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Rate of Screening for Obstructive Sleep Apnea Syndrome in Patients with Apparent Resistant Hypertension Attending a Tertiary Care Hospital

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ABSTRACT

Objectives: This study aimed to evaluate the screening rate and the prevalence of obstructive sleep apnea syndrome (OSAS) in patients with apparent resistant hypertension (ARH) attending Sultan Qaboos University Hospital, and to assess sex differences. ***Methods***: A cross-sectional retrospective study was conducted using the data from 500 patients with ARH between January 2018 and January 2023. The cohort included 270 women and 230 men. Data extracted from hospital records included demographic and clinical characteristics, antihypertensive medications, results of OSA screening tools (e.g., Epworth Sleepiness Scale and STOP-Bang questionnaire), and polysomnography outcomes. ***Results:*** Of the 500 patients with ARH, 54 (10.8%) were diagnosed with OSAS. Only 6.6% (n = 33) were screened for OSA using the Epworth Sleepiness Scale or STOP-Bang questionnaire, while the majority (93.4%, n = 467) were not screened. Women constituted 54.0% of the cohort and had a higher mean body mass index than men (32.7 kg/m^2 vs. 30.2 kg/m^2, $p < 0.001$). OSAS prevalence was significantly higher in women than men (14.1% vs. 7.0%, $p = 0.013$). ***Conclusions:*** There was a low rate of screening for OSAS among patients with ARH at Sultan Qaboos University Hospital, which may explain the lower-than-expected prevalence observed. Contrary to published literature, OSAS was more frequently diagnosed in women, who were screened more often, suggesting that OSA may be underdiagnosed in men.

Hypertension or high blood pressure (BP) is defined as systolic BP reaching 140 mmHg or more and/or diastolic BP of 90 mmHg or more.[1] It is considered the world's leading risk factor for stroke, cardiovascular diseases, disability, and mortality.[2] One of the clinical phenotypes of hypertension in which BP is difficult to control is resistant hypertension (RH). RH is the BP of a hypertensive patient that stays elevated above goal despite using three antihypertensive medications of different classes administered at maximally tolerated doses or BP that is controlled by four or more antihypertensive agents.[2] RH is estimated to be prevalent in around 10–30% of the hypertensive population,[3] and is associated with a higher risk of developing cardiovascular events compared to non-RH.[4] It was also found to be associated with an increase in the prevalence and severity of target organ damage in the heart and kidney due to the persistent elevation of BP.[5]

Several factors contribute to RH including poor adherence to antihypertensive therapy, obesity, excess alcohol intake, and certain drugs, in addition to other secondary causes. Common secondary causes of RH include obstructive sleep apnea, renal parenchymal disease, primary aldosteronism, and renal artery stenosis.[6]

Apparent RH (ARH) is an office BP reading of > 140/90 mmHg while taking three or more antihypertensive medications without excluding the white coat effect and nonadherence to medication. Once adherence to ≥ 3 antihypertensive medications and a mean 24-hour ambulatory BP of > 130/80 mmHg have been confirmed, along with the elevated office BP, the patient is considered to have true RH.[7]

Obstructive sleep apnea (OSA) is a sleep disorder characterized by episodes of complete or partial

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obstruction of the upper airway associated with a decrease in oxygen saturation or arousal from sleep, leading to nonrestorative sleep. Symptoms accompanying OSA include loud disruptive snoring, observed apneas during sleep, and excessive daytime sleepiness.[8] Depending on the apnea-hypopnea index (AHI), OSA is classified as mild with an AHI of 5–14.9, moderate with 15–29.9, and severe with ≥ 30.[9]

The most common screening tests used to identify patients with daytime sleepiness and OSA include the Epworth Sleepiness Scale (ESS) and the STOP-Bang questionnaire. The ESS evaluates the severity of sleepiness using a questionnaire. The ESS score ranges from 0 to 24. Any score > 10 indicates the presence of excessive daytime sleepiness with any cause of sleep disorders and is not specific to OSA and further assessment is required to confirm the presence of the disease.[10] The STOP-Bang questionnaire is the most widely accepted screening tool for assessing OSA. It evaluates the presence of snoring, fatigue or daytime sleepiness, observed apnea during sleep, presence of hypertension, body mass index (BMI) of ≥ 35 kg/m^2, age > 50 years, neck circumference > 40 cm, and male sex. The STOP-Bang questionnaire assesses the probability of having moderate to severe OSA with the risk being high if 'YES' to ≥ 3 items and low risk if 'YES' to < 3 items.[8] In-laboratory polysomnography (PSG) is used to confirm the diagnosis of OSA.[11]

Sleep apnea and sleep-disordered breathing are associated with systemic hypertension in different age groups.[12] OSA was specifically found to be the most common secondary condition related to RH.[13] Furthermore, it was reported that treating OSA with continuous positive airway pressure (CPAP) reduced the 24-hour BP of patients with RH.[14]

Sex is an essential factor that impacts the relationship between OSA and RH, where it was found that a significantly higher number of men with RH had OSA than women.[15] However, this might not be the case as research indicates that, despite having a similar probability of developing OSA side effects, women with OSA symptoms may have been under diagnosed and under-treated compared to men.[16]

The link between OSA syndrome (OSAS) and RH is mediated by several interrelated pathophysiological mechanisms, which involve complex neurohumoral, vascular, and metabolic interactions. The most significant mechanism involves the activation of sympathetic activity triggered by OSA, which extends beyond the apnoea/hypopnoea episodes and results in a persistent increase in sympathetic activation even during the daytime when patients are awake. This elevated sympathetic activity leads to increased vascular resistance and cardiac output while stimulating the renin-angiotensin-aldosterone system, all contributing to elevated BP. Additionally, other pathophysiological impacts of OSA, such as increased oxidative stress, greater vascular stiffness, and proinflammatory responses, further exacerbate the rise in BP.[17]

Studies that evaluate the screening of OSA among RH patients are scanty. It indicates that the awareness among physicians regarding the link between the two disorders is sub-optimal. A study done at a primary care hospital revealed that over 60% of the patients treated for hypertension did not achieve the desired result and had not properly controlled hypertension,[18] which may suggest that further screening for other factors including OSA should have been done. Furthermore, it has been shown that the primary reason patients were referred to a sleep study was because OSA was suspected and not to screen for RH.[19]

This study aimed to evaluate the rate of screening and the rate of OSA in patients with apparent RH in the local population and to elicit any differences between men and women.

METHODS

This retrospective, cross-sectional study was conducted at Sultan Qaboos University Hospital (SQUH), a tertiary care academic hospital in Muscat, Oman. The study included adult patients (≥18 years old) with a diagnosis of ARH who were seen in various clinics between 1 January 2018 and 31 December 2022. The RH criteria were those defined by the American Heart Association—having elevated BP despite using three antihypertensive medications of different classes administered at maximum tolerated doses or BP controlled by four or more antihypertensive agents.

Data were extracted from the hospital's electronic medical record system, including demographics (age and sex), BMI, BP readings, duration of hypertension, number and classes of antihypertensive medications, and relevant comorbidities such as diabetes mellitus and dyslipidemia. Documentation of screening

for OSAS—using tools such as the STOP-Bang questionnaire, overnight pulse oximetry, or referral for PSG—was reviewed. Patients with confirmed OSAS diagnoses and their corresponding treatment plans (e.g., CPAP therapy) were also recorded. Statistical analysis was done using SPSS Statistics (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Descriptive statistics were presented as mean and standard deviation (SD). Mann-Whitney U test was used for continuous variables that did not follow the normal distribution, while the chi-square and Fisher's Exact tests were used to test the association between categorized variables. The *p*-values of ≤ 0.05 were considered statistically significant.

Ethical approval was granted by the ethics committee of the College of Medicine and Health Sciences SQUH (MREC # 3050).

RESULTS

Data was collected from the medical records of 500 patients eligible for the study according to the inclusion criteria.

The main characteristics of these patients are presented in Table 1. Two hundred and seventy (54.0%) patients were women. The age of patients ranged from 22–103 years, with a mean age of 67.4 ± 12.4 years. The mean BMI was 31.6 ± 10.6 kg/m^2, and the mean systolic and diastolic BP were 140.6 ± 25.5 mmHg and 69.6 ± 13.9 mmHg, respectively.

The most common comorbidities, in addition to hypertension in these patients, were diabetes mellitus (64.0%) followed by dyslipidemia and ischemic heart disease (40.4% and 39.8%, respectively). The most common class of antihypertensives prescribed was diuretics (97.8%), and the least common was vasodilators (29.2%) [Table 1].

Only 6.6% (n = 33) of patients with ARH were screened for OSA using the ESS or STOP-Bang questionnaire. All had a sleep study and were positive for OSAS. The sleep study was done for 21 patients without the initial questionnaire screening. Therefore, 54 patients out of the 500 patients (10.8%) were found to have OSAS.

Women represented 54.0% (n = 270) of the study population with a tendency to be older than men (mean age 68.46 ± 11.693 vs. 66.11 ± 13.04 years, $p = 0.08$). In contrast to men, women had a significantly higher BMI (32.7 ± 10.3 vs. 30.2 ± 10.7, $p < 0.001$), while men had a significantly higher diastolic BP (mean diastolic BP = 70.7 ± 13.1 vs. 68.7 ± 14.6, $p = 0.029$) [Table 2].

Table 1: General characteristics, co-morbidities and the main antihypertensive classes prescribed in the study population.

Variables	Percentage, %
Age, years, mean ± SD	67.4 ± 12.4
Body mass index, kg/m^2, mean ± SD	31.6 ± 10.6
SBP, mmHg, mean ± SD	140.6 ± 25.5
DBP, mmHg, mean ± SD	69.6 ± 13.9
Comorbidities,	
Heart failure	17.4
Ischemic heart disease	39.8
Chronic kidney disease	26.2
Diabetes mellitus	64.0
Dyslipidemia	40.4
Hyperthyroidism	1.0
Hypothyroidism	6.8
Main antihypertensive agent	
Diuretic	97.8
ACEI/ARB	85.0
Beta-blocker	80.0
Calcium channel blockers	80.0
Vasodilator	29.2

SBP: systolic blood pressure; DBP: diastolic blood pressure; ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker.

When comparing co-morbidities, ischemic heart disease was higher in men (47.4% vs. 33.3%, $p = 0.002$), while hypothyroidism was more prevalent in women (8.9% vs. 4.3%, $p = 0.050$).

OSA was significantly higher in women than men (14.1% vs. 7.0%, $p = 0.013$) [Table 2].

DISCUSSION

To the best of our knowledge, this is the first study to evaluate the screening rates and OSAS rates in patients with ARH in Oman, and to examine sex differences.

Data was gathered from 500 patients treated at a tertiary care hospital; OSAS was diagnosed in 10.8% of the patients with ARH. Other studies have reported a significantly higher prevalence of OSAS in RH patients (71–83%).[20–22] In those prospective studies, all patients with RH underwent full-night PSG to assess OSAS and its severity. Therefore, our analysis likely underestimates the true prevalence of OSAS in these patients due to the absence of sleep studies.

Table 2: Comparison of the general characteristics, co-morbidities and prevalence of obstructive sleep apnea between male and female patients with resistant hypertension.

Variables	Men, % (n = 230)	Women,% (n = 270)	*p*-value
Age, years, mean ± SD	66.1 ± 13.0	68.5 ± 11.7	0.080
Body mass index, kg/m², mean ± SD	30.2 ± 10.7	32.7 ± 10.3	< 0.001
SBP, mmHg, mean ± SD	139.40 ± 25.1	141.6 ± 25.7	0.301
DBP, mmHg, mean ± SD	70.7 ± 13.1	68.7 ± 14.6	0.029
Comorbidities			
Obstructive sleep apnea	7.0	14.1	0.013
Heart failure	15.2	19.3	0.240
Ischemic heart disease	47.4	33.3	0.002
Chronic kidney disease	25.2	27.0	0.684
Diabetes mellitus	65.7	62.6	0.513
Dyslipidemia	37.0	43.3	0.170
Hyperthyroidism	0.9	1.1	1.000
Hypothyroidism	4.3	8.9	0.050

SBP: systolic blood pressure; DBP: diastolic blood pressure.

Only 6.6% of our study participants were screened using the ESS or STOP-Bang questionnaire. This suggests that physicians were selective in administering the questionnaire or referring patients to a sleep specialist, likely focusing on patients who exhibited clear symptoms or signs of OSAS. This assumption is supported by the fact that all patients who were screened had a positive sleep study result.

Consistent with previous studies, we found that more women had ARH, and they tended to be older and more obese than the men.[23,24]

Interestingly, OSAS was significantly more prevalent in women (14.1%) than men (7.0%). This contradicts existing literature, which generally shows that while OSAS is common in women,[25] it is more prevalent in men, with a male-to-female ratio estimated at 2:1.[15,26,27] This discrepancy in our results may be attributed to the higher BMI in women, which could have led to more frequent screening and sleep studies, thereby increasing the detection of OSAS among women with RH at SQUH.

As the findings of this study indicate a low screening rate of OSAS among patients with ARH, it is strongly recommended that OSAS screening be integrated into the management plans for all patients with true RH. Early identification and diagnosis of OSAS in these patients will allow timely initiation of CPAP treatment, leading to improved BP control and better cardiovascular outcomes.

There are limitations to our study that should be considered when interpreting its findings. First, the sample does not represent true RH as white coat hypertension and non-adherence to medications were not excluded from some of these patients. This was a single-center study conducted exclusively at SQUH, and some patients with RH may have been treated or screened for OSA at sleep clinics in other hospitals without their records being reflected at SQUH. As a result, some patients with OSA may have been missed. Additionally, the study's retrospective nature is based on the data gathered from medical records. The results of OSA screenings or PSG may have been incomplete or missing from the records.

CONCLUSION

The rate of screening and investigation for OSAS among patients with ARH at our hospital was low, resulting in a lower observed prevalence of OSAS. Contrary to published literature, OSA was more prevalent in women, who were screened more frequently, suggesting that OSA in men may have been underdiagnosed. Although this rate may not reflect the true prevalence of OSAS in RH patients, it highlights the need for increased screening efforts to identify OSAS in this population, which could improve BP control and other cardiovascular outcomes. A multicenter, prospective study should

be conducted to evaluate the true prevalence of OSAS in RH in Omani population.

Disclosure
The authors declare no conflicts of interest. No funding was received for this study.

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