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Clinical Factors Associated with Very Severe Obstructive Sleep Apnea in Mongolian Patients: A Case-Control Study

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Objectives: To determine risk factors and clinical characteristics of obstructive sleep apnea patients (OSA) according to the severity of the value of AHI ≥ 60 (Apnea-Hypopnea Index). **Methods:** A hospital-based, case-control study, December 2018 - 2020. Patients were grouped by severity of AHI as moderate, severe, and very severe. **Results:** Of 103 male cases, 52 were very severe obstructive sleep apnea (vsOSA). The control group consisted of 16 moderate OSA (mOSA) and 35 severe OSA (sOSA) patients. The case group consisted of 52 vsOSA patients. The average age was 48.7 ± 12.6. There was statistically significant increased body mass index ($p < 0.003$), systolic blood pressure, and abdominal circumference ($p < 0.006$) in the vsOSA group. Moreover, on polysomnography there was less deep sleep ($p < 0.004$), a greater arousal index ($p < 0.000$), higher apnea-hypopnea index ($p < 0.000$), and higher night systole pressure ($p < 0.010$). According to a bivariate analysis, abdominal circumferences were the variable with the closest association to the vsOSA group (crude OR: 9.14, $p > 0.004$), followed by decreased maximum saturation of O2 (crude OR: 6.6, $p > 0.451$). **Conclusion:** Of male OSA patients, 50.1% have vsOSA (AHI > 60) and most of them were obese and suffered from high blood pressure. Lower levels of O2 saturation and increased abdominal and neck circumferences were significant risk factors for the very severe obstructive sleep apnea group.

Keywords: Obstructive Sleep Apnea, Case-Control Study, Apnea-Hypopnea Index

Introduction

Obstructive sleep apnea (OSA) is a common condition characterized by repetitive obstruction of the upper airway during sleep with resultant episodic hypoxia and arousal. The severity of the OSA is determined by the apnea-hypopnea index (AHI), the frequency in which apnea or hypopnea is produced, and expressed as the number of events per hour [1]. With these values, the severity of OSA can be grouped as: mild OSA (mOSA) -5 > AHI < 15 events/hour; moderate OSA (mod OSA) 15 > AHI < 30; severe OSA (sOSA) AHI > 30) [2]. This is assessed by polysomnography (PSG) [3, 4]. The comprehensive overnight PSG

is currently the most widely used diagnostic test to document obstructive sleep apnea. This is the gold standard for diagnosis of OSA [5, 6].

OSA prevalence is greater in men and associated with obesity [7, 8]. OSA risk factors with strong associations are obesity, male sex, and older age, while those with moderate associations include craniofacial/upper-airway abnormalities, smoking, alcohol drinking, nasal congestion, cardiovascular disease, and family history of sleep apnea [9]. Increased body-mass index (BMI) and neck circumference are mostly measured in individuals with obesity and fat deposition around the upper airway who are at increased risk of having OSA. It is known that OSA is associated with a range of negative outcomes including sleepiness, sleep disruption, cognitive dysfunction, and cardiovascular disease [5]. Subjects with OSA may complain of excessive daytime sleepiness (EDS) or insomnia, nocturia, and morning headaches. Specifically, there has been increasing social concern regarding sleep quality due to traffic accidents caused by daytime sleepiness, which is a major sleep apnea symptom, and other large-scale disasters caused by a lack of attention [5, 10, 11].

The prevalence of symptomatic OSA in the general population has been estimated at about 3-9% [1-3]. In Western countries, the overall population prevalence ranged from 9% to 38% [1]. Moreover, up to 5% of the western population has undiagnosed OSA syndrome characterized by an elevated apnea-hypopnea index (AHI) and symptoms) [7]. In the Wisconsin Sleep Cohort, a stratified random sample of Wisconsin state employees ages 30 – 60 years, the prevalence of OSA defined by an AHI > 5 events/hour was 9% in women and 24% in men [8]. The prevalence of OSA has been shown to increase with age in adults, up to the age of 65. On the other hand, in Asian countries OSA prevalence ranged from 3.7% to 97.3% [4]. This huge difference is possibly explained by the sample size as well as some risk factors such as age and BMI. In the study by Okabayashi et al. where the participants underwent home pulse oximetry, the OSA patients with highest AHI were overweight and hypertensive [12].

Previously researchers found that patients with sOSA had higher rates of morbidity and mortality compared to mild and moderate AHI level patients [13]. Several studies demonstrated that the severity of OSA was significantlty different between white and asian ethnic groups. Asian populations had a higher mallampati oropharyngeal score (the distance from the tongue base to the roof of the mouth), a higher thryomental angle, and shorter thyromental distance morphology compared to white ethnic groups. Moreover, obese subjects had an abnormal craniofacial profile which resulted in structural narrowing of the upper airway. Further more, in the Korean population, Koo et al. revealed that during REM (rapid eye movement) sleep, modOSA and sOSA was significantly associated with metabolic syndrome after adjusting for age and BMI [14].

Some studies used different cut-off values for very severe OSA (vs OSA) with AHI ≥ 60 to AHI > 100 to determine the association between clinical characteristics to PSG parameters [14 - 16]. Based on a previous study we hypothesized that patients with vsOSA (AHI > 60) are associated with increased comorbidities in comparison with AHI < 60 levels. To our knowledge, no study has analyzed the diagnosis of OSA and sleep related breathing disorders using polysomnography in the Mongolia population. Therefore, in the present study, we aimed to determine risk factors and clinical characteristics of OSA patients with the value of AHI ≥ 60 in Mongolian male patients admitted at the Sleep Research Center of the General Hospital for State Special Servants (GHSSS) in Mongolia.

Materials and Methods

Study design

Hospital based, retrospective, case-control design was used for the study. All patient data and PSG recordings were used from the Sleep Center of the General Hospital for State Special Servants (GHSSS), Ulaanbaatar, Mongolia.

Study population

There were a total of 233 PSG acquisitions performed during the 2-year period, December 2018-2020 and 158 patients were diagnosed with OSA, 103 males, and 55 females. We excluded all females and patients with a diagnosis other than OSA. Male patients were divided into three categories according to their AHI: moderate 16 (15.5%) (modOSA < 15, AHI < 29.9), severe 35 (34.0%) (sOSA > 30, AHI > 59.9) and very severe 52 (50.5%) (vsOSA, AHI > 60). We considered vsOSA (AHI > 60) category as a case and modOSA with sOSA groups as controls. Cases and controls were matched randomly according to their AHI category.

Inclusion criteria: age older than 18 years old, AHI > 15, and

male. Exclusion criteria: controls with AHI < 15, sleep disease comorbidity, diagnosis other than OSA, and women.

Variables

Demographic, anthropometric, clinical and PSG variables included for the analysis were: age (years), weight (kg), height (m), body mass index (BMI: kg/m^2), neck and abdomen circumference (cm), Mallampati's classifications parameters, blood pressure, SPO2 measurement and selected PSG indicators.

We defined obesity as a BMI ≥ 30. A hypertension diagnosis was considered as systolic blood pressure > 140 mmHg or diastolic blood pressure > 90. Arterial blood pressure measurements were done according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, Hypertension [17].

We followed National Cholesterol Education Program's Adult Treatment Panel III criteria to define metabolic syndrome, with the cut-off value for abdominal obesity of 90 cm for men, as recommended by the World Health Organization guidelines for South Asians [18, 19].

Clinical examinations

Participants' body weight (in kg) and height (in cm) were measured by trained medical assistants or physicians using a standardized protocol, and BMI (in kg/m^2) was subsequently calculated. Patients with BMI values between 25 and 30kg/m^2 were considered overweight, and patients with BMI values > 30 kg/m^2 were considered obese. Body weight was measured to the nearest 0.5kg in standing position without footwear, wearing light indoor clothes, with body composition analyzer, "AQUNICC BC 360" of AQUNICC brand, by "SELVAS" Korea. Abdominal circumference was measured midway between lower rib margin and anterior superior iliac spine using a non-elastic measuring tape and reported in cm. Neck circumferences in cm were measured at the level of the cricothyroid membrane. An automatic sphygmomanometer "Ray come" with a digital display was used to measure blood pressure with patients in the sitting position after at least 5 minutes of rest.

The oropharynx examination: a) The Mallampati score was obtained during the physical examination of each patient. The score was assessed by asking the patient to open his or her mouth as wide as possible while protruding the tongue as far as possible. A standard I to IV grading system was used. Similarly, tongue position grading was performed as follows: I, if uvula and the entire tonsils/pillar were clearly visible; II, if most of the uvula was visible but tonsils or the pillar was invisible; III, if only the soft palate was partially visible; and IV, if only the hard palate was visible [15]. b) Tonsil grade was graded from I to IV; cases, where the tonsil tissue was not visible, were defined as I; cases where the tonsil was visible in the pillars as II; cases with tonsils outside the pillars as III; and cases where tonsils reached the midline as grade IV [20].

Polysomnography

All patients underwent one night laboratory polysomnography recording from 10:00 pm to 6:00 am, who were sent from sleep doctors and neurologists of the outpatient department. We used a PSG device with name "SOMNO screen TM plus 6962" by SOMNO medics GmbH, Germany. The software is DOMINO, version 2.6.0. All PSG tests were carried out according to standardized techniques with digital data recording. Preparation of examinations and placement of electrodes lasted approximately 50 to 60 minutes. For the PSG, the recordings took place under the vigilance of specialized technicians with the supervision of a physician, in a room with appropriate technical conditions. The PSG recording scorings followed according to the American Academy of Sleep Medicine 2007 recommendations, with automatic staging followed by manual staging in phases of 30 seconds, according to modified Rechtschaffen and Kales criteria, carried out by experienced technicians and analyzed by sleep specialists [20, 21]. Data were obtained from two central derivations (C4-A1, C3-A2), two occipital derivations (O2-A1, O1-A2), two frontal derivations (F4-A1, F3-A2), two derivations for the detection of ocular movement (ROC-A1, LOC-A2), three chin electromyogram (EMG) derivation, two electrocardiogram electrodes, a nasal pressure sensor, a nasal thermistor, a piezoelectric snore sensor, respiratory movement sensors with thoracic and abdominal piezoelectric bands, pulse oximetry, EMG of the right and left tibialis muscle, and body position. Hypoapnea was defined as a decrease in amplitude of the thermistor ≥ 30%, with desaturation desaturation of 4% compared to the prior baseline value, over at least 90% of the duration of an event ≥ 10 seconds. OSA was classified as moderate (AHI 15.1–30 events/h), severe (AHI > 30 events/h), and very severe (AHI > 60 events/h) [22].

Statistical analysis

Frequencies, percentages, and an ANOVA test was used to examine the difference among different groups. The Turkey test was applied for multiple comparisons after the Bonferroni corrections. A conditional logistic regression model was used to estimate crude Odds Ratios (crude OR) with a 95% confidence interval (CI). A p-value of < 0.05 was used as the cut-off point for determining the statistical significance. The data were collected using quantitative methods and were analyzed using Statistical Packages for Social Sciences (SPSS) version 20 statistical software.

Ethical statement

The study was approved by the Research Ethics Committee of the Mongolian National University of Medical Sciences on March 23, 2019 (No. 2019/3-03). All patients signed an informed consent form before clinical examination, anthropometric measurement, and acquisition of polysomnography.

Results

In our database, we identified 103 male cases of OSA and 52 (50.5%) patients with an AHI > 60 during 2 years. Case-patients that met the inclusion criteria were matched with 16 (15.5%) modOSA controls and 35 (34.0%) sOSA controls. The mean age of all subjects was 48.7 ± 12.6 years. There are no significant differences in OSA groups by age ($p > 0.791$). Socio-demographic characteristics of all patients is shown in Table 1.

72 (70%) of all patients included in the study had day arterial hypertension, 88 (85%) had night arterial hypertension, 10 (9%) patients had normal weight, 29 (28%) were overweight, and 64 (62%) suffered from morbid obesity. There was no statistically significant difference between groups in terms of age, education, and place of living with a p value of 0.92-0.13 following the chi-square test (Table 1).

Multiple comparison test revealed that there was statistically significantly more body weight ($p < 0.016$), BMI ($p < 0.012$), night systolic blood pressure, abdominal ($p < 0.009$) and neck ($p < 0.014$) circumference in the AHI > 60 group than the moderate OSA group. In contrast, there was no statistical difference in height, day systolic blood pressure, sleep efficiency and Mallampati index between groups (Table 2). PSG variables of sleep architecture revealed increased sleep arousal index ($p < 0.000$), high AHI ($p < 0.000$), desaturation of O2 ($p < 0.000$), night systole blood pressure increasing ($p < 0.010$) in patients with vsOSA compared to moderate to severe groups (Table 2).

Logistic regression analysis of associations of different groups of OSA revealed that abdominal circumferences have the highest association with vsOSA (crude OR: 9.14, $p > 0.004$), followed by maximum saturation of O2 (crude OR: 6.6, $p > 0.401$), BMI > 30 (crude OR: 5.3 $p > 0.001$) and blood pressure >140 (crude OR: 4.62, $p > 0.015$). However, neck circumference > 36 with crude OR of 3.08 was not statistically significant ($p > 0.151$) (Table 3).

Table 1. Demographic characteristics of patients.

Characteristics	Obstructive Sleep Apnea				*p- value
	Moderate (n = 65)	Severe (n = 83)	Very severe (n = 66)	Total (n = 214)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age, years[a]	48.41 ± 12.2	51.85 ± 10.7	47.8 ± 11.3	48.7 ± 12.6	0.058
Education	N (%)	N (%)	N (%)	N (%)	
Primary	3 (18.8)	7 (20.0)	14 (26.9)	24 (23.3)	0.915
Middle	13 (81.2)	28 (80.0)	38 (73.1)	79 (76.7)	
Residency					
Ulaanbaatar city	12 (75.0)	25 (71.4)	34 (65.4)	71 (69.0)	0.920
County	4 (25.0)	10 (28.6)	18 (34.6)	32 (31.0)	
Employment					
Primary	5 (31.3)	12 (34.3)	17 (32.7)	34 (33.0)	0.131
High	7 (43.8)	17 (48.6)	16 (30.8)	41 (39.8)	
University	4 (25.0)	6 (17.1)	19 (36.5)	29 (28.2)	

*ANOVA test; multiple comparison: [a]Very severe vs. severe, p = 0.074.

Table 2. Anthropometric and sleep characteristics of all patients (cases (AHI > 60) and controls).

Characteristics	Obstructive Sleep Apnea				*p-value
	Moderate (n = 65)	Severe (n = 83)	Very severe (n = 66)	Total (n = 214)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
BMI [a]	27.91 ± 5.18	30.94 ± 6.6	34.86 ± 5.55	29.60 ± 6.5	0.003
Neck circumference[b, c]	38.8 ± 3.9	40.54 ± 5.19	41.87 ± 3.89	37.26 ± 5.19	0.041
Abdominal circumference[d]	100.3 ± 12.52	105.3 ± 19.0	113.8 ± 15.17	99.21 ± 18.19	0.006
Malampatti score*	1.62 ± 0.8	1.48 ± 0.6	1.82 ± 0.9	1.49 ± 0.78	0.151
Apnoe-hypoapnea index[e]	21.06 ± 3.88	45.65 ± 8.25	83.5 ± 17.5	38.59 ± 29.41	0.000
SpO2 min[f]	84.12 ± 5.41	76.6 ± 8.4	67.23 ± 9.53	78.97 ± 10.67	0.000
SpO2 max[g]	93.0 ± 1.46	92.9 ± 2.18	91.4 ± 2.74	92.71 ± 2.7	0.007
BP day systole max[h]	134.3 ± 26.57	144.5 ± 22.4	150.8 ± 22.5	136.13 ± 22.35	0.044
BP night systole max[i, j]	152.5 ± 34.3	169.57 ± 26.8	174.13 ± 29.2	148.92 ± 30.37	0.011
Total sleep time, hours [k, l, m]	7.27 ± 0.96	6.84 ± 1.03	7.25 ± 0.83	7.00 ± 1.00	0.108
Sleep efficiency	87.5 ± 6.65	86.3 ± 10.6	88.8 ± 9.04	86.61 ± 10.3	0.460
REM sleep [n, o]	19.3 ± 5.28	15.7 ± 6.36	13.94 ± 4.65	16.89 ± 6.55	0.004
Arousal index [p]	31.3 ± 12.4	45.6 ± 15.47	53.2 ± 17.4	39.44 ± 20.90	0.000

*ANOVA test; multiple comparisons: [a]moderate vs. very severe, $p < 0.011$; [b]moderate vs. severe, $p < 0.051$; [c]moderate vs. very severe, $p < 0.045$; [d]severe vs. very severe, $p < 0.051$; [e]moderate vs. very severe, $p < 0.053$; [f]severe vs. very severe, $p < 0.031$; [g]moderate vs. severe, $p < 0.012$; [h]moderate vs. severe, $p < 0.013$; [i]moderate vs. severe, $p < 0.013$; [j]moderate vs. very severe, $p < 0.052$; [k]moderate vs. severe, $p < 0.024$; [l]severe vs. very severe, $p < 0.051$; [m]moderate vs. very severe, $p < 0.001$; [n]moderate vs. very severe, $p < 0.001$; [o]sever vs. very severe, $p < 0.000$; [o]moderate vs. very severe, $p < 0.000$.
REM-Rapid Eye Movement.

Table 3. Bivariate analysis of associations with the severity of OSA.

Characteristics	OR	CI 95%	p-value
Age	1.16	1.00-1.01	0.078
Gender			
Femalee*	1.00	Reference	
Male	1.33	0.80-2.20	0.086
Apnea-hypoapnea index, scores			
Moderate (15-30)*	1.00	Reference	
Severe (31-60)	2.07	2.41-6.87	0.041
Very severe (60 <)	4.24	3.49-23.7	0.053
Total sleep time, hours			
> 8 hours*	1.00	Reference	
< 7 hours	3.41	2.32-8.72	0.054
REM sleep, minutes			
< 90 min*	1.00	Reference	
> 91 min	1.78	1.65-4.69	0.056
Arousal index, scores			
< 39*	1.00	Reference	
> 40	1.15	0.69-1.91	0.586

Continued

Sleep efficiency, percentages			
> 90%*	1.00	Reference	
< 91%	1.78	1.65-4.69	0.056
Deep sleep latency, minutes			
< 30 min*	1.00	Reference	
> 31 min	2.87	1.69-4.78	0.001
BMI, kg			
< 29 kg*	1.00	Reference	
> 30 kg	0.57	0.17-1.80	0.335
SpO2 %			
> 92 %*	1.00	Reference	
< 91 %	0.51	0.06 - 2.46	0.494
BP day systole, mmHg			
< 136 mmHg*	1.00	Reference	
> 137 mmHg	2.65	2.12-6.28	0.061
BP night systole, mmHg			
< 148 mmHg*	1.00	Reference	
> 149 mmHg	4.25	4.12-6.28	0.061
Abdominal circumference, cm			
< 99 cm*	1.00	Reference	
> 100 cm	1.31	0.32 - 4.58	0.602
Neck circumference > 36			
< 37 cm*	1.00	Reference	
> 38 cm	1.64	0.36 - 6.90	0.549

*Reference value; BMI-Body Mass Index; REM-Rapid Eye Movement

Discussion

Currently there are a limited number of studies about risk factors and clinical characteristics of vsOSA. In Argentine, one study recruited 10 patients with AHI > 100 for 1.5 years in 2019, while in South America 19 patients were recorded with AHI >100 in 6 years, and in Mongolia we found the same AHI category in 9 patients over a period of 2 years [17-20].

Men are prone to have OSA compared to women at the ratio of 2:1 which is similar to other studies [19]. In our study, vsOSA tends to occur at a younger age (AHI > 60, mean age 47.2 ± 11.3) than in Western and Asian countries [21, 22]. The anthropometric measurements like abdominal, neck circumferences, and BMI are close to the performance of other studies.

PSG architecture of our patients shows higher AHI, with the same total sleep time (TST), and similar sleep efficiency, deep sleep (N3), rapid eye movement sleep (REM), and arousal index compared to other similar studies. The decreased SPO2 level in PSG had the strongest association ($p < 0.000$) with AHI severity in Mongolian men, which was similar to other studies [23]. In addition, our bivariate analysis is consistent with the associations found in the study conducted by Jurcevic et al. and Jorge Rey de Castro Rey de Castro [11, 20]. They concluded that the group with vsOSA has a consistent association with high blood pressure (HBP), more often with increased BMI, and higher abdominal circumferences. Yasimin Unal and H Kang also reported BMI and abdominal circumference having strong association with the severity of the AHI category [14, 15]. We also found differences in the magnitude of these associations depending on whether the vsOSA cases were compared with moderate or severe OSA controls, suggesting that the differences are more notable when compared to vsOSA than with moderate OSA.

The association between day systole blood pressure,

night systole blood pressure, and vsOSA is high compared to patients with sOSA, and increases, even more, when compared to patients with moderate OSA, which is consistent with the findings of previous studies [18, 19]. These findings suggest that the principal clinical characteristic of patients with vsOSA is that of having a greater probability of arterial hypertension depending on the severity of the OSA, which is in keeping with other studies [24, 25]. In the bivariate analysis, obesity had an intense association (OR: 5.3) with AHI category and it was consistent with the results obtained by Preis et al. in the Framingham study [26].

The limitation of our study was the lack of an standardized sleep quality questionnaire for Mongolian patients. We didn't evaluate the clinical laboratory analysis of patients with OSA which was another limitation of our study. Clinical studies including the laboratory analyses such as blood sugar, cholesterol, and lipids may have more significance in the identification of further prognosis of different stages of OSA.

Half of male OSA patients observed during the 2018-2020 years at the Sleep Center in Ulaanbaatar have very severe OSA with AHI > 60. Patients with vsOSA have a consistent association with HBP, more often with elevated BMI, and higher abdominal circumferences. PSG shows the lowest SPO2 saturation in patients with vsOSA as compared to patients with severe and moderate OSA.

Conclusions

50.1% of male OSA patients in Mongolia have vsOSA (AHI > 60) and most of them are obese and suffered from high blood pressure. Lower level of O_2 saturation and increased abdominal and neck circumferences are significant risk factors for the very severe obstructive sleep apnea group.

Conflict of Interest

The following authors have no conflict of interest.

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