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Clinical characteristics of non-sleepy obstructive sleep apnea patients: a study in a tertiary care sleep clinic in India

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Abstract

Obstructive sleep apnea (OSA) encompasses a diverse population, manifesting with or without symptoms of excessive daytime sleepiness. There is contention surrounding the significance of non-sleepy OSA within clinical contexts and whether routine treatment is warranted. This study aims to evaluate epidemiological and clinical distinctions between sleepy and non-sleepy OSA patients. A retrospective analysis was conducted on consecutive patients undergoing polysomnography for OSA assessment at tertiary care hospitals between 2018 and 2023. For 176 of 250 patients, complete polysomnography records with OSA diagnoses were available. Non-sleepy OSA was defined when a patient had an Epworth sleepiness scale score <10 and polysomnography demonstrated an apnea hypopnea index 5/hour. Non-sleepy OSA patients were matched with sleepy OSA patients in terms of age and gender distribution (mean age 51.24±13.25 years *versus* 50.9±10.87 years, male 70.4% *versus* 73.3%). The sensitivity of STOP-BANG 3 for the non-sleepy OSA group was 87.7%, 89.3%, and 95.2% for any OSA severity, moderate to severe OSA, and severe OSA, respectively, while the corresponding sensitivity for the sleepy OSA group was 96.5%, 98.6%, and 100% for any OSA severity, moderate to severe OSA, and severe OSA, respectively. A novel symptom scoring tool, HASSUN (hypertension, nocturnal apneas, snoring, sleep disturbance, unrefreshing sleep, and nocturia), demonstrated a sensitivity of over 90% for all severity categories of OSA in both non-sleepy and sleepy OSA groups. The prevalence of cardiovascular and metabolic comorbidities did not significantly differ between non-sleepy and sleepy OSA patients. The physiological parameters, including forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio, arterial partial pressure of oxygen, and bicarbonate at baseline, were comparable between the two groups. To conclude, non-sleepy OSA patients are less obese, exhibit fewer symptoms, and have less severe OSA in comparison to sleepy OSA. Non-sleepy OSA patients display a similar likelihood of cardiovascular and metabolic comorbidities compared to sleepy OSA patients. Further investigations are warranted to elucidate the mechanisms underlying cardiovascular metabolic comorbidities in non-sleepy OSA patients. The proposed HASSUN scoring tool for non-sleepy OSA screening necessitates validation in future studies.

Key words: obstructive sleep apnea, polysomnography, daytime sleepiness, apnea-hypopnea index, sensitivity and specificity.

Introduction

Obstructive sleep apnea (OSA) represents a prevalent sleep disorder linked with significant cardiovascular and metabolic implications. It is characterized as sleep-related breathing disorder typified by recurrent apneas and hypopneas, objectively defined via polysomnography, often resulting in excessive daytime sleepiness and potential cognitive impairment [1]. Current estimates suggest a global prevalence of 938 million adults affected by OSA [2]. Studies have indicated a mean prevalence of OSA of approximately 6% (ranging from 3% to 18%) in men and 4% (ranging from 1% to 17%) in women. Similarly, the prevalence of OSA ranges from 27.3% (9% to 86%) in men to 22.5% (3.7% to 63.7%) in women [3]. STOP-BANG is the most widely utilized screening tool for OSA owing to its documented sensitivity.

The Epworth Sleepiness Scale (ESS) emerges as a pivotal tool for distinguishing between patients with and without Excessive daytime sleepiness (EDS), employing a questionnaire to assess the likelihood of falling asleep in everyday scenarios. Scores on the ESS scale ranges from 0 to 24, with an ESS score 10 indicative of a sleepy patient, while an ESS score <10 suggests a non-sleepy patient [4,5]. Some OSA patients experience the burden of EDS, while others remain asymptomatic during the day [2,3]. The mechanisms causing different clinical presentations in OSA patients are still unclear.

There is paucity of data in the literature regarding how non-sleepy OSA patients differ when compared to sleepy OSA patients. Here in this retrospective study, we scrutinized the data of sleepy and non-sleepy OSA patients and explored whether the demographic and/or polysomnographic comparison could bring out meaningful findings. We also attempted to propose a novel symptom-scoring tool to screen suspected cases of OSA.

Materials and Methods

A retrospective analysis encompassed all patients presenting to our sleep clinic at a tertiary care center between 2018 and 2023 for OSA evaluation. Patient records were retrieved from our existing database and scrutinized for demographic parameters, symptoms, comorbidities at presentation, ESS, STOP-BANG score (Soring, Tiredness, Observed apnea, high blood Pressure, Body mass index 35 kg/m2, Age>50, Neck circumference>40 cm, Male Gender), Berlin score, and Charlson Comorbidities Index. Additionally, physiological parameters including Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, arterial blood gas (ABG) analysis including partial pressure of oxygen (pO2), and bicarbonate (HCO3) were evaluated. In the final data analysis, patients with incomplete polysomnography data and those with AHI<5/hour were excluded. OSA was defined as apnea-hyponea index (AHI) of 5/hour of sleep with symptoms or AHI 15/hour without

symptoms. Mild OSA was defined as those with AHI 5 <15/hour, moderate OSA (AHI 15 - 30/hour), and severe OSA (AHI >30/hour) [1]. Patient population was divided into non-sleepy OSA and sleepy OSA groups, with non-sleepy OSA being ESS<10 and sleepy OSA patient ESS 10. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Variables with normal distribution were presented as mean ± standard deviation (SD) and subjected to independent samples t-test to analyze differences between non-sleepy and sleepy OSA groups. Categorical variables were presented as number (percentage) and analyzed using the Chi-square test for statistical significance. All significance tests were two-sided. Sensitivity analysis of STOP-BANG, based on two different cutoffs (STOPBANG 3, 4) as described in various studies [6-8], was conducted for the overall cohort and for non-sleepy versus sleepy OSA groups. A screening tool (HASSUN) was developed for non-sleepy OSA patient detection based on symptom analysis in the non-sleepy OSA group. The HASSUN score consisted of Hypertension, Apnea, Snoring, Sleep Disturbance, Unrefreshing sleep and Nocturia, with each parameter constituting one point, total maximum score being 6 and minimum score being 0. Sensitivity of the HASSUN score was assessed for OSA detection in the non-sleepy OSA population at two different cutoffs, namely HASSUN score 2 and HASSUN score 3.

Results

Sample size and exclusion criteria

A total of 250 subjects were initially screened for analysis, with complete polysomnographic data available for 184 patients. Following exclusion criteria, eight patients with AHI<5/hour on PSG were removed from the analysis, resulting in a final sample size of 176 patients. Among the included patients, 71 were classified into the non-sleepy group (ESS 10), while 105 were categorized into the sleepy group (ESS > 10).

Non-sleepy OSA and sleepy OSA groups had a comparable age and gender distribution. The prevalence of cardiovascular and metabolic comorbidities, the Charlson Comorbidity Index, spirometry, and ABG parameters did not significantly differ between the two groups. (Table 1 and *Supplementary Table 1*)

The non-sleepy OSA group demonstrated a significantly lower BMI compared to the sleepy OSA group. The non-sleepy OSA group exhibited significantly lower mean AHI and a lesser prevalence of severe OSA compared to the sleepy OSA group (Tables 1 and 2).

Scores and sensitivity

Sensitivity of STOP-BANG for the overall cohort with a cutoff of 3 was 93%, 95% and 98.7% for any OSA, moderate-severe OSA, and severe OSA respectively. The sensitivity for STOP-BANG 4 was 82.5%, 86% and 90.9% for any OSA, moderate-severe OSA and severe OSA respectively.

Sensitivity of STOP-BANG 3 for non-sleepy OSA group was 87.7%, 89.3% and 95.2% for any OSA severity, moderate to severe OSA and severe OSA respectively, while corresponding sensitivity for sleepy OSA group was 96.5%, 98.6% and 100% any OSA severity, moderate to severe OSA and severe OSA respectively.

Sensitivity of STOP-BANG 4, again, was lower for non-sleepy OSA group as compared to the sleepy OSA group. Sensitivity for non-sleepy OSA group was 71.9%, 74.4% and 80.9% for any OSA severity, moderate to severe OSA and severe OSA respectively, while corresponding sensitivity for sleepy OSA group was 89.5%, 93.3% and 94.5% any OSA severity, moderate to severe OSA and severe OSA respectively.

We devised a score for screening of non-sleepy OSA patients, termed as HASSUN score, consisting of Hypertension, Apnea, Snoring, Sleep Disturbance, Unrefreshing sleep and Nocturia. Sensitivity of this score for predicting OSA in the non-sleepy group was 98.5%, 98.3% and 96.7% at cutoff of 2 for any OSA, moderate to severe OSA and severe OSA respectively, and 95.5%, 94.9% and 96.7% at the cutoff of 3 for any OSA, moderate to severe OSA and severe OSA respectively (Table 3).

Discussion

Excessive daytime sleepiness (EDS) in obstructive sleep apnea (OSA) patients presents a complex pathogenesis. EDS has been linked to sleep fragmentation or alterations in oxygenation, independent contributions of nocturnal hypoxemia, and sleep fragmentation [9-15]. However, the relationship between EDS and the risk of cardiovascular and metabolic comorbidities in OSA patients remains unclear.

The current study aimed to investigate differences in demographic parameters, symptoms, polysomnographic variables, and comorbidities between OSA patients with and without EDS. We found no significant disparities in age or gender distribution. However, patients without EDS (non-sleepy OSA patients) tended to be less obese, reported lesser symptoms. They also exhibited lower STOPBANG and Berlin scores. Additionally, non-sleepy OSA patients had a significantly lower mean apnea-hypopnea index (AHI) and were less likely to have severe OSA compared to sleepy OSA patients. However, the proportion of patients with moderate to severe OSA did not significantly differ between the groups.

Regarding the association between OSA and cardiovascular and metabolic comorbidities, our findings were consistent with previous studies reporting similar prevalence rates of hypertension, coronary artery disease (CAD), heart failure, and stroke between OSA patients with and without EDS [16-24]. Despite conflicting findings in previous studies, current study did not observe a statistically significant difference in hypertension prevalence between the two groups [19-24].

Among various screening tools for identifying OSA, STOP-BANG is the most widely utilized owing to its documented sensitivity in predicting OSA. Chung et al., focusing on preoperative OSA assessment, demonstrated STOPBANG 3 sensitivities of 83.6%, 92.9%, and 100% for AHI thresholds of >5, >15, and >30, respectively [6]. Similarly, Ong TH et al., reported sensitivities of 86.1%, 92.8%, and 95.6% for STOP-BANG with a cutoff of 3 for the same AHI thresholds in patients presenting to sleep clinics [7]. Meta-analysis by Pivetta et al. reported a pooled sensitivity of STOP-BANG 3 to be 91.4%, 95%, and 97% for any OSA, moderate to severe OSA, and severe OSA, respectively, with slightly lower figures for the South Asian/Southeast Asian population [25]. In current study, the overall sensitivity of STOP-BANG 3 was 93%, 95%, and 98.7% for any OSA, moderate-severe OSA, and severe OSA, respectively. Notably, the sensitivity of STOP-BANG 3 for moderate-severe OSA was 89.3% for non-sleepy OSA patients compared to 98.6% for sleepy OSA patients, indicating a significantly lower sensitivity for the non-sleepy group. Rida Waseem MA et al. reported, the sensitivity of STOP-Bang score 4 (with a BMI cutoff of 27.5) for predicting moderate-to-severe OSA was 73.9% in Indian ethnic origin [8]. In the present study, STOP-BANG score 4 exhibited an overall sensitivity of 86% for moderate to severe OSA, with sensitivity values of 74.4% for non-sleepy OSA patients and 93.3% for sleepy OSA patients, again suggesting a notably lower sensitivity of STOP-BANG for predicting moderate to severe OSA in the non-sleepy group.

In the present study, we developed a screening tool based specifically on symptoms observed in the non-sleepy group, acknowledging the lower sensitivity of STOP-BANG for detecting non-sleepy OSA. This tool, termed the HASSUN score, comprises six parameters: Hypertension, Apnea, Snoring, Sleep disturbance, Unrefreshing sleep, and Nocturia. Evaluating the sensitivity of the HASSUN score for the non-sleepy group at two cutoffs (2 and 3), we observed sensitivities of 98.5%, 98.3%, and 96.7% for any OSA, moderate to severe OSA, and severe OSA, respectively, for HASSUN 2, and 95.5%, 94.9%, and 96.7% for HASSUN 3. Consequently, the sensitivity of HASSUN as a screening tool outperformed STOP-BANG for the non-sleepy group. However, further validation through prospective studies is warranted.

In conclusion, the current study adds to the existing literature by demonstrating that the prevalence of cardiovascular and metabolic comorbidities does not significantly differ between OSA patients with and without EDS. This finding suggests that the presence of EDS may not independently predict the risk of these comorbidities in OSA patients. Consequently, when managing OSA, clinicians should consider individual patient characteristics beyond EDS to determine the appropriate treatment approach.

Despite the insights provided by current study, it is essential to acknowledge its limitations, including its retrospective design and cross-sectional nature. Future prospective studies are needed to explore the longitudinal impact of EDS on the development of cardiovascular and metabolic comorbidities in OSA patients.

Conclusions

Non-sleepy OSA patients are as likely to suffer from cardiovascular and metabolic comorbidities as sleepy OSA patients. STOP-BANG, a commonly used screening tool performs worse at screening non-sleepy OSA patients compared to sleepy OSA patients. Future studies are needed to characterize any differences in future risk of the same between the two groups and to validate the new proposed tool for screening non-sleepy and sleepy OSA patients.

References

1. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med 2017;13:479-504.
2. Benjafield A, Valentine K, Ayas N. Global prevalence of obstructive sleep apnea in adults: estimation using currently available data. Am J Respir Crit Care Med 2018;197:A3962.
3. Theorell-Haglöw J, Miller CB, Bartlett DJ, et al. Gender differences in obstructive sleep apnoea, insomnia and restless legs syndrome in adults – what do we know? A clinical update. Sleep Med Rev 2018;38:28-38.
4. Johns MW. Sensitivity and specificity of the multiple sleep latency test (MSLT), the maintenance of wakefulness test and the epworth sleepiness scale: failure of the MSLT as a gold standard. J Sleep Res 2000;9:5-11.
5. Murray W. Johns, A New method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991:14:540-5.
6. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology 2008;108:812-21.

7. Ong TH, Raudha S, Fook-Chong S, et al. Simplifying STOP-BANG: use of a simple questionnaire to screen for OSA in an Asian population. Sleep Breath 2010;14:371-6.
8. Waseem R, Chan MTV, Wang CY, et al. Diagnostic performance of the STOP-Bang questionnaire as a screening tool for obstructive sleep apnea in different ethnic groups. J Clin Sleep Med 2021;17:521-32.
9. Guilleminault C, Partinen M, Quera-Salva MA, et al. Determinants of daytime sleepiness in obstructive sleep apnea. Chest 1988;94:32-7.
10. Bedard MA, Montplaisir J, Richer F, Malo J. Nocturnal hypoxemia as a determinant of vigilance impairment in sleep apnea syndrome. Chest 1991;100:367-70.
11. Colt HG, Haas H, Rich GB. Hypoxemia vs sleep fragmentation as cause of excessive daytime sleepiness in obstructive sleep apnea. Chest 1991;100:1542-8.
12. Gottlieb DJ, Whitney CW, Bonekat WH, et al. Relation of sleepiness to respiratory disturbance index: the sleep heart health study. Am J Respir Crit Care Med 1999;159:502-7.
13. Miliauskas S, Sakalauskas R. Peculiarities of nocturnal oxygen saturation in obstructive sleep apnea. Medicina (Kaunas) 2005;41:217-20. [Article in Lithuanian].
14. Punjabi NM, O'Hearn DJ, Neubauer DN, et al. Modeling hypersomnolence in sleep-disordered breathing. A novel approach using survival analysis. Am J Respir Crit Care Med 1999;159:1703-9.
15. Johns MW. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth sleepiness scale. Chest 1993;103:30-6.
16. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep heart health study. JAMA 2000;283:1829-36.
17. Sharma SK, Kumpawat S, Banga A, Goel A. Prevalence and risk factors of obstructive sleep apnea syndrome in a population of Delhi, India. Chest 2006;130:149-56.
18. Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 2001;163:19-25.
19. Oksenberg A, Arons E, Nasser K, et al. Severe obstructive sleep apnea: sleepy versus nonsleepy patients. Laryngoscope 2010;120:643-8.
20. Bravo M, de LP, Serpero LD, et al. Inflammatory proteins in patients with obstructive sleep apnea with and without daytime sleepiness. Sleep Breath 2007;11:177-85.
21. Koutsourelakis I, Perraki E, Bonakis A, et al. Determinants of subjective sleepiness in suspected obstructive sleep apnoea. J Sleep Res 2008;17:437-43.

22. Barcelo A, Barbe F, la Pena de M, et al. Insulin resistance and daytime sleepiness in patients with sleep apnoea. Thorax 2008;63:946-50.
23. Huang JF, Chen LD, Lin QC, et al. The relationship between excessive daytime sleepiness and metabolic syndrome in severe obstructive sleep apnea syndrome. Clin Respir J 2016;10:714-21.
24. Wang Q, Zhang C, Jia P, et al. The association between the phenotype of excessive daytime sleepiness and blood pressure in patients with obstructive sleep apnea-hypopnea syndrome. Int J Med Sci 2014;11:713-20.
25. Pivetta B, Chen L, Nagappa M et al. Use and performance of the STOP-Bang questionnaire for obstructive sleep apnea screening across geographic regions: a systematic review and meta-analysis. JAMA Netw Open 2021;4:e211009.

Online supplementary material:
Supplementary Table 1. Respiratory physiological parameters.

Table 1. Demographic profile of the study cohort (n=176).

Parameter	Non-sleepy OSA (n=71)	Sleepy OSA (n=105)	p-value
Age	51.4±13.25	50.9±10.87	0.851
Sex Male Female	50 (70.4%) 21 (29.6%)	77 (73.3%) 28 (26.7%)	0.673
Height (cm)	165.78 ± 11.2	165.02 ± 8.95	0.685
Weight (kg)	80.69 ± 16.08	90.01 ± 17.99	0.005
BMI (kg/m^2)	29.64 ± 5.88	32.73 ± 7.54	0.022
Symptoms			
Sleep Disturbance	56 (78.9%)	99 (94.3%)	0.002
Breathing difficulty at night	39 (54.9%)	90 (86.5%)	0.000
Snoring	67 (94.4%)	105 (100%)	0.015
Prolonged apneas in sleep	45 (65.2%)	87 (84.5%)	0.003
Unrefreshing sleep	52 (73.2%)	100 (95.2%)	0.000
Headache & Neck pain in morning	36 (52.9%)	62 (59.0%)	0.429
Hypertension	42 (60%)	61 (58.7%)	0.859
Chest pain	23 (32.4%)	41 (39%)	0.368
Nocturia	57 (81.4%)	88 (84.6%)	0.580
Anxiety	13 (29.5%)	24 (29.3%)	0.974
Depression	8 (17.4%)	13 (16.7%)	0.917
Comorbidities			
Diabetes	17/60 (28.3%)	31/91 (34.1%)	0.459
Hypertension	32/64 (50%)	54/97 (55.7%)	0.480
Hyperlipidemia	10/46 (21.7%)	25/79 (31.6%)	0.234
CAD	6/58 (10.3%)	11/91 (12.1%)	0.744
Heart Failure	2/47 (4.3%)	1/82 (1.2%)	0.271
Stroke/CVA/TIA	4/59 (6.8%)	4/91 (4.4%)	0.526
Charlson's comorbidities Index	0.41 ± 0.72	0.45 ± 0.65	0.709
STOP-BANG	4.33 ± 1.61 (n=57)	5.31 ± 1.47 (n=86)	0.000
Berlin score	5.49 ± 2.01 (n=57)	6.81 ± 1.79 (n=86)	0.000

BMI, body mass index; CAD, coronary artery disease; CVA, cerebrovascular accident; STOP-BANG, soring, tiredness, observed apnea, high blood pressure, body mass index 35 kg/m2, age>50, neck circumference>40 cm, male gender; TIA, transient ischemic attac.

Table 2. Polysomnography parameters of the study cohort.

Parameter	Non-sleepy OSA (n=71)	Sleepy OSA (n=105)	p value
AHI	32.95 ± 20.62	47.79 ± 28.72	0.000
Mild OSA	10 (14.3%)	14 (13.3%)	0.025
Moderate OSA	28 (40%)	23 (21.9%)	
Severe OSA	32 (45.7%)	68 (64.8%)	

AHI**,** apnea hypopnea index; OSA, obstructive sleep apnea,

Table 3. Hypertension, apnea, snoring, sleep disturbance, unrefreshing sleep, nocturia score analysis.

HASSUN Score cutoff	Sensitivity in non-sleepy OSA group		
	Any OSA	Moderate to severe OSA	Severe OSA
2	98.5%	98.3%	96.7%
3	95.5%	94.9%	96.7%

HASSUN**,** hypertension, apnea, snoring, sleep disturbance, unrefreshing sleep, nocturia; OSA, obstructive sleep apnea.