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Predictors for Obesity Hypoventilation Syndrome in Thai Population

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Background and Objective Obesity Hypoventilation Syndrome (OHS), is a condition with high morbidity and mortality. Body Mass Index (BMI) of more than 30 kg/m^2 is used, to diagnose OHS. As BMI for obesity for Thais is 25 kg/m^2, BMI more than 25 kg/m^2 is used in our institution, to diagnose OHS. The purpose of this study was to evaluate if BMI of 25 kg/m^2 is appropriate criterion for OHS in Thai patients.

Methods This study was a retrospective study conducted at Khon Kaen University. Inclusion criteria were adult patients diagnosed with OHS in 2016. Patients diagnosed with obstructive sleep apnea (OSA), were randomly selected as control subjects. The ratio of OHS:OSA, was 1:4. Clinical factors associated with OHS were examined, using multivariate logistic regression analysis.

Results During the study period, there were 25 OHS and 108 OSA patients. The OHS group had a significantly higher average BMI (48.9 kg/m^2 vs. 29.2 kg/m^2), than the OSA group. The OHS group also had higher proportions of patients with pulmonary hypertension (50% vs. 2%), and heart failure (76% vs. 6.5%). There were two independent predictors for OHS, including BMI and serum bicarbonate levels. Adjusted odds ratio (95% CI) for each of these factors was 1.08 (1.01, 1.17) and 1.96 (1.15, 3.34), respectively. Body mass index greater than 25 kg/m^2 and serum bicarbonate more than 25 mEq/L, yielded 100% sensitivity for OHS.

Conclusions Appropriate diagnostic criteria for OHS for the Thai population, may be different from those for populations in Western countries. **Sleep Med Res 2019;10(1):13-16**

Key Words Obstructive sleep apnea, Sensitivity, Diagnosis, Obesity, Serum bicarbonate.

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INTRODUCTION

Obesity Hypoventilation Syndrome (OHS) is defined as the combination of obesity [Body Mass Index (BMI) ≥ 30 kg/m^2] and daytime hypoventilation [arterial carbon dioxide pressure ($PaCO_2$) ≥ 45 mm Hg], in absence of other possible causes of hypoventilation [1]. Although obstructive sleep apnea (OSA) and OHS are classified as sleep-related breathing disorders, OHS patients tend to have lower quality of life, greater health care expenses, greater risk of pulmonary hypertension, and higher mortality rate, compared with OSA patients [2].

Prevalence of OHS in the general population is unknown, but has been estimated between 0.15% and 0.30% in the United States adult population [3]. However, prevalence estimates for OHS, vary significantly across studies. One review article found the estimated prevalence of OHS in patients with OSA, was between 4–50% [4]. This considerable range, likely reflects

variations in patient populations across studies.

Additionally, clinical features of OHS patients vary considerably by ethnicity. For example, Japanese OHS patients are younger, than those with pure OSA [5,6]. OHS was found in older patients, than in OSA patients in Saudi Arabia or the United Arab Emirates [3,7,8]. East Asian populations are also known to develop OHS at lower BMI, compared with non-Asian populations [4].

As mentioned above, criteria for OHS may differ among ethnic groups. Current diagnostic criteria for OHS, are BMI more than 30 kg/m^2. However, BMI criterion may not be applicable in Thai or other Asian populations, as criterion for obesity used in Asian populations is BMI more than 25 kg/m^2. So, BMI of more than 25 kg/m^2 is used in our institution, to diagnose OHS. The purpose of this study was to evaluate if BMI of 25 kg/m^2 is appropriate criterion, for OHS in Thai patients.

METHODS

This was a retrospective study conducted at Khon Kaen University's Srinagarind Hospital. Inclusion criteria were adults (older than age 15), and had been diagnosed with OHS. Patients were excluded, if they had one of the following conditions: hypothyroidism, Chronic Obstructive Pulmonary Disease, neuromuscular diseases, opiate overdose, or severe electrolyte abnormalities such as hypophosphatemia, hypokalemia, or hypercalcemia. The study period was January−December 2016.

Table 1. Baseline clinical features of OHS and OSA

Factors	OHS (n = 25)	OSA (n = 108)	p-value
Age (yr)	48 (35–59)	49 (37–59)	0.167
Male sex (%)	10 (40)	57 (52.8)	0.250
Weight (kg)	83 (67–106)	78.4 (65–95)	-
Height (cm)	161 (155–170)	162 (155–170)	-
BMI (kg/m^2)	48.9 (39.5–57.5)	29.2 (25.7–35.4)	< 0.001
Mallampati (%)			
Class 1	1 (7.1)	4 (5.4)	
Class 2	1 (7.1)	27 (36.5)	
Class 3	3 (21.4)	31 (41.89)	0.001
Class 4	9 (64.3)	12 (15.22)	
Hypertension (%)	13 (52)	84 (77.8)	0.009
Diabetes mellitus (%)	12 (48)	27 (25)	0.023
Stroke (%)	0 (0)	7 (6.5)	0.191
Coronary artery disease (%)	1 (4)	8 (7.4)	0.541
Heart failure (%)	19 (76)	7 (6.5)	< 0.001
Atrial fibrillation (%)	2 (8)	1 (0.9)	0.032
SBP (mm Hg)	140 (127.5–150.5)	140 (129–151)	0.087
DBP (mm Hg)	85 (76–94)	85 (78–94)	0.223
Hct (%)	40.0 (37.1–44.8)	39.7 (36.3–44.0)	0.024
WBC (cell/mm^3)	7700 (6400–9900)	7450 (5700–8850)	0.050
Plt (cell/mm^3)	241000 (198000–285000)	245000 (198000–280000)	0.547
BUN	12.7 (9.5–16.3)	12.8 (9.7–16.2)	0.891
Cr	0.8 (0.7–1.0)	0.85 (0.7–1.1)	0.413
Serum HCO_3 (mg/dL)	49 (37–59)	24.8 (22.7–26.8)	< 0.001
AHI	21.5 (12–43)	20 (10–39)	0.110
Lowest spO_2 (%)	83.5 (71–88)	83.5 (72–89.5)	0.948
EF	60 (56–65)	67 (64–72)	0.001
PHT (%)	9 (50)	2 (2.11)	0.000

Data presented as median (interquartile range) or number (percentage).
OHS: Obesity Hypoventilation Syndrome, OSA: obstructive sleep apnea, BMI: Body Mass Index, SBP: systolic blood pressure, DBP: diastolic blood pressure, Hct: hematocrit, WBC: white blood cells, Plt: platelet, BUN: blood urea nitrogen, Cr: creatinine, HCO_3: bicarbonate, AHI: apnea hypopnea index, spO_2: oxygen saturation from polysomnography, EF: ejection fraction, PHT: pulmonary hypertension.

All patients diagnosed as OHS, were included in the study. Patients diagnosed with OSA were randomly selected as controls, from the OSA database at the hospital. Ratio of OHS:OSA was 1:4. Study protocol was approved by the Ethics Committee in Human Research, Khon Kaen University, Thailand (HE541373).

Clinical data of all eligible patients in both groups were recorded including baseline characteristics, co-morbid diseases, physical signs, and laboratory results. All patients underwent polysomnography, and OSA was diagnosed according to the apnea-hypopnea index (AHI; evidence of five or more apnea or hypopnea events per hour).

Statistical Analyses

Descriptive statistics were used, to compare differences between OHS and OSA groups. Clinical predictive factors of OHS were calculated, using logistic regression analysis. Factors with a p value less than 0.20 by univariate logistic regression, were included in subsequent multivariate logistic regression analysis. If significant factors for OHS were expressed as numerical data, cutoff points to determine risk of OHS were computed, using a receiver operating characteristic (ROC) curve. All statistical analyses were performed, using STATA software version 10.0 (College Station, TX, USA).

RESULTS

There were 25 OHS and 108 OSA patients, included in this study. Median values of pCO2 and pO2 of the OHS group was 56 mm Hg (first to third interquartile range of 52−72), and 57 (first to third interquartile range of 50−65). The OHS group had significantly higher average BMI (48.9 kg/m^2 vs. 29.2 kg/m^2), than the OSA group. The OHS group also had higher proportions of patients with pulmonary hypertension (50% vs. 2%) and heart failure (76% vs. 6.5%), than the OSA group (Table 1).

There were two independent predictors for OHS, including BMI and serum bicarbonate level. Adjusted odds ratio (95% confidence interval) of these factors were 1.08 (1.01, 1.17) and 1.96 (1.15, 3.34), respectively (Table 2). BMI greater than 25 kg/m^2 and serum bicarbonate more than 25 mEq/L yielded 100% sensitivity for OHS (Table 3). Areas under the ROC curves of body mass index and serum bicarbonate for OHS, were 88.37% and 93.88%, respectively (Figs. 1 and 2).

Table 2. Factors associated with obesity hypoventilation syndrome by multivariate logistic regression analysis

Factors	Adjusted odds ratio	95% confidence interval
Male sex	5.95	0.30–118.17
Systolic blood pressure	0.95	0.87–1.04
Apnea hypopnea index	1.01	0.97–1.06
Body Mass Index	1.09	1.01–1.17
Serum bicarbonate	1.96	1.15–3.33

Table 3. Various cutoff points and its diagnostic properties of body mass index and serum bicarbonate for obesity hypoventilation syndrome

Cutoff points	Sensitivity	Specificity
Body mass index		
25	100	22
28	100	43
30	92	53
Serum bicarbonate		
25	100	52
27	92	76
29	76	98

DISCUSSION

This study found that body mass index and serum bicarbonate, were two independent predictors for OHS among OSA pa-

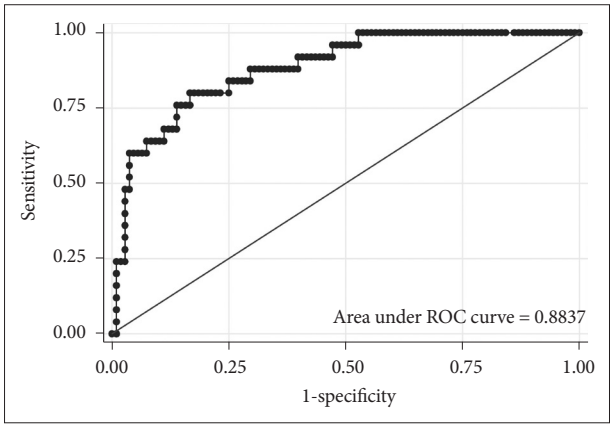

Fig. 1. A receiver operating characteristic (ROC) curve, of Body Mass Index and Obesity Hypoventilation Syndrome.

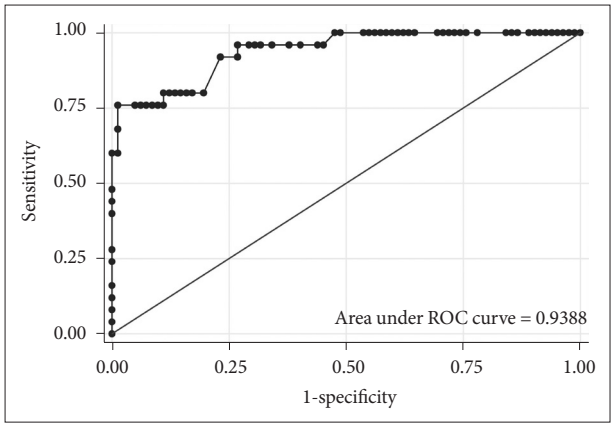

Fig. 2. A receiver operating characteristic (ROC) curve, of serum bicarbonate and Obesity Hypoventilation Syndrome.

tients (Table 2). This is in contrast to a previous study in the U.S., in which AHI was not found to be a significant factor for OHS (Table 3) [9]. Two other studies conducted in Turkey, also confirmed that serum bicarbonate was an independent predictor for OHS [10,11]. No previous study has evaluated if body mass index is a predictor for OHS, because obesity is a diagnostic criteria for the condition.

Although BMI criterion for OHS is 30 kg/m^2, a report in Japan found that average BMI of OHS patients in the Japanese population was 37 [5]. This study also found that median BMI of OHS patients was also more than 30 kg/m^2 (48.9 kg/m^2) as shown in Table 1. However, the appropriate BMI cutoff point may not be 30 kg/m^2 in this study. There were 8% of Thai OSA patients with OHS, who may not be diagnosed with BMI of 30 kg/m^2 (Table 3). Findings may imply that Thai OSA patients could develop OHS, even if they have lower BMI than 30 kg/m^2.

Likewise, setting the cutoff point of serum bicarbonate at 27 mEq/L or more may lead to under-diagnoses of OHS, in approximately 8% of Thai OSA patients (Table 3). This cutoff point has been shown to yield a sensitivity of 92% in the U.S. population, and 76−88% in the Turkish population [9-11]. However, according to our research, if the cutoff point for serum bicarbonate is set at 25 mEq/L, sensitivity increases to 100%, as it is when BMI is set at 25 kg/m^2 (Table 3). Findings raise the concern that current diagnostic criteria for OHS, may not be suitable in Thai or other Asian populations.

There are limitations to this study. First, all participants had been diagnosed with OSA. However, OHS may develop without presence of OSA, in approximately 10% of patients. So, findings are applicable only to patients with OSA. Second, this study was conducted in only one university hospital setting in Thailand. Further studies in other settings in Asia are needed. Third, there are some missing values, such as serum HCO_3 in the OSA group. Finally, the study population is small. However, other OHS studies also had study populations of fewer than 200 participants.

In conclusion, appropriate diagnostic criteria for OHS in Thai patients, may be different from those in Western populations.

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Conflicts of Interest

The authors have no financial conflicts of interest.

Authors' Contribution

Conceptualization: Sawanyawisuth K, Saeseow S, Chattakul P. Data curation: Saeseow S. Methodology: Chattakul P, Khamsai S, Limpawattana P, Chindaprasirt J. Supervision: Chotmongkol V, Silarucks S, Senthong V, Sawanyawisuth K. Writing—original draft: Sawanyawisuth K. Writing—review & editing: all authors.

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