted in Table 1.

Rapid eye movement OSA has a prevalence of 24.12% in this population. Between REM OSA and NREM OSA, there was a statistically significant difference in sex ratio (male: female), snoring index, AHI, and mean apnea duration. Male: female ratio was more in NREM OSA in comparison with REM OSA. The average age of patients showed no statistically significant difference between the two groups (p-value = 0.270). The median of arousal index for REM OSA was 13.5 (5.93–25.4), and in NREM OSA was 18 (9.7–34). It shows that arousal was more frequent in the NREM OSA group. The median of the snoring index in REM OSA was 369 (IQR 230–504), and in NREM OSA was 292 (IQR 192–429). The median of minimum oxygen saturation in REM OSA was 81.4 (IQR 74.35–87), and in NREM OSA was 79.1 (IQR 65–89.6). The median of AHI in REM OSA was 10.7 (8.23–15.83), and in NREM OSA was 25 (11.1–44). This shows that most of the patients with REM OSA belonged to mild OSA group as per the AHI, but most NREM OSA patients were in the severe or moderate OSA group. The median of mean apnea duration in REM OSA was 19.5 (IQR 17–22.56), and in NREM OSA was 16 (IQR 9.1–26). The median of REM duration in REM OSA was 19.8 (10.6–36.5), and in NREM OSA was 21.5 (8.6–39.6). The median of REM% in REM OSA was 5.9 (3.0–9.7), and in NREM OSA was 4.5 (0.3–9.5). Snoring index, AHI, and mean apnea duration showed a statistically significant difference between NREM OSA and REM OSA ($p = 0.045$, $p < 0.001$ and $p = 0.008$, respectively). In contrast, minimum oxygen saturation, REM duration, and REM percentage did not show any difference statistically between the two groups.

Among 113 patients with age ≥50, 30.1% had REM-related OSA compared with 16.3% in age <50 years, which was statistically significant ($p = 0.024$). About 43% of the females had REM OSA

Table 1: Baseline demographic and polysomnographic variables

	Mean ± SD			
	Total study population	*REM OSA*	*NREM OSA*	*p-value*
n	199	48	151	
Age (years)	52.02 ± 12.63	53.77 ± 11.8	51.46 ± 12.9	0.270[a]
Male: Female	177:22	38:10	139:12	0.013
BMI	30.98 ± 5.27	31.08 ± 6.2	30.96 ± 4.98	0.887[a]
Arousal index	23.31 ± 20.72	18.99 ± 17.04	24.68 ± 21.64	0.061[b]
Snoring index	324.37 ± 168.65	356.2 ± 155	314.26 ± 172	0.045[b]
Min Ox sat (%)	76.7 ± 15.42	79.09 ± 12.46	75.94 ± 16.21	0.425[b]
AHI	25.96 ± 19.97	13.39 ± 8.05	29.95 ± 20.97	<0.001[b]
Mean apnea duration (sec)	19.07 ± 9.5	21.22 ± 7.74	18.38 ± 9.93	0.008[b]
REM duration (mins)	26.94 ± 23.2	26.37 ± 23.9	27.2 ± 22.9	0.781[b]
REM%	6.49 ± 6.39	6.16 ± 6.5	7.34 ± 6.03	0.060[b]

[a]Student's *t*-test, [b]Mann–Whitney *U* test

Table 2: Comparison of demographic and polysomnographic features between REM OSA and NREM OSA

	Type of OSA		
Variable	*REM predominant OSA n (%)*	*NREM predominant OSA n (%)*	*p-value*
Age (years)			
<50	14 (16.4)	72 (83.7)	0.024
≥50	34 (30.1)	79 (69.9)	
Gender			
Male	38 (21.6)	138 (78.4)	0.021
Female	10 (43.5)	13 (56.5)	
BMI			
≤25	5 (33.3)	10 (66.7)	0.586
25–30	18 (21.4)	66 (78.6)	
>30	25 (25)	75 (75)	
ODI			
≤5	5 (31.3)	11 (68.8)	0.565
>5	38 (24.7)	127 (75.3)	
Supine			
Supine-isolated OSA	22 (25.3)	65 (74.7)	0.869
Supine-predominant OSA	10 (21.3)	37 (78.7)	
Position-independent OSA	16 (24.6)	49 (75.4)	
T88%			
T88% <20	46 (28.2)	117 (71.8)	0.015
T88% >20	1 (3.8)	25 (96.2)	
AHI			
5–15	35 (41.2)	50 (58.8)	<0.001
15–30	10 (20.4)	39 (79.6)	
>30	3 (4.6)	62 (95.4)	

compared with 21.6% of males with REM OSA that was statistically significant (p-value = 0.021). Most patients had NREM-related OSA irrespective of the BMI. Across different BMI categories, there was no statistically significant difference between REM- and NREM-related OSA. There was no statistically significant difference in oxygen desaturation index and position dependence of OSA between NREM-related OSA and REM-related OSA groups. Despite the fact that there was no statistically significant difference in ODI between the two groups, more NREM-related OSA patients spend a larger proportion of their sleep duration with saturation below 88–96.2% vs 3.8%. It was statistically significant. Therefore, in univariate analysis, T88% >20% was linked with NREM OSA, while age >50 years and female sex were the characteristics associated with REM-predominant OSA. The results of multivariate analysis showed >50 years REM predominant OSA [$p = 0.031$, odds ratio (95% confidence interval)–2.20 (1.07–4.5)] and T88% >20% associated with NREM OSA [$p = 0.031$, odds ratio (95% confidence interval)–9.36 (1.22–71.56)] showed significant factors.

About 56.95% of the patients in NREM-related OSA group were prescribed CPAP, while 41.67% of the patients in REM-related OSA group were prescribed CPAP (Table 2).

Discussion

In the Indian population, the prevalence of OSA ranges from 4.4 to 13.7%.[6–9] Depending on the criterion used, REM-related OSA affects anywhere from 10% to 36% of people worldwide.[10–13] There are very few studies on REM-related OSA in India. Nair et al. studied the proportion of REM OSA in patients with sleep-related breathing in India and found 56.3% of the study population had REM-related OSA.[14] Our study showed a prevalence of 24.2%, comparable with the global data but in contrast to a similar study from India. The discrepancy in prevalence may result from variations in the study population's inclusion criteria. This study has taken patients who are diagnosed as OSA based on an AHI cut-off value of five as the study population, while the study by Nair et al. has taken patients referred for PSG who have attained REM stage.

The mean age of the REM- and NREM-related OSA groups did not differ significantly. In contrast, the study by Nair et al. found that the mean age of the REM-related OSA cohort was lower than that of the NREM-related OSA population.[14]

The male-to-female ratio of the groups that were predominately REM or NREM differed significantly. Though the disease was more common in males among both groups, the male: female ratio was smaller in the REM OSA group. This female preponderance in NREM-related OSA was observed by Nair et al.,[14] Al Oweidat et al.,[15] and Conwell et al.[2] The fact that females were predominant despite the vast difference in male: female ratio between the two groups

points to the silent epidemic of undiagnosed OSA in the Indian population. These cases of undiagnosed REM OSA may be one of the reasons for the underdiagnosis of OSA among Indian females.

The AHI varied significantly between the two groups. While most of the patients in the REM OSA group had mild OSA, most patients in NREM-related OSA had moderate or severe OSA. Nair et al.,[14] Gabryelska and Białasiewicz,[16] and Nishio et al.[17] report a similar finding. The high prevalence of REM OSA in the mild OSA group is one of the reasons for the underdiagnosis and consequent undertreatment of this OSA phenotype.

In comparison to NREM OSA, the apnea duration was greater in the REM OSA group. It is comparable to the outcomes from Muraki et al.[18]

Between the REM OSA and NREM OSA groups, there were statistically significant differences in AHI values. It is in concurrence with the study by Gabryelska and Białasiewicz[16] and Su CS et al.[19] Most of the REM-related OSA patients were in the mild OSA group, which was similar to the finding by Nair et al.[14] These REM-related OSA may be untreated when limited-channel polysomnography is used for diagnosis.

In contrary to Nair et al.'s conclusion, there was a statistically significant difference in the snoring index between the two groups.[14]

In comparison to the NREM-related OSA group, the mean apnea duration was longer in the REM OSA group, which was a statistically significant difference. The longer apnea duration might be a pointer to the risk of comorbidity despite the low AHI value in REM-related OSA.

Similar to the results of the study by Gabryelska and Białasiewicz, there was statistically no significant difference between the two groups for minimum oxygen saturation and percentage of REM sleep.[16]

In univariate analysis, the factors linked with REM-related OSA were age >50 years and female sex. The study by Koo et al. on the effects of gender and age on REM-related OSA revealed the relationship between the feminine sex and REM-related OSA.[11] We discovered a link between age >50 and REM-related OSA. In contrast, REM-related OSA was more common in younger age groups in the study by Koo et al.[11]

Limitations of the Study

This study was done in a hospital-based population. A clearer picture of the prevalence of REM-related OSA in the Indian population would be provided by community-based studies. Though PAP prescription was studied, adherence to PAP therapy was not followed up in this study.

The cardiovascular and metabolic profiles of the patients were not included in this study, which would have provided insights into the possible difference in comorbidities between these two patient populations.

Conclusion

The population of south India has a high prevalence of REM-related OSA. Given that this illness is associated with middle age and female sex, the subgroup requires targeted case-finding approaches.

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