Original Article

The prevalence of rapid eye movement-related obstructive sleep apnea in a sample of Saudi population

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Abstract:

BACKGROUND: This study aimed to estimate the prevalence of rapid eye movement-related obstructive sleep apnea (REMrOSA) using common definitions.

METHODS: This was a retrospective cohort study that used three sets of criteria to identify patients with REMrOSA. These criteria were defined as strict, intermediate, and lenient depending on the apnea-hypopnea index (AHI), AHI during REM sleep/(AHI during non-REM sleep [NREM-AHI]), NREM-AHI and REM duration.

RESULTS: The study included 609 patients with OSA and full sleep study. The prevalence of REMrOSA was 26%, 33%, and 52% using the strict, intermediate, and lenient criteria, respectively. There were no differences in the patients' general and demographic characteristics between the different groups of the three definitions. REMrOSA patients were more likely to be younger females than non-REMrOSA (NREMrOSA) patients. Comorbidities were more frequent in the REMrOSA group compared to NREMrOSA when using strict and intermediate definitions. In contrast, AHI, mean O2 saturation, and time spent <90% O2 saturation were significantly worse during NREMrOSA compared to REMrOSA, regardless of the criteria used. Our study reported higher AHI, lower mean oxygen saturation, lower minimum oxygen saturation, and longer time of desaturation during REMrOSA when lenient definition was used compared to when strict and intermediate definitions were used.

CONCLUSIONS: REMrOSA is a common condition with a prevalence ranging between 26% and 52% depending on what definition is applied. Although OSA tends to be more severe with lenient definition, however, the clinical and polysomnographic features were similar among REMrOSA groups regardless of the definition used.

Keywords:

Nonrapid eye movement, obstructive hypopnea, sleep efficiency, sleep-disordered breathing

Obstructive sleep apnea (OSA) is a common disorder that affects sleep quality. It is estimated that the prevalence of OSA exceeds 50% in some countries and affects 1 billion individuals globally.[1] Local data suggest that OSA affects 8.5% of the Saudi population, with a predominance among males.[2] The main characteristics of OSA are repeated episodes of complete or partial collapse of the upper airway with concomitant hypoxemia and hypercapnia and fragmentation of sleep.[3,4] Obstruction of the upper airway may occur during the rapid eye movement (REM) or non-REM (NREM) sleep stages. The incidence of airway collapse increases with REM sleep due to suppressed tonicity of the genioglossus muscle secondary to the inhibition of hypoglossal nerve cholinergic activity.[5,6] Therefore, the severity of OSA can be magnified due to the occurrence of upper airway collapse throughout REM sleep.

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Furthermore, the frequency and duration of respiratory events and the severity of oxygen desaturation are more profound in REM-related OSA (REMrOSA).[7-9] Moreover, it is generally acknowledged that REM sleep is associated with increased sympathetic activity with a surge in blood pressure, which leads to instability of the metabolic and cardiovascular systems.[10] Conceptually, respiratory events during REM sleep could detrimentally affect the cardiovascular system. Recent studies have shown that REMrOSA is associated with metabolic complications, as patients with type 2 diabetes and REMrOSA have higher levels of hemoglobin A1C than type 2 diabetes patients with non-REMrOSA (NREMrOSA).[11] Additionally, REMrOSA is highly associated with hypertension (HTN), which jeopardizes patient quality of life and makes them vulnerable to cardiovascular complications.[12] Therefore, identifying the characteristics of patients with REMrOSA is clinically important, as it may have an impact on their treatment.

The criteria for defining patients with REMrOSA differ, which likely contributes to the wide range of prevalence rates reported for REMrOSA. Previous studies have shown that the prevalence of REMrOSA ranges from 2.7% to 62%.[13] Additionally, this variability in the criteria used to define this condition has led to inconsistent clinical and polysomnographic features being observed among studies.

In this study, we aimed to estimate the prevalence of REMrOSA among Saudi population and distinguish the clinical and polysomnographic characteristics of REMrOSA from those of NREMrOSA patients using three different sets of diagnostic criteria.

Methods

Patients

This retrospective, cohort chart review study was conducted in two centers in Jeddah, Saudi Arabia. It included data from 902 adult patients with full polysomnography (PSG) from January 2015, until December 2017. Of these patients, 96 were excluded because they never achieved REM sleep during the sleep study, resulting in a cohort of 609 patients who achieved REM (11% of the original cohort). The study protocol and study methodology were approved by the Institutional Review Board (IRB) in each center: King Abdulaziz Medical City (IRBC\1271\17) and King Abdulaziz University Hospital (234-20). The ethical principles of the Declaration of Helsinki were adhered to during collection, handling, and storage of data, and all care was taken to protect patient confidentiality. Due to retrospective nature of the study, IRB in each center: King Abdulaziz Medical City and King Abdulaziz University Hospital has waived informed consent statement for the study. We included all patients aged >18 years who were referred to the sleep centers at King Abdulaziz Medical City and King Abdulaziz University Hospital for a sleep study during the study period. Patients with a total sleep time (TST) of <200 min were excluded to ensure that the data included more than one sleep cycle; those with no REM stage sleep were also excluded. Detailed demographic data, including age, sex, body mass index (BMI), daytime sleepiness using the Epworth Sleepiness Scale (ESS), and comorbidities, were obtained from the patients' medical records.[14]

In our study, the diagnosis of sleep apnea was based on an apnea-hypopnea index (AHI) of ≥5 events per hour of sleep. Patients who had an AHI <5 were excluded from the analysis, leading to a population of 609 patients who have an AHI >5 (197 patients were excluded, 24.4% of the REM cohort). Furthermore, we categorized our patients into two groups: REMrOSA and NREMrOSA patients based on three definitions used in the literature for REMrOSA:[13,15-18]

a. Strict definition: Its criteria include AHI ≥5, AHI during REM sleep/AHI during non-REM sleep ≥2, NREM AHI <15, and REM duration ≥30 min
b. Intermediate definition: Its criteria include AHI ≥5, REM AHI/NREM AHI ≥2, and NREM AHI <15
c. Lenient definition: Its criteria include AHI ≥5 and REM AHI/NREM AHI ≥2.

Patients with an AHI ≥5 who did not meet any of the three definitions of REMrOSA mentioned above were considered to have NREMrOSA.

Polysomnography

PSG consisted of continuous recordings from surface leads for electroencephalography (EEG), electrooculography, electromyography (submental and bilateral anterior tibialis muscles), electrocardiography, nasal pressure, and nasal and oral airflow (thermocouple); chest and abdominal impedance belts for respiratory muscle efforts; pulse oximetry for oxygen saturation and pulse rate; a tracheal microphone for snoring; and body position sensors for sleep position. PSG records were scored manually by a certified sleep technologist and reviewed by a certified sleep physician according to scoring rules of the American Academy of Sleep Medicine (AASM) 2012 scoring.[19]

Abnormal obstructive breathing events were defined according to the AASM as (1) apnea with a decrease in airflow by 90% or more from baseline for at least 10 s and (2) hypopnea with a reduction in airflow of at least 30% of the preevent baseline value determined using nasal pressure associated with a reduction in oxygen saturation of at least 3% and/or followed by EEG arousal. All these events occurred despite persistent chest and

abdominal muscle efforts to overcome the obstruction.[20] The average number of these apnea and hypopnea events per hour of sleep (AHI) was then calculated. Subjects with an AHI of ≥5 were categorized as having OSA.[4]

The following parameters were obtained from the polysomnographic data:

- AHI: ([Number apnea + Number hypopnea]/TST [h])
- AHI in REM: ([Number apnea + Number hypopnea]/TST [h]) in REM sleep
- AHI in NREM: ([Number apnea + Number hypopnea]/TST [h]) in NREM sleep
- Time in bed (TIB): Period of time between the lights off and lights on markers
- TST: Period of time between the lights off and lights on markers excluding all the wake stages
- Sleep efficiency (%): TST/TIB
- Sleep onset: Period of time between the lights off marker and the beginning of wake
- Mean O_2 saturation: Average value of the complete SpO_2 curve
- Time spent with O_2 saturation <90%: Percentage of sleep time with oxygen saturation < 90%.

Statistical analysis

All statistical analyses were performed using R software version 4.0.2 (R Core Team, 2020). R is A language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

For continuous variables with a normal distribution, the mean was used as a measure of central tendency, and the standard deviation (SD) was used as the measure of variation. Either the two-sample *t*-test or Welch's two-sample *t*-test was conducted based on the group variance (equal versus unequal variance). Continuous variables that were not normally distributed were reported using the median and interquartile range and were compared using the Wilcoxon rank sum test. Categorical variables were reported using frequencies and percentages. Chi-square or Fisher's exact test, as appropriate, was used to examine relationships in categorical variables. For ordinal attributes, the Kruskal–Wallis test was used. To identify differences between groups, we started with overall ANOVA testing. All statistical tests were two-tailed, and results with $P < 0.05$ were considered significant.

Results

Patient characteristics

The final cohort included 609 patients who achieved REM and had an AHI >5. The mean age was 49 years (SD = 4), the mean BMI was 38.06 kg/m^2 (SD = 21.01), and 58% were males. Of these patients, 40.9%, 39.9%, 36.1%, 26.9%, 45.3%, and 40.9% had diabetes mellitus, Chronic obstructive pulmonary disease (COPD), asthma, HTN, ischemic heart disease (IHD), and hypothyroidism, respectively.

Sleep-related characteristics of the study population

All 609 patients underwent diagnostic PSG. The mean ESS score of the available data was 11.4 (SD = 5.8). The mean AHI was 30.35 (SD = 28.74). The mean TST was 267.73 min. On average, patients spent approximately 12.04%, 51.77%, 22.59%, and 15.05% of their sleep in NREM stage 1, NREM stage 2, NREM stage 3, and REM sleep, respectively [Table 1].

Characteristics of rapid eye movement-related obstructive sleep apnea patients based on the strict definition

Using strict criteria, the patients were divided into two

Table 1: Demographic data and sleep study characteristics of the study population

Patients	*n*=609, *n* (%)
Age (years), mean (SD)	49 (4)
BMI (kg/m^2), mean (SD)	38.06 (21.01)
Male sex	353 (58.0)
DM	249 (40.9)
COPD	243 (39.9)
Asthma	220 (36.1)
HTN	164 (26.9)
IHD	276 (45.3)
Hypothyroid	249 (40.9)
Type of study	
PSG	565 (92.8)
Split night	44 (7.2)
Epworth Sleepiness Scale, mean (SD)	11.40 (5.78)
TST minutes, mean (SD)	267.73 (70.64)
Sleep efficiency, mean (SD)	73.38 (14.96)
Sleep onset minutes, mean (SD)	23.53 (34.37)
Wake after sleep onset minutes, mean (SD)	76.88 (49.72)
Stage n1 proportion, mean (SD)	12.04 (10.02)
Stage n2 proportion, mean (SD)	51.77 (20.27)
Stage n3 proportion, mean (SD)	22.59 (18.56)
REM minutes, mean (SD)	40.85 (23.44)
REM proportion, mean (SD)	15.05 (7.85)
AHI, mean (SD)	30.35 (28.74)
AHI in REM, mean (SD)	59.81 (45.89)
AHI in NREM, mean (SD)	34.82 (38.93)
Mean oxygen saturation during the study, mean (SD)	93.27 (4.12)
Minimal oxygen saturation during the study, mean (SD)	79.50 (10.57)
Period the oxygen saturation during the study was <90% (min), mean (SD)	17.69 (28.15)

BMI=Body mass index, SD=Standard deviation, DM=Diabetes mellitus, COPD=Chronic obstructive lung disease, HTN=Hypertension, IHD=Ischemic heart disease, TST=Total sleep time, REM=Rapid eye movement, PSG=Polysomnography

groups: the REMrOSA group (26%) and the NREMrOSA group (74%). REMrOSA patients were younger than those with NREMrOSA (46.3 vs. 49.9; $P = 0.006$). Males were more likely to suffer from NREMrOSA (63.9%, $P \leq 0.001$). Patients with REMrOSA and patients with NREMrOSA had similar BMI values (38.42 kg/m^2 vs. 37.07 kg/m^2, respectively; $P = 0.494$). Furthermore, the percentage of comorbidities including obstructive airway diseases and IHD was higher in REMrOSA patients although they had milder sleep apnea than did NREMrOSA patients (AHI of 12.74 compared to 36.47; $P \leq 0.001$) as well as milder severity of oxygen desaturation [Table 2].

Characteristics of rapid eye movement-related obstructive sleep apnea patients based on the intermediate definition

Based on the abovementioned intermediate criteria, the 609 patients were divided into 2 groups: patients with REMrOSA (33%) and patients with NREMrOSA (67%). Age was significantly different across all two groups ($P = 0.029$). Males were still more likely to suffer from NREMrOSA than females (67.6%, $P \leq 0.001$). Patients with REMrOSA and patients with NREMrOSA had similar BMI values (37.6 kg/m^2 vs. 38.3 kg/m^2, respectively; $P = 0.703$). Furthermore, there was a significant difference between the REMrOSA patients and NREMrOSA patients in comorbidities including obstructive airway diseases and IHD ($P \leq 0.05$). The REMrOSA patients still had a milder average AHI than the NREMrOSA patients (AHI 12.98 compared to 38.91; $P \leq 0.001$) [Table 3].

Characteristics of rapid eye movement-related obstructive sleep apnea patients based on the lenient definition

When the 609 patients were divided based on the abovementioned lenient criteria, the prevalence of patients with REMrOSA and NREMrOSA was (52%) and (48%) respectively [Table 4].

Age was significantly different across all two categories ($P = 0.01$). Males were more likely to suffer from NREMrOSA (73.3%, $P \leq 0.001$). Interestingly, BMI was slightly higher in REMrOSA patients than in NREMrOSA patients (38.14 kg/m^2 vs. 37.98 kg/m^2, respectively; $P = 0.0351$). ESS was significantly different between the two groups, with NREMrOSA patients being more sleepy when compared to REMrOSA patients (12.3 vs. 10.62, $P = 0.003$). Furthermore, the presence of comorbidities was not found to be significantly different between the REMrOSA patients and NREMrOSA patients. Unlike the NREMrOSA patients, the REMrOSA patients had moderate sleep apnea (AHI of 17 compared to 44.8 events/hour: $P \leq 0.001$). Furthermore, the oxygenation parameters were different between these groups [Table 4].

The differences between the three sets of definitions

There was no significant difference among the three sets of definitions (criteria) with regard to age, sex, or the presence of comorbidities. There was a trend toward having more respiratory-related illnesses (COPD and

Table 2: General characteristics of rapid eye movement-related obstructive sleep apnea categories based on the strict definition

Patient characteristics	NREMrOSA (*n*=452; 74), *n* (%)	REMrOSA (*n*=157; 26), *n* (%)	*P*
Age (years), mean (SD)	49.90 (14.32)	46.34 (12.51)	0.006*
BMI (kg/m^2), mean (SD)	38.42 (23.52)	37.07 (11.18)	0.494
Male sex	289 (63.9)	64 (40.8)	<0.001*
DM	181 (40.0)	68 (43.3)	0.533
COPD	162 (35.8)	81 (51.6)	0.001*
Asthma	143 (31.6)	77 (49.0)	<0.001*
HTN	123 (27.2)	41 (26.1)	0.871
IHD	188 (41.6)	88 (56.1)	0.002*
Hypothyroid	157 (34.7)	65 (41.4)	0.162
Epworth Sleepiness Scale, mean (SD)	11.34 (5.74)	11.57 (5.92)	0.722
Total AHI, mean (SD)	36.47 (30.84)	12.74 (6.97)	<0.001*
AHI in REM, mean (SD)	64.08 (49.04)	47.52 (32.39)	<0.001*
AHI in NREM, mean (SD)	44.42 (40.98)	7.18 (3.76)	<0.001*
AHI in supine, mean (SD)	32.09 (41.58)	13.05 (9.28)	<0.001*
Total obstructive apnea index, mean (SD)	8.24 (42.78)	0.86 (1.83)	0.031*
Average oxygen saturation, mean (SD)	92.92 (3.93)	94.28 (4.51)	<0.001*
Minimum oxygen saturation, mean (SD)	78.03 (11.18)	83.72 (7.07)	<0.001*
Time spent <90% oxygen saturation, mean (SD)	20.29 (29.39)	9.81 (22.31)	<0.001*

*Statistical significance <0.05. Strict definition=Category 4 criteria, AHI equal to or >5 (respiratory frequency/TST), REM AHI/NREM AHI ratio at least 2, NREM AHI <15, and REM duration at least 30 min. REM=Rapid eye movement, REMrOSA=REM-related obstructive sleep apnea, NREMrOSA=Non-REMrOSA, BMI=Body mass index, DM=Diabetes mellitus, COPD=Chronic obstructive lung disease, HTN=Hypertension, IHD=Ischemic heart disease, AHI=Apnea-hypopnea index, SD=Standard deviation, TST=Total sleep time

Table 3: General characteristics of rapid eye movement-related obstructive sleep apnea categories based on the intermediate definition

Patient characteristics	NREMrOSA (*n*=408; 67), *n* (%)	REMrOSA (*n*=201; 33), *n* (%)	*P*
Age (years), mean (SD)	49.85 (14.19)	47.23 (13.32)	0.029*
BMI (kg/m^2), mean (SD)	38.30 (24.56)	37.59 (10.83)	0.703
Male sex	276 (67.6)	77 (38.3)	<0.001*
DM	162 (39.7)	87 (43.3)	0.449
COPD	144 (35.3)	99 (49.3)	0.001*
Asthma	128 (31.4)	92 (45.8)	0.001*
HTN	109 (26.7)	55 (27.4)	0.942
IHD	167 (40.9)	109 (54.2)	0.003*
Hypothyroid	143 (35.0)	79 (39.3)	0.349
Epworth Sleepiness Scale, mean (SD)	11.43 (5.79)	11.36 (5.78)	0.906
Total AHI, mean (SD)	38.91 (31.29)	12.98 (8.10)	<0.001*
AHI in REM, mean (SD)	64.55 (48.98)	50.19 (37.17)	<0.001*
AHI in NREM, mean (SD)	48.22 (41.36)	7.61 (3.85)	<0.001*
AHI in supine, mean (SD)	34.12 (42.82)	13.10 (12.15)	<0.001*
Average oxygen saturation, mean (SD)	92.86 (3.97)	94.10 (4.30)	0.001*
Minimum oxygen saturation, mean (SD)	77.56 (11.05)	83.43 (8.23)	<0.001*
Time spent <90% oxygen saturation, mean (SD)	20.06 (28.60)	12.73 (26.59)	0.004*

*Statistical significance <0.05. Strict definition: Category 4 criteria, AHI equal to or <5 (respiratory frequency/TST), REM AHI/NREM AHI ratio at least 2, NREM AHI <15, and REM duration at least 30 min. REM=Rapid eye movement, REMrOSA=REM-related obstructive sleep apnea, NREMrOSA=Non-REMrOSA, BMI=Body mass index, DM=Diabetes mellitus, COPD=Chronic obstructive lung disease, HTN=Hypertension, IHD=Ischemic heart disease, AHI=Apnea-hypopnea index, SD=Standard deviation, TST=Total sleep time

Table 4: General characteristics of rapid eye movement-related obstructive sleep apnea categories based on the lenient definition

Patient characteristics	NREMrOSA (*n*=292; 48), *n* (%)	REMrOSA (*n*=317; 52), *n* (%)	*P*
Age (years), mean (SD)	50.50 (14.32)	47.59 (13.48)	0.01*
BMI (kg/m^2), mean (SD)	37.98 (27.66)	38.14 (11.93)	0.0351
Male sex	214 (73.3)	139 (43.8)	<0.001*
DM	109 (37.3)	140 (44.2)	0.103
COPD	112 (38.4)	131 (41.3)	0.506
Asthma	98 (33.6)	122 (38.5)	0.238
HTN	72 (24.7)	92 (29.0)	0.262
IHD	126 (43.2)	150 (47.3)	0.342
Hypothyroid	109 (37.3)	113 (35.6)	0.729
Epworth Sleepiness Scale, mean (SD)	12.28 (5.81)	10.62 (5.66)	0.003*
Total AHI, mean (SD)	44.76 (34.17)	17.08 (12.08)	<0.001*
AHI in REM, mean (SD)	50.16 (40.60)	68.70 (48.67)	<0.001*
AHI in NREM, mean (SD)	54.57 (45.64)	16.62 (17.45)	<0.001*
AHI in supine, mean (SD)	39.12 (48.85)	16.19 (13.88)	<0.001*
Average oxygen saturation, mean (SD)	92.78 (4.16)	93.71 (4.04)	0.006*
Minimum oxygen saturation, mean (SD)	77.04 (11.65)	81.76 (8.89)	<0.001*
Time spent <90% oxygen saturation, mean (SD)	20.26 (28.49)	15.32 (27.67)	0.037*

*Statistical significance <0.05. Strict definition: Category 4 criteria, AHI equal to or >5 (respiratory frequency/TST), REM AHI/NREM AHI ratio at least 2, NREM AHI <15, and REM duration at least 30 min. REM=Rapid eye movement, REMrOSA=REM-related obstructive sleep apnea, NREMrOSA=Non-REMrOSA, BMI=Body mass index, DM=Diabetes mellitus, COPD=Chronic obstructive lung disease, HTN=Hypertension, IHD=Ischemic heart disease, AHI=Apnea-hypopnea index, SD=Standard deviation, TST=Total sleep time

asthma) going from lenient toward the strict definition, however, it did not reach statistical significance. The main differences were in the oxygenation parameters as they improved going from lenient toward the strict definition. Furthermore, patients meeting the lenient definition were more likely to have a higher AHI ($P \leq 0.001$). Additionally, the minimum oxygen saturation levels were lower ($P = 0.019$ and $P = 0.019$, respectively) in the lenient group, and this group had a longer duration of desaturation ($P = 0.114$), however, the desaturation time was not statistically different [Table 5].

Discussion

The present study aimed to assess the prevalence of REMrOSA among Saudi population, using three different definitions, and to identify differences in patient characteristics based on those definitions. The

Table 5: Demographic data and oxygenation parameters of patients across rapid eye movement-related obstructive sleep apnea definitions

Patient characteristics	All patients (*n*=609), *n* (%)	Lenient (*n*=317; 52), *n* (%)	Intermediate (*n*=201; 33), *n* (%)	Strict (*n*=157; 26), *n* (%)	*P*
Age (years), mean (SD)	48.99 (13.96)	47.59 (13.48)	47.23 (13.32)	46.34 (12.51)	0.625
BMI (kg/m^2), mean (SD)	38.06 (21.01)	38.14 (11.93)	37.59 (10.83)	37.07 (11.18)	0.622
Male sex	353 (58.0)	139 (43.8)	77 (38.3)	64 (40.8)	0.45
DM	249 (40.9)	140 (44.2)	87 (43.3)	68 (43.3)	0.975
COPD	243 (39.9)	131 (41.3)	99 (49.3)	81 (51.6)	0.06
Asthma	220 (36.1)	122 (38.5)	92 (45.8)	77 (49.0)	0.061
HTN	164 (26.9)	92 (29.0)	55 (27.4)	41 (26.1)	0.788
IHD	276 (45.3)	150 (47.3)	109 (54.2)	88 (56.1)	0.128
Hypothyroid	222 (36.5)	113 (35.6)	79 (39.3)	65 (41.4)	0.436
Epworth Sleepiness Scale, mean (SD)	11.40 (5.78)	10.62 (5.66)	11.36 (5.78)	11.57 (5.92)	0.279
Total AHI, mean (SD)	30.35 (28.74)	17.08 (12.08)	12.98 (8.10)	12.74 (6.97)	<0.001
AHI in REM, mean (SD)	59.81 (45.89)	68.70 (48.67)	50.19 (37.17)	47.52 (32.39)	<0.001
AHI in NREM, mean (SD)	34.82 (38.93)	16.62 (17.45)	7.61 (3.85)	7.18 (3.76)	<0.001
AHI in supine, mean (SD)	27.19 (37.07)	16.19 (13.88)	13.10 (12.15)	13.05 (9.28)	0.005
Average oxygen saturation, mean (SD)	93.27 (4.12)	93.71 (4.04)	94.10 (4.30)	94.28 (4.51)	0.339
Minimum oxygen saturation, mean (SD)	79.50 (10.57)	81.76 (8.89)	83.43 (8.23)	83.72 (7.07)	0.019
Time spent <90% oxygen saturation, mean (SD)	17.69 (28.15)	15.32 (27.67)	12.73 (26.59)	9.81 (22.31)	0.114

REM=Rapid eye movement, NREM=Non-REM, BMI=Body mass index, DM=Diabetes mellitus, COPD=Chronic obstructive lung disease, HTN=Hypertension, IHD=Ischemic heart disease, AHI=Apnea-hypopnea index, SD=Standard deviation

prevalence of REMrOSA when applying the strict criteria was 26%. However, the prevalence rates based on the intermediate and lenient criteria were 33% and 52%, respectively. There were no significant differences when comparing patients' demographic and medical backgrounds across the three definitions. However, when REMrOSA compared to NREMrOSA, patients tend to be younger with female predominance as strict and intermediate definitions are used. In contrast, patients tend to be younger, more obese with male predominance when the lenient definition was used.

The prevalence of REMrOSA reported in our study seems to conform with other studies. The prevalence of REMrOSA has been reported widely in the literature, and it is affected by the diagnostic definition used. Bahammam *et al*.[13] reported a prevalence of 17% using almost similar strict criteria but with a minimum REM sleep duration of 15 min. Furthermore, Conwell *et al*.[15] used three different definitions. The first definition was our lenient definition and showed a prevalence of 37%, while their second definition, with the addition of the criterion of NREM AHI of <15/h, demonstrated a prevalence rate of 24.4%. The third definition used by Conwell *et al*.[15] included total AHI ≥5, AHI REM/AHI NREM ≥2, AHI NREM <8 and at least 10.5 min of REM sleep duration. This definition lessened the rate to 13.5%.[15] Mano *et al*.[16] used the same criteria as those in the Conwell *et al*.[15] study. The prevalence rates observed in their study for the first, second, and third definitions were 24.6%, 18.6%, and 12.2%, respectively.[16]

REMrOSA is expected to be associated with increased sympathetic tone and hence more likely to be complicated by medical conditions such as IHD. Our study concurs with such link between REMrOSA and comorbidities since it has shown that COPD, asthma, and IHD were found to be more predominant in the REMrOSA group compared to NREMrOSA when using strict and intermediate definitions. However, when lenient criteria are used, there was no significant difference between the prevalence of the abovementioned medical conditions between NREMrOSA and REMrOSA, reflecting the increase of the prevalence of these conditions among NREMrOSA when lenient criteria compared to strict and intermediate criteria being used. In contrast, AHI, mean O2 saturation, and time spent <90% O2 saturation were significantly worse during NREMrOSA compared to REMrOSA, regardless of the criteria used. Interestingly, we found that REMrOSA tends to have worse AHI and sleep related oxygen parameters when lenient criteria are used compared to strict and intermediate criteria [Table 5]. Our study reported higher AHI, lower mean oxygen saturation, lower minimum oxygen saturation, and longer time of desaturation during REMrOSA when lenient definition was used compared to when strict and intermediate definitions were used.

Although our study showed no significant difference in BMI between REMrOSA and NREMrOSA patients when using the strict (P = 0.494) and intermediate (P = 0.73), the BMI tends to be significantly higher in the REMrOSA compared to NREMrOSA when the lenient definition is applied (P = 0.0351). In contrast, Campos-Rodríguez *et al*.[21] showed no difference in the BMI between the REMrOSA and NREMrOSA groups using the lenient, strict, or intermediate definition. Similarly, Oksenberg

et al.[22] and Sunnetcioglu *et al*.[23] did not find statistically significant differences regarding BMI using the same definition as that used by Campos-Rodríguez *et al*.[21] Therefore, it remains difficult to favor any criteria, strict, intermediate, or lenient, to identify REMrOSA based on the finding of higher BMI.

ESS in our study again showed no significant difference between patients with REMrOSA and NREMrOSA according to the strict, intermediate criteria. However, when lenient definition is applied, patients with NREMrOSA were more sleepy than REMrOSA patients. This conforms with other studies. Sakao *et al*.[24] did not find a significant difference in the ESS value between REMrOSA and NREMrOSA patients using two definitions: (1) AHI ≥5, AHI-REM/AHI-NREM >2, and AHI-NREM <15 and (2) as definition 1 plus AHI-NREM <8 and at least 10.5 min of REM sleep. Moreover, several other studies support our findings and did not detect a difference in the ESS value between patients with REMrOSA and NREMrOSA.[9,15,16,21,22] However, a study of a sample of Saudi populations, similar to ours, reported that the ESS value was higher in patients with NREMrOSA.[13] These conflicting data necessitate the need for further large study to decide the best criteria to define REMrOSA.

To date, there are no consensus or standard criteria to diagnose REMrOSA. However, we examine REMrOSA independently of NREMrOSA using three different criteria to define the former. Our study demonstrated that when lenient definition (criteria) was used, REMrOSA is likely to be associated with a trend of increased prevalence of comorbid diseases, though weaker when compared with strict and intermediate criteria. Furthermore, we observed that respiratory events became more severe as the diagnostic criteria became more lenient, which may favor these criteria to define REMrOSA rather than strict and intermediate ones. However, there are several conflicting data in the literature and the question of which criteria can be used to identify REMrOSA remains to be answered.

Conclusion

REMrOSA is a common condition regardless of the definition used. However, to date, no standard definition has been agreed upon. Although OSA tends to be more severe with lenient definition, the clinical and polysomnographic features were similar among REMrOSA groups regardless of the definition used.

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Conflicts of interest

There are no conflicts of interest.

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