Original Article

Factor associated with severity of obstructive sleep apnea in Thammasat University hospital

Wadee Wongpradit, M.D.[1], Prapasri Kulalert, M.D., Ph.D.[2], Nithita Sattaratpaijit, M.D.[3*]

Abstract

Introduction: Obstructive sleep apnea (OSA) is a prevalent chronic disease and is associated with many adverse health outcomes, but OSA is underrecognized by physicians.

Objectives: To identify factors associated with severity of OSA

Methods: This was a retrospective cross-sectional study. 587 OSA patients were enrolled and classified into 3 groups: mild, moderate, and severe OSA. Demographic and comorbidity data, anthropometric measurement, and Epworth sleepiness scale were reviewed. Ordinal regression was used to analyze the associated factors.

Results: The prevalence of mild, moderate, and severe OSA were 39.0%, 23.9% and 56.7% respectively. Univariable analyses showed that male sex, body mass index (BMI) ≥ 25 kg/m^2, neck circumference (NC) > 40 cm, excessive daytime sleepiness, hypertension, and diabetes mellitus were associated with severity of OSA. Multivariable ordinal analysis showed that age ≥ 60 years old, male sex, BMI ≥ 25 kg/m^2, NC > 40 cm, excessive daytime sleepiness, and diabetes mellitus were associated with severity of OSA.

Conclusions: Our identifying factors assist to recognize adult patients at risk of OSA by severity.

Keywords: Obstructive sleep apnea, Factor, Severity, Diabetes mellitus

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[1] Department of Community Medicine and Family Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, 12121, Thailand

[2] Department of Clinical Epidemiology, Family Medicine, Faculty of Medicine, Thammasat University, Pathum Thani, 12121, Thailand

[3] Department of Otolaryngology-Head and Neck Surgery, Faculty of Medicine, Thammasat University, Pathum Thani, 12121, Thailand

* **Corresponding author:** Nithita Sattaratpaijit, MD., Department of Otolaryngology-Head and Neck Surgery, Faculty of Medicine, Thammasat University, Pathum Thani, 12121, Thailand. Tel.: +66 8964 60560 Email: nithita@tu.ac.th

Introduction

Obstructive sleep apnea (OSA) is a prevalent sleep disorder, characterized by repetitive partial or complete obstruction of the upper airway during sleep, which leads to recurring episodes of hypoxemia, sleep fragmentation, and increased sympathetic activity.[1] The prevalence of OSA ranges from 9% to 38% in the general population[2] and is 11.4 % in the Thai population.[3]

OSA is associated with various adverse health outcomes including hypertension, diabetes mellitus, atrial fibrillation, heart failure, coronary artery disease, stroke, cognitive impairment, and decreased quality of life.[4,5] Moreover, more severe OSA is associated with more risk of cardiovascular outcomes and mortality.[6,7]

Despite increasing awareness of OSA by physicians, it is often underrecognized because initial presentations such as snoring, seem harmless.[8] OSA is also underdiagnosed because the standard diagnostic procedure is overnight polysomnography (PSG), which is not generally available, has a long waiting list, is costly, and requires a sleep specialist for interpretation.[9] OSA is treatable by continuous positive airway pressure therapy, which decreases sleepiness and fatigue and improves quality of life.[10,11] Thus, identifying, and prioritizing patients at risk who require early PSG or treatment are important for primary prevention of adverse health consequences.

Most published studies concern risk factors for diagnosing OSA, but factors associated with severity of OSA are less recognized. Therapeutic approaches can vary according to severity, which is affected by ethnic differences such as obesity, fat distribution, and craniofacial structure.[12] Therefore, the aim of this study was to identify factors related to mild, moderate, and severe OSA in Thai patients.

Methods

Participants and Study Design

This study was a retrospective chart review study conducted at the sleep clinic, Thammasat University Hospital, Thailand between November 2019 and October 2020. The study protocol was approved by the Human Research Ethics Committee of University of Thammasat University (Medicine) (approval no.MTU-EC-CF-0-311/64).

We included all patients over 18 years old who were diagnosed with OSA. The diagnosis of OSA was made by evidence of AHI $\geq$ 5 per hour from standard in-laboratory PSG (either split-night or full-night). Patients were excluded from the study if PSG data was incomplete or total sleep time < 100 min.

Data Collection

Demographic data, anthropometric measurement, self-reported questionnaire, and Thai Epworth sleepiness scale were routinely recorded prior to PSG and retrieved from electronic medical records. Comorbidities such as hypertension, diabetes mellitus, asthma, COPD, and chronic rhinitis were obtained from medical records or current drug treatment.

Anthropometric measurements were taken by trained sleep technicians using standard techniques.[13] Weight in kilograms (kg) was measured while wearing light clothing and without shoes, using a digital scale to the nearest 100 grams. Height in meters (m) was measured without shoes, with stadiometer to the nearest 0.5 centimeters (cm). Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2). Neck circumference (NC) was measured (cm) using an inelastic tape with 1 millimeter precision at the level of the cricothyroid membrane in upright position.[14]

Daytime sleepiness was evaluated using the Thai version of the Epworth Sleepiness Scale (ESS) questionnaires.[15] A score > 10 was considered to indicate excessive daytime sleepiness.[16]

Polysomnography

All patients underwent standard in-laboratory PSG. Recording techniques and data scoring followed American Academy of Sleep Medicine (AASM) recommendations[17] by using a digital polysomnography monitor (Greal Series, Compumedics, Victory, Australia). The following parameters were recorded continuously: electroencephalography, electrooculography, submental and anterior tibial electromyography, nasal and oral thermal airflow, nasal pressure, thoracoabdominal movement, pulse oximetry (SpO2), position, snoring, and electrocardiography. All recordings were visually analyzed, and manually scored by two sleep specialists according to the AASM scoring system.[17]

Apnea was defined as ≥ 90% reduction of airflow lasting ≥ 10 seconds. Hypopnea was defined as ≥ 30% reduction of nasal pressure lasting ≥ 10 seconds and associated with either ≥ 3% arterial oxygen desaturation or arousal. AHI was calculated as the number of apneas and hypopneas per hour of total sleep time.

OSA was defined as AHI ≥ 5 per hour and severity was classified into 3 ordinal categories: mild for AHI ≥ 5 and <15, moderate for AHI ≥ 15 and < 30, and severe for AHI ≥ 30.[18]

Statistical Analysis

Continuous variables were described as mean ± standard deviation for normally distributed variables or median and interquartile range (IQR) for non-normally distributed variables. Continuous variables were converted into categorical variables based on clinical significance or previous study[14]; age was classified into < 60 years and ≥ 60 years, and BMI was classified into < 25 kg/m^2 and ≥ 25 kg/m^2 according to the Asian-Pacific cutoff value for obesity.[19] The NC was classified into ≤ 40 cm and > 40 cm. Categorical variables were described as number and percentage. Comparisons of differences among the three groups were analyzed using the analysis of variance (ANOVA) test for continuous variables with normal distribution and equal variance, the Kruskal Wallis test for continuous variables with normal distribution and unequal variance or non-normal distribution variables, and the Chi-square test or Fisher's exact test for categorical variables. Potentially associated factors of OSA severity were included in the univariable and multivariable ordinal logistic regression model to calculate the odds ratios (ORs) and 95% confidence intervals (CIs). All factors, including age, sex, BMI, NC, excessive daytime sleepiness (ESS > 10), and comorbidities such as hypertension and diabetes mellitus were chosen according to previously published studies. All analyses were performed using Stata version 14 (STATA Corp., Texas, USA). A two-sided p-value of < 0.05 was considered statistically significant.

Results

A total of 634 patients were included in our study. After exclusion (n=47), the 587 remaining patients showed median age of 51 (37, 62) years old and 358 (61%) were male. The 587 patients were classified as follows: mild OSA: 114 (39.0%); moderate OSA: 140 (23.9%); and severe OSA: 333 (56.7%).

The characteristics of patients according to severity of OSA are described in Table 1. Characteristics significantly associated with severity of OSA were sex, BMI, NC, ESS, hypertension, and diabetes mellitus. There were no significant differences in age, proportion of asthma, COPD, or chronic rhinitis.

Table 1 Characteristics of patients regarding severity of OSA.

Variables	Total (n = 587)	Mild OSA (n = 114)	Moderate OSA (n = 140)	Severe OSA (n = 333)	*P*-value
Age (years), median (IQR)	51 (37, 62)	48 (35, 58)	50.5 (35, 61)	52 (38, 63)	0.059
Age, n (%)					0.151
< 60 years	412 (70.2)	88 (77.2)	99 (70.7)	225 (67.6)	
≥ 60 years	175 (29.8)	26 (22.8)	41 (29.3)	108 (32.4)	
Sex, n (%)					0.003
Male	358 (61.0)	56 (49.1)	81 (57.9)	221 (66.4)	
Female	229 (39.0)	58 (50.9)	59 (42.1)	112 (33.6)	
BMI (kg/m2), median (IQR)	29.4 (25.7, 34.3)	26.5 (23.6, 31.6)	28.8 (25.4, 32.35)	30.9 (26.7, 35.8)	< 0.001
BMI classification, n (%)					< 0.001
< 25 kg/m2	126 (21.5)	44 (38.6)	31 (22.1)	51 (15.3)	
≥ 25 kg/m2	461 (78.5)	70 (61.4)	109 (77.9)	282 (84.7)	
NC, n (%)					<0.001
≤ 40 cm	339 (57.8)	93 (81.6)	96 (68.6)	150 (45.1)	
> 40 cm	248 (42.2)	21 (18.4)	44 (31.4)	183 (54.9)	
ESS, median (IQR)	8 (5, 12)	7 (4, 11)	8 (5, 11)	9 (5, 13)	0.003
EDS, n (%)					0.008
No	389 (66.3)	83 (72.8)	103 (73.6)	203 (61.0)	
Yes	198 (33.7)	31 (27.2)	37 (26.4)	130 (39.0)	
Comorbidities, n (%)					
Hypertension	329 (56.1)	52 (45.6)	71(50.7)	206 (61.9)	0.004
Diabetes mellitus	156 (26.6)	21 (18.4)	25 (17.9)	110 (33.0)	< 0.001
Asthma	21 (3.6)	6 (5.3)	5 (3.6)	10 (3.0)	0.533
COPD	6 (1.0)	0 (0.0)	3 (2.1)	3 (0.90)	0.221
Chronic rhinitis	118 (20.1)	28 (24.6)	27 (19.3)	63 (18.9)	0.415
AHI, median (IQR)	35 (18, 63)	9.5 (7.2, 11.6)	21.1 (18.2, 26.1)	58.7 (42.2, 78.7)	< 0.001

Abbreviations: OSA, obstructive sleep apnea; IQR, interquartile range; BMI, body mass index; ESS, Epworth Sleepiness Scale; EDS, excessive daytime sleepiness; COPD, chronic obstructive pulmonary disease; AHI, apnea hypopnea index.

By univariable analysis, ordinal odds ratios were obtained as shown in Table 2. All parameters were selected for further multivariable analysis, including age ≥ 60 years, male, BMI ≥ 25 kg/m^2, NC > 40 cm, ESS > 10, hypertension and diabetes mellitus.

The ordinal multivariable analysis showed significant association between severity of OSA and age ≥ 60 years (OR, 1.57; 95% CI, 1.05 - 2.33; p=0.027), male sex (OR, 1.55; 95% CI, 1.08-2.21; p=0.017), BMI ≥ 25 kg/m2 (OR, 1.71; 95% CI, 1.12-2.61; p=0.013), NC > 40 cm (OR, 2.71; 95% CI, 1.82-4.02; p<0.001) , excessive daytime sleepiness (OR, 1.53; 95% CI, 1.07-2.20; p=0.020) and diabetes mellitus (OR, 1.57; 95% CI, 1.01-2.44; p=0.048), as shown in Table 3.

Table 2 Results of univariable ordinal logistic model using three severities of OSA.

Variables	Crude OR	(95% CI)	*P*-value
Age			
< 60 years	Ref		
≥ 60 years	1.38	0.98 - 1.96	0.068
Sex			
Male	1.72	1.25 - 2.38	0.001
Female	Ref		
BMI ≥ 25 kg/m²	2.56	1.76 - 3.73	< 0.001
NC > 40 cm	3.64	2.57 - 5.14	< 0.001
EDS	1.68	1.19 - 2.38	0.003
Comorbidities			
Hypertension	1.72	1.25 - 2.36	0.001
Diabetes mellitus	2.14	1.45 - 3.14	< 0.001

Abbreviations: OR, odds ratio; CI, confidence interval; Ref, reference; BMI, body mass index; NC, neck circumference; EDS, excessive daytime sleepiness.

Table 3 Results of multivariable ordinal logistic model using three severities of OSA.

Variables	Adjusted OR	(95% CI)	*P*-value
Age			
< 60 years	Ref		
≥ 60 years	1.57	1.05 - 2.33	0.027
Sex			
Male	1.55	1.08 - 2.21	0.017
Female	Ref		
BMI ≥ 25 kg/m²	1.71	1.12 - 2.61	0.013
NC > 40 cm	2.71	1.82 - 4.02	< 0.001
EDS	1.53	1.07 - 2.20	0.020
Comorbidities			
Hypertension	1.19	0.82 - 1.72	0.356
Diabetes mellitus	1.57	1.01 - 2.44	0.047

Abbreviations: OR, odds ratio; CI, confidence interval; Ref, reference; BMI, body mass index; NC, neck circumference; EDS, excessive daytime sleepiness.

Discussion

Our study reported that independent factors associated with severity of OSA included age ≥ 60 years old, male sex, BMI ≥ 25 kg/m², NC > 40 cm, excessive daytime sleepiness, and diabetes mellitus.

Age is a well-known risk factor for OSA. Our study supported a previous study in that old age increased risk of more severe OSA.[20] The SHIP-Trend study[21] reported that the prevalence of moderate to severe OSA in the general population was 36.6% in age ≥ 60 years compared with 13.4% in age < 60 years.

Many studies revealed that OSA was more prevalent in males than in females.[14,22] Similar to findings of Dosman JA et al., our study found that male sex was associated with more severe OSA.[23] The explanation might be the differences in upper airway anatomy, function, and female sex hormones.[24]

Obesity is considered a significant risk factor for the development and progression of OSA.[25] Dong Z et al. reported that increased body mass index (BMI) has been associated with greater severity of OSA.[26] Our study also affirmed that BMI $\geq$ 25 kg/m^2 in Thai population was a factor associated with severity of OSA. The pathophysiology of OSA in obese people might be affected by fat distribution. Fat deposits around the upper airway may result in a smaller lumen and increased collapsibility of the upper airway. Fat deposits in the tissues surrounding the thorax might increase demand for oxygen by reducing chest compliance and functional residual capacity.[25]

Neck circumference (NC) over 40 cm was the strongest factor associated with severity of OSA in our study. NC is considered a marker of localized adipose tissue distribution around the neck. It is a more reliable factor in determining OSA and severity of OSA than BMI.[27] Kim SE et al. also found that NC had the strongest positive correlation with AHI in an Asian population.[28]

We assessed daytime sleepiness by the Thai version of the ESS questionnaire, which is the standard measurement of subjective sleepiness. An ESS score above 10 is regarded as an indicator of excessive daytime sleepiness.[16] The correlation between ESS score, or excessive daytime sleepiness, and severity of OSA is still inconclusive because some of the OSA patients did not report excessive sleepiness despite severe OSA. However, the association between excessive daytime sleepiness and severity of OSA observed in this study was similar to that in many other studies.[29,30]

The relationship between OSA and diabetes seems to be bidirectional.[31] Several studies have found a high prevalence of OSA in patients with diabetes and shown that OSA may be a risk factor for the development of type 2 diabetes.[32] Our study related having diabetes to severity of OSA.

This study has some limitations which need to be considered. First, we enrolled patients who suspected OSA at a sleep clinic, so they might not reflect the features of a more general population. Second, this was a cross-sectional retrospective study. Thus, we could not determine the actual causes and effects of risk and development of OSA severity. However, this is the first study investigating factors associated with severity of OSA in Thai patients. Previous studies found independent factors associated with OSA by treating final clinical outcomes of interest as binary (no OSA versus OSA). In our study, we defined 3 groups of outcomes in routine practice (mild, moderate, and severe OSA) and used ordinal regression analysis to provide more details of differences between the groups.

Further investigations should develop simple and generalizable screening tools for physicians to differentiate OSA by severity.

In conclusion, our study strongly suggests that elderly people, males, those who have BMI $\geq$ 25 kg/m^2, NC > 40 cm, excessive daytime sleepiness, and diabetes mellitus are more likely to have higher OSA severity which need early diagnosis and treatment without delay. These factors assist physician to differentiate OSA by severity.

References

1. Eckert DJ, White DP, Jordan AS, Malhotra A, Wellman A. Defining phenotypic causes of obstructive sleep apnea. Identification of novel therapeutic targets. *Am J Respir Crit Care Med.* 2013;188(8):996-1004.
2. Senaratna CV, Perret JL, Lodge CJ, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. *Sleep Med Rev*. 2017;34:70-81.
3. Neruntarat C, Chantapant S. Prevalence of sleep apnea in HRH Princess Maha Chakri Srinthorn Medical Center, Thailand. *Sleep Breath.* 2011;15(4):641-648.
4. Yeghiazarians Y, Jneid H, Tietjens JR, et al. Obstructive sleep apnea and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2021;144(3):e56-e67.
5. Bonsignore MR, Baiamonte P, Mazzuca E, Castrogiovanni A, Marrone O. Obstructive sleep apnea and comorbidities: a dangerous liaison. *Multidiscip Respir Med.* 2019;14(1):8.
6. Xie C, Zhu R, Tian Y, Wang K. Association of obstructive sleep apnoea with the risk of vascular outcomes and all-cause mortality: a meta-analysis. *BMJ open.* 2017;7(12):e013983.
7. Won CH, Chun HJ, Chandra SM, Sarinas PS, Chitkara RK, Heidenreich PA. Severe obstructive sleep apnea increases mortality in patients

with ischemic heart disease and myocardial injury. *Sleep Breath.* 2013;17(1):85-91.
8. Rundo JV. Obstructive sleep apnea basics. *Cleve Clin J Med.* 2019;86(9 suppl 1):2-9.
9. Miller JN, Berger AM. Screening and assessment for obstructive sleep apnea in primary care. *Sleep Med Rev.* 2016;29:41-51.
10. Avlonitou E, Kapsimalis F, Varouchakis G, Vardavas CI, Behrakis P. Adherence to CPAP therapy improves quality of life and reduces symptoms among obstructive sleep apnea syndrome patients. *Sleep Breath.* 2012;16(2): 563-569.
11. Tomfohr LM, Ancoli-Israel S, Loredo JS, Dimsdale JE. Effects of continuous positive airway pressure on fatigue and sleepiness in patients with obstructive sleep apnea: data from a randomized controlled trial. *Sleep.* 2011;34(1):121-126.
12. Hnin K, Mukherjee S, Antic NA, et al. The impact of ethnicity on the prevalence and severity of obstructive sleep apnea. *Sleep Med Rev.* 2018;41:78-86.
13. Fryar CD, Gu Q, Ogden CL, Flegal KM. Anthropometric reference data for children and adults: United States, 2011-2014. *Vital Health Stat 3 Anal Stud.* 2016;(39):1-46.
14. Banhiran W, Junlapan A, Assanasen P, Chongkolwatana C. Physical predictors for moderate to severe obstructive sleep apnea in snoring patients. *Sleep Breath*. 2014;18(1):151-158.
15. Banhiran W, Assanasen P, Nopmaneejumruslers C, Metheetrairut C. Epworth sleepiness scale in obstructive sleep disordered breathing: the reliability and validity of the Thai version. *Sleep Breath.* 2011;15(3):571-577.
16. Pallesen S, Nordhus IH, Omvik S, Sivertsen B, Tell GS, Bjorvatn B. Prevalence and risk factors of subjective sleepiness in the general adult population. *Sleep.* 2007;30(5):619-624.
17. Berry RB, Brooks R, Gamaldo C, et al. AASM scoring manual updates for 2017 (version 2.4). *J Clin Sleep Med.* 2017;13(05):665-666.
18. 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(3):479-504.
19. World Health Organization. Regional Office for the Western P. The Asia-Pacific perspective: redefining obesity and its treatment. Sydney: Health Communications Australia; 2000.
20. Heinzer R, Vat S, Marques-Vidal P, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *Lancet Respir Med.* 2015;3(4):310-318.
21. Fietze I, Laharnar N, Obst A, et al. Prevalence and association analysis of obstructive sleep apnea with gender and age differences – results of SHIP-Trend. *J Sleep Res.* 2019; 28(5):e12770.
22. Hein M, Lanquart JP, Loas G, Hubain P, Linkowski P. Prevalence and risk factors of moderate to severe obstructive sleep apnea syndrome in insomnia sufferers: a study on 1311 subjects. *Respir Res.* 2017;18(1):135.
23. Dosman JA, Karunanayake CP, Fenton M, et al. Obesity, sex, snoring and severity of OSA in a first nation community in Saskatchewan, Canada. *Clocks & sleep.* 2022;4(1):100-113.
24. Bonsignore MR, Saaresranta T, Riha RL. Sex differences in obstructive sleep apnoea. *Eur Respir Rev.* 2019;28(154):e190030.
25. Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea: implications for treatment. *Chest.* 2010;137(3):711-719.
26. Dong Z, Xu X, Wang C, Cartledge S, Maddison R, Shariful Islam SM. Association of overweight and obesity with obstructive sleep apnoea: a systematic review and meta-analysis. *Obes Med.* 2020;17:100185.
27. Soylu AC, Levent E, Sariman N, Yurtlu S, Alparslan S, Saygi A. Obstructive sleep apnea syndrome and anthropometric obesity indexes. *Sleep Breath.* 2012;16(4):1151-1158.
28. Kim SE, Park BS, Park SH, et al. Predictors for presence and severity of obstructive sleep apnea in snoring patients: significance of neck circumference. *J Sleep Med.* 2015;12(2):34-38.
29. Bjorvatn B, Lehmann S, Gulati S, Aurlien H, Pallesen S, Saxvig IW. Prevalence of excessive sleepiness is higher whereas insomnia is lower with greater severity of obstructive sleep apnea. *Sleep Breath.* 2015;19(4):1387-1393.
30. Proimos E, Kiagiadaki D, Kaprana A, Chimona TS, Maroudias NJ, Papadakis CE. Clinical

application of subjective measurements for OSAS assessment: predictive factors of syndrome severity. *ORL.* 2012;74(5):240-245.
31. Reutrakul S, Mokhlesi B. Obstructive sleep apnea and diabetes: a state of the art review. *Chest.* 2017;152(5):1070-1086.
32. Subramanian A, Adderley NJ, Tracy A, et al. Risk of incident obstructive sleep apnea among patients with type 2 diabetes. *Diabetes care.* 2019;42(5):954-963.