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ORIGINAL ARTICLE

Assessment of obstructive sleep apnea among Malaysians with open-angle glaucoma using the STOP-Bang Questionnaire

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Introduction

Glaucoma is the most common cause of irreversible loss of vision worldwide. Numerous studies have confirmed an association between open-angle glaucoma (OAG) and obstructive sleep apnea (OSA) among Caucasian and Chinese populations; however, there has been no published study from South East Asia on this subject.

Materials and Methods

Therefore, our objectives were to use the STOP-BANG questionnaire (SBQ) to determine the factors (socio-demography, medical comorbidities) associated with the risk of OSA among patients with OAG and the association between glaucoma parameters and OSA. The SBQ was used for classifying patients as OSA low risk (score ≤ 2) to moderate/high risk (score ≥ 3).

Results

We found that the mean patient age was 64.2 ± 8.9 years, of which 55.4% (245 subjects) were males. The prevalence of moderate/high risk of OSA among the open angle glaucoma patients was 247 (55.9%), which comprised of mostly males(n=196,44.34%) compared to females (n=51,11.54%). Multiple logistic regression analysis showed that the predictors of moderate/high risk of OSA were males [odds ratio (OR) = 189.7, 95% confidence interval (CI) = 55.21, 651.69], high body mass index (OR = 1.23, 95% CI = 1.14, 1.33), diabetes (OR = 3.1, 95% CI = 1.45, 6.63) and hypertension (OR = 70.73, 95% CI = 22.59,221.50).

Conclusion

The identification of modifiable risk factors will be beneficial in the prevention of visual loss from glaucoma. The prevalence of moderate to high risk OSA risk was 56.9% among patients with OAG, that supports the vascular theory causing glaucomatous damage.

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Glaucoma remains a major global health problem with the risk for irreversible loss of vision.[1] It is known as the "Silent thief of sight" as it steals vision slowly and painlessly, therefore, most patients present late with permanent visual disability.[2] Identifying modifiable risk factors for this disorder is of vital importance as it will delay it progression and reduce the cost of treatment for patients. The objective of this study was to determine the prevalence of moderate and high-risk OSA among patients with open-angle glaucoma (OAG) and also determine the co-morbidity of these patients. This would bridge the gap of knowledge, raise the awareness among clinicians, enable the implementation for early intervention and prevent complications of OSA.

MATERIALS AND METHODS

A cross-sectional study was conducted from November 2019 - January 2021 to determine the factors (socio-demographic and medical comorbidities) associated with OSA risk among the OAG patients attending the ophthalmology clinic in Hospital Pengajar Universiti Putra Malaysia (HPUPM). Respondents were also assessment for the association between the severity of OSA with their most recent glaucoma parameters. Ethical approval was obtained from the relevant ethical boards. We used the STOP-BANG questionnaire, which consists of eight (yes, no) questions and according to the patient's response, the dependent variable in this study is the obstructive sleep apnea among patients with open-angle glaucoma and the independent variable are demographic characteristics, medical and co-morbidities factors, and glaucoma parameters.[3] The comparison of numerical categories between the two separate groups, usually normally distributed, was tested using the T-test, while the Chi-square and Fisher Test were used for two independent categorical groups. Version 25.0 of the Statistical Package for the Social Sciences (SPSS) was used to analyse the results.

This study classified the risk of having OSA as low for those scored ≤ 2, moderate for those scored 3-4 and high for those who scored 5-8. The study included patients aged ≥40 years with OAG or normotensive glaucoma (NTG) in one or both eyes who were able to give consent and who attended the ophthalmology clinic. Patients confirmed as having OSA by questionnaire were also examined by an ear, nose and throat (ENT) specialist to exclude any other pathology for their symptoms. We excluded from the study patients with secondary glaucoma, such as post-traumatic, uveitis, and surgical complication, also closed-angle glaucoma; patients who were unable to perform reliable visual field testing; patients with pulmonary disease, chronic steroid use, with previous diagnosis of OSA, diuretics or fluid restriction for congestive cardiac failure or chronic renal failure; patients on anticoagulants, atrial fibrillation or myocardial infarction in the last 6 months; patients with central and mixed sleep apnoea, and insomnia.

RESULTS

A total of 442 patients aged >40 years participated in this study. The mean participant age was 64.2 ± 9.0 years; of which 55.4% were male. Malay was the most common ethnicity (40.3%), followed by Chinese (38.2%) then Indians (21.3%) (Table 1 and Figure 1). More than half of the participants had secondary education (43.9%) and tertiary education (29.4%). The majority of participants were non-smokers (83.7%) and did not drink alcohol (93.9%). Family history of glaucoma was absent in most participants (82.6%).

Hypertension (71.2%) was the most prevalent comorbidity among the patients, followed by hyperlipidaemia (67.2%) and diabetes mellitus (54.3%) (Table 2). Other than these comorbidities, less than one-fifth of the participants had ischemic heart disease, chronic kidney disease, asthma, migraine, stroke, or peripheral vascular disease, and less than 1% had hypothyroidism and depression.

Being male ($p < 0.001$), still working ($p = 0.026$), in the M40 income stratum ($p = 0.018$), high body mass index (BMI) ($p < 0.001$), smoking ($p < 0.001$) and alcohol drinking ($p = 0.002$) all were highly associated with moderate and high risk of OSA as assessed with the STOP-BANG questionnaire among glaucoma

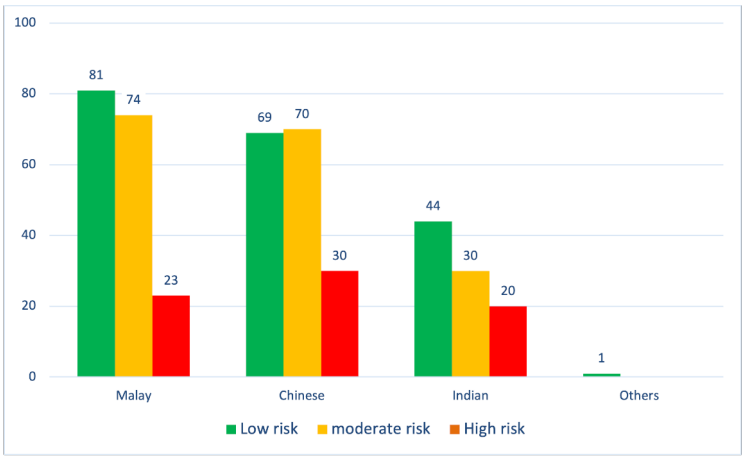

Figure 1 Distribution of OSA risk among glaucoma patients by ethnicity using SBQ N=442

Table 1 *Socio-demographic characteristics of the respondents. (N= 442)*

		Frequency (n)	Percentage (%)
Gender	Male	245	55.4
	Female	197	44.6
Ethnicity	Malay	178	40.3
	Chinese	169	38.2
	Indian	94	21.3
	Others	1	0.2
Education level	None	18	4.1
	Primary	100	22.6
	Secondary	194	43.9
	Tertiary	130	29.4
Occupation	Retiree or housewives	320	72.6
	Working	121	27.4
	Commercial vehicle driver	75	17.0
Body mass index, (BMI)	Underweight	9	2.0%
Male (n= 245), 26.31±4.89	Normal	87	19.7%
Female (n=197), 27.14±5.17	Overweight	184	41.6%
	Obese	162	36.7%
Smokers	Yes	72	16.3%
	No	370	83.7%
Alcohol drinkers	Yes	27	6.1%
	No	415	93.9%
Family history of OSA	Yes	77	17.4%
	No	365	82.6%
Income group	B40 <RM5,000)	390	88.2%
	M40 (>RM5,000)	52	11.8%
Age (Mean± SD) = 64.20±8.95 years			

Table 2 *The frequency of medical comorbidities among the respondents. (N= 442)*

Medical comorbidities	Frequency (n)	Percentage (%)
Diabetes mellitus	240	54.3
Hypertension	314	71.2
Hyperlipidemia	298	67.4
Ischaemic heart disease	74	16.7
Stroke	19	4.3
Migraine	21	4.8
Peripheral vascular disease	10	2.3
Chronic kidney disease	40	9.0
Hypothyroidism	4	0.9
Depression	2	0.5
Asthma	32	7.2

Table 3 Association between the respondents' socio-demographic factors and OSA risk (N = 442)

Variable		Low-risk OSA STOP-BANG ≤2 (195) N (%)	Moderate & high risk OSA STOP-BANG ≥3 (247) N (%)	p-value
Age (Mean± SD)	63.35±9.44	64.87±8.50	0.081	
Gender	Male	49 (20.0)	196 (80.0)	*<0.001*
	Female	146 (74.1)	51 (25.9)	
Ethnicity	Chinese	69 (40.8)	100 (59.2)	0.489
	Malay	81 (45.5)	97 (54.5)	
	Indian	44 (46.8)	50 (53.2)	
	Others	1 (100.0)	0 (0.0)	
Education level	None	13 (72.2)	5 (27.8)	*0.050*
	Primary	47 (47.0)	53 (53.0)	
	Secondary	85 (43.8)	109 (56.2)	
	Tertiary	50 (38.5)	80 (61.5)	
Occupation	Retiree or housewives	152 (47.4)	109 (52.6)	*0.026*
	Working	43 (35.5)	78 (64.5)	
Income group	B40 (<RM5,000)	180 (46.1)	210 (53.9)	*0.018*
	M40 (>RM5,000)	15 (28.8)	37 (71.2)	
Body mass index, kg/m² (Mean± SD) Male 25.49±4.30 Female 27.62±5.36	Underweight	9	2.0%	*<0.001*
	Normal	87	19.7%	
	Overweight	184	41.6%	
	Obese	162	36.7%	
Smokers	Yes	11 (15.3)	61 (84.7)	*<0.001*
	No	184 (49.7)	186 (50.3)	
Alcohol drinkers	Yes	4 (14.5)	23 (85.2)	*0.002*
	No	191 (46.0)	224 (54.0)	
Family history of OSA	Yes	27 (35.1)	50 (64.9)	0.078
	No	168 (46.0)	197 (54.0)	

patients who attended the Hospital Pengajar UPM ophthalmology clinic (Table 3).

Having hypertension ($p < 0.001$), diabetes ($p = 0.026$), hyperlipidaemia ($p = 0.018$), ischaemic heart disease ($p < 0.001$), smoking ($p < 0.001$) and alcohol drinking ($p = 0.002$) all were also significantly associated with moderate and high risk of OSA as assessed with the STOP-BANG questionnaire among glaucoma patients who attended the Hospital Pengajar UPM ophthalmology clinic (Table 4).

Multiple logistic regression analysis showed that the predictors of moderate/high risk of OSA were males [odds ratio (OR) = 189.7, 95% confidence interval (CI) = 55.21 - 651.69], high body mass index (OR = 1.23, 95% CI = 1.14, 1.33), diabetes (OR = 3.1, 95% CI = 1.45 - 6.63) and hypertension (OR = 70.73, 95% CI = 22.59 - 221.50).

DISCUSSION

To the best of our knowledge, this study is the first to evaluate the prevalence of OSA in OAG patients in Malaysia. Here, we used the STOP-BANG questionnaire to identify the risk of OSA in OAG patients who attended the ophthalmology clinic, and included 442 patients with OAG. The STOP-BANG questionnaire has been validated in the local language in Malaysia and therefore was a suitable instrument to determine the objectives of this study.[4] In addition, it has good sensitivity and specificity.[5-6] The questionnaire requires just a few minutes to complete and its sensitivity using a cut-off score of > 3 are 84% to 100% in detecting sleep apnea, depending on its severity.[5-6]The specificity is also acceptable, ranging from 37% to 56.4%, once again depending on the severity of the sleep apnea.[5-6]

Table 4 Association between the respondents' medical comorbidities and OSA risk (N = 442)

Variable		Low-risk OSA STOP-BANG ≤2 (195) N (%)	Moderate & high risk OSA STOP-BANG ≥3 (247) N (%)	p-value
Diabetes mellitus	Yes	87 (36.3)	153 (63.7)	*<0.001*
	No	108 (53.5)	94 (46.5)	
Hypertension	Yes	101 (32.2)	213 (67.8)	*<0.001*
	No	94 (73.4)	34 (26.6)	
Hyperlipidemia	Yes	112 (37.5)	187 (62.5)	*<0.001*
	No	83 (58.0)	60 (42.0)	
Ischemic heart disease	Yes	24 (32.4)	50 (67.6)	*0.027*
	No	171 (46.5)	197 (53.5)	
Stroke	Yes	5 (26.3)	14 (73.7)	0.110
	No	190 (44.9)	233 (55.1)	
Migraine	Yes	10 (47.6)	11 (52.4)	0.741
	No	185 (43.9)	236 (56.1)	
Peripheral vascular disease	Yes	3 (30.0)	7 (70.0)	0.363
	No	192 (44.4)	240 (55.6)	
Chronic kidney disease	Yes	16 (40.0)	24 (60.0)	0.582
	No	179 (44.5)	223 (55.5)	
Hypothyroidism	Yes	3 (75.0)	1 (25.0)	0.325
	No	192 (43.8)	246 (56.2)	
Depression	Yes	2 (100.0)	0 (0.0)	0.111
	No	193 (43.9)	247 (56.1)	
Asthma	Yes	14 (43.8)	18 (56.2)	0.965
	No	181 (44.1)	229 (55.9)	

We found that the prevalence of moderate to severe OSA among the patients was 56.9%. Male gender (odds ratio (OR) = 189.7), BMI (OR = 1.23), diabetes (OR = 3.1) and hypertension (OR = 70.73) were predictors of moderate to high risk of OSA in the OAG patients; we also found that the prevalence of NTG was 59.5% compared to OAG.[7] These findings are consistent with the results of previous global literature, which had also reported that people with OAG and diabetes mellitus had higher odds for moderate to high risk of OSA symptoms as compared to non-diabetics.[8] Our findings are also consistent with several previous studies in which the OR of diabetes mellitus for OSA was 1.23–1.78.[9-10] Diabetes may disturb vascular autoregulation of the retina, and the resulting vascular dysfunction, which induces glaucomatous optic neuropathy diabetes also disturb glial cell function and neuronal metabolism.[11] The high relation between OSA and diabetes mellitus could be because diabetes affects the control of respiration and the upper airway neural reflexes, which in turn lead to respiratory disorders during sleep.[12] Therefore, OSA is common among diabetics, with a prevalence of 54.50%. A lower prevalence of OSA has been reported in men (63.26%) compared to women (66.22%).[13] Diabetes may stimulate OSA via many mechanisms, as patients with diabetes mellitus also have high oxidative stress, inflammation and sympathetic activation with hypothalamic-pituitary-adrenal hyperactivity.[14] OSA in diabetic patients could be also mediated by decreased physical activity and changes related to lung volume.[15] There is evidence that non-diabetic and overweight (OR = 2.2) and obese (OR = 8.29) are associated with OSA; furthermore, diabetic patients with relatively high BMI have increased odds for OSA (OR = 1.1) in comparison to patients with low BMI.[9] Patients with hypertension had 70 times greater odds of developing moderate to high risk of OSA than normotensive patients. As is the case in obesity and

diabetes mellitus, hypertension and OSA have a bidirectional relationship, and a fairly high proportion (50%) of hypertensive people also have associated OSA, where hypertensive patients had 1.32 greater odds of having OSA than normotensive patients.[9,16] Males have 2.27 greater odds for OSA risk; this finding can be explained by the clear statistically significant difference of the mean STOP-BANG score between men (3.36) and women (2.12).[9] Furthermore, among the findings were the increased proportion of smokers among men (29.4%) compared to women (0.0%), as well as the higher number of alcohol drinkers among men (12.7%) than women (0.5%). From an anatomical and physical viewpoint, a higher percentage of men (24.1%) had neck circumference > 40 cm, and this is much higher by about 3-fold compared to that in women (7.6%). So, according to gender-stratified analysis, it is unsurprising that males with OAG were predicted to have moderate to severe OSA. Men are 2–3 times more prone to OSA than women, and the prevalence in both increases with age. This may indicate that sex hormones play a role OSA development. Estimates of sex differences for OSA have been made globally. In the USA, 24% of men and 9% of women have an apnoea-hypopnea index ≥ 5. A highly interesting case was that women with polycystic ovary syndrome, secreting high testosterone, are at higher risk of developing OSA. This may be due to sex hormone- and sex-related anatomical distribution of fatty tissue deposition around the respiratory passages.[17] Sex hormones determine the deposition of fatty tissue around the airway structures.

An interesting finding in the present study was that the prevalence of NTG was much more common (59.5%) compared to OAG in the patients (N = 442), and this is consistent with the previous literature. A recent population-based study stated that NTG prevalence is higher in Asia (76.3%) compared to the white population (33.7%), whatever the glaucoma parameters (intraocular pressure (IOP), IOP above the target, Hodapp-Parrish visual field damage, cup/disc ratio, visual field index, visual acuity, clinical progression); compared to OSA in this study, the p-value was not significant (>0.05).[18]

The main limitation was as it is cross-sectional study and observed the problem temporary in one time make it difficult to find the causality of the effect and therefore there is a possible association between OSA and glaucoma but not a definite link, the second is that most of the patients were old and they had their own conditions and not easy for them to be attended regularly to the clinic to be rechecked. Thirdly, any of the patients had secondary glaucoma who were excluded from the study.

CONCLUSION

This study was conducted among open-angle glaucoma patients, to assess their risk for OSA using the validated STOP-BANG questionnaire. We found that male gender, high BMI, hypertension and diabetes mellitus were highly significantly associated with moderate to high risk of OSA among patients with OAG; the prevalence of moderate to high OSA risk was 56.9% in those with OAG; the prevalence of NTG was 59.5% versus that of primary angle glaucoma (40.5%). Finally, our findings are all consistent with all of the previous findings on this subject.

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ETHICS APPROVAL

Ethical approval was obtained from the Medical Research and Ethics Committee of the Ministry of Health Malaysia, reference number NMRR-18-2796-43737 ('IR) and by the Ethics Committee for Human Study of Universiti Putra Malaysia.

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