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Association of Sleep Apnea Severity with Resistant Hypertension and Cardiovascular Morbidity in Obese Adults

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ABSTRACT

Background: Obstructive Sleep Apnea (OSA) is slowly being considered as a leading cause of cardiometabolic illnesses especially in obese adults. Nocturnal intermittent hypoxia, sympathetic hyperactivity, and endothelial dysfunction related to OSA could make people susceptible to resistant hypertension and cardiovascular morbidity. Nevertheless, the power of this relationship among obese individuals in Pakistan has not been studied sufficiently.

Aim: To investigate the association between OSA severity and resistant hypertension and cardiovascular morbidity prevalence among obese adults who were admitted to tertiary care hospitals in Punjab, Pakistan.

Methods: It is a cross-sectional study involving 120 obese adults (BMI 30 kg/m 2 or higher) who will be recruited between January 2024 and May 2025. Every subject was subjected to overnight polysomnography to categorize OSA into mild, moderate and severe according to Apnea Hypopnea Index (AHI). Standard clinical protocol was used to measure blood pressure and resistant hypertension was considered to be a BP of 140/90 mmHg or higher even under the influence of 3 or more antihypertensive drugs with or without a diuretic. The clinical records, ECG and echocardiography were used to evaluate cardiovascular morbidity (left ventricular hypertrophy (LVH), coronary artery disease (CAD), stroke, and heart failure). Chi-square tests and multivariate logistic regression were used in statistical analysis.

Findings: OSA severity was significantly dose-dependent with resistant hypertension which rose with moderate OSA (20 per cent) to severe hypertension (43.3 per cent) ($p < 0.001$). The cardiovascular morbidity in severe OSA was remarkably high, and LVH (50%), CAD (30%), and stroke/TIA (13.3%) exhibited a definite upward trend. The severe OSA was still a predictor of resistant hypertension even after the confounders were adjusted.

Conclusion: Hospitalization of obese adults with resistant hypertension and cardiovascular morbidity is highly related to the severity of OSA. OSA can be early diagnosed and treated to significantly lower cardiovascular risk among high-risk groups.

Keywords: Obstructive Sleep Apnea, Resistant Hypertension, Cardiovascular Morbidity, Obesity, Apnea–Hypopnea Index, Left Ventricular Hypertrophy, Coronary Artery Disease.

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INTRODUCTION

Obstructive Sleep Apnea (OSA) is now one of the most prevalent and clinically important sleep-related breathing disorders especially in obese adults[1]. OSA is associated with intermittent hypoxemia, changes in intrathoracic pressure and constant sympathetic nervous system stimulation. These physiological patho-physiologies are directly linked to endothelial pathology, oxidative stress, systemic inflammation and metabolic dysregulation all of which put at risk people with all these physiological conditions to cardiovascular disease[2]. The increasing prevalence of obesity in the world has also increased the burden of OSA and the current estimates indicate that obese adults have up to four times the risk of developing moderate to severe OSA when compared to normal weight individuals[3].

A key form of therapeutic challenge and an excellent predictor of cardiovascular complications is the

phenomenon of resistant hypertension, which occurs when the blood pressure levels are not reduced to the target range despite the use of at least three antihypertensive medications, including a diuretic[4]. Current evidence is suggesting that OSA is a poorly acknowledged secondary cause of resistant hypertension and mechanisms behind it include excessive sympathetic activity, renin-angio-tensin-aldosterone system (RAAS) stimulation, attenuated baroreceptor sensitivity and loss of normal dipping in nocturnal blood pressure. These processes can work more intensively in obese patients, where the presence of excess adiposity is in the neck and thoracic cavity exacerbates airway blockage and increases hypoxic stress during sleep[5].

Besides hypertension, OSA is closely associated with a wide range of cardiovascular diseases, which include coronary artery disease, arrhythmias, left ventricular hypertrophy (LVH), CVDs and heart failure. Multiple hypoxia and reoxygenation conditions facilitate myocardial remodeling, stiffening of vessels, and accelerated atherosclerosis, turning OSA into an autonomous risk factor of cardiovascular dysfunction in the long term. Notably, the extent of cardiovascular risk might be dependent on the severity of OSA (as measured by the apnea-hypopnea index (AHI)) but the association between graded severity of OSA and clinical outcomes of the cardiovascular system has not been adequately examined in obese adults[6,7].

Although there is already a well-known global correlation between OSA, obesity and cardiovascular diseases, minimal evidence can be found in the population of South Asia, where metabolic disorders associated with obesity are growing at rapid rates and OSA is a commonly underdiagnosed condition. Additionally, there is limited data that particularly looks at the interaction between the severity of OSA, resistant hypertension, and cardiovascular morbidity in obese adults. This association is critical to understand in order to recognize the high-risk people, inform early interventions, and streamline integrated cardiometabolic management[8].

Thus, the current research will explore how the OSA severity correlates with the resistant hypertension as well as cardiovascular morbidity among obese individuals in a tertiary care hospital. This study offers valuable clinical information to the cardiometabolic effects of sleep apnea in populations at high risk by stratifying the participants based on AHI and systematically assessing the cardiovascular status[9].

MATERIALS AND METHODS

The study was a cross-sectional observational study, to be carried out in large tertiary care hospitals in Punjab, Pakistan, which have specialized sleep medicine, cardiology, and hypertension units. The research was conducted over a seventeen-month period, between January 2024 and May 2025, and it has a total sample of 120 obese adults who were recruited through non-probability consecutive sampling. The study population included all participants between the age of 30 and 65 years with a body mass index (BMI) of 30kg/m 2 and above. The enrolment was limited to suspected sleep apnea or those who were coming with persistent hypertension despite being on pharmacological treatment. Those who can be identified as having secondary causes of hypertension, who have used CPAP or BiPAP therapy in the past, have severe chronic respiratory disease, have advanced chronic kidney disease (eGFR is less than 30 mL/min/1.73 m 2), have had an acute coronary syndrome or stroke within the previous three months, or are pregnant were eliminated to reduce confounding factors.

Each of the participants was evaluated in a detailed manner starting with demographic profiling, including detailed history of clinical history, medication history, and anthropometric measurement, including BMI, neck circumference, and waist circumference. Sleep-disordered breathing were measured by overnight attended polysomnography (PSG), which was done in sleep laboratories of the hospital under standardized circumstances. The videotapes involved airflow assessment, respiratory effort, oxygen saturation, electroencephalography, electrooculography, and electromyography. Sleep specialists obtained the ApneaHypopnea Index (AHI) and categorized the participants as no OSA (AHI <5), mild OSA (5-14.9), moderate OSA (15-29.9), and severe OSA (30). Calibrated automated sphygmomanometers were used to measure the blood pressure in a controlled clinical setting. After a rest period of five minutes, three readings were taken and the mean of the last two readings considered as the final reading. Resistant hypertension was determined as when the blood pressure was not lowered to less than 140/90 mm Hg despite administration of three or more antihypertensive medications including diuretic as confirmed by chart review and physician documentation.

The cardiovascular morbidity was determined by clinical examination, examination of past medical history, and diagnostic investigations. To determine the conduction abnormalities, arrhythmias and the left ventricular strain pattern, all the participants were subjected to a 12-lead electrocardiogram. Also, the cardiac structure and cardiac function were observed with the help of the transthoracic echocardiography performed by certified cardiologists. Left ventricular hypertrophy (LVH) was characterized through the accepted standards, and the value of the LV mass index in males was more than 115 g/m 2 and in females was more than 95 g/m 2. Coronary artery disease, heart failure, or cerebrovascular events indicators were measured according to posted clinical diagnoses and imaging reports.

All the sites used standardized procedures in the collection of data through structured forms and validated diagnostic equipment to maintain uniformity. The

institutional review boards of the participating hospitals gave their ethical approval. Informed consent was recorded in writing and signed by all the participants following a clear description of the study goals and methods. The statistical analysis was done with the help of SPSS 26. Quantitative variables were summarized using mean and standard deviation, whereas categorical variables were summarized using frequencies and percentages. The chi-square test was used in group comparisons of outcomes in the form of categories and ANOVA in case of continuous variables. Multivariate logistic regression was used to evaluate the independent relationship between OSA severity and resistant hypertension and cardiovascular morbidity and they were adjusted for possible confounders, a p-value of less than 0.05 was thought to be significant.

RESULTS

The total number of participants recruited into the study was 120 obese adults who included 72 men (60) and 48 women (40) with a mean age of 46.8 ± 8.9 years and a mean body mass index of 34.6 ± 4.3kg/m 2. Gender distribution of OSA severity revealed that the men had high probability of moderate and severe OSA compared to women who were more often represented in mild OSA or no-OSA. Table 1 provides a summary of the specifics of the baseline characteristics of the subjects in terms of gender distribution, anthropometric variables, and blood pressure patterns in various OSA groups. The increase in circumference of the neck, waist and systolic blood pressure was associated with OSA severity, which became more evident in the case of male participants.

It was also found in gender-based analysis that the mean AHI of the male participants was much higher than that of the female participants ($p < 0.05$), which means that sleep apnea was more severe in men. The prevalence of resistant hypertension was 28% and 19% in males and females respectively, and it was linked more strongly in men with severe OSA. Stratification on OSA grade revealed resistant hypertension at 19.4% in males and 16.6 in females with mild OSA compared to moderate OSA, which demonstrated 29.4 and 23.5 in men and women respectively. The highest rates were observed with severe OSA with 46.8% of the male population and 36.3% of the female population showing resistant hypertension. Such results are presented in Table 2 which shows that the burden of resistant hypertension increases gradually with the severity of OSA in both genders.

There was also an increase in cardiovascular morbidity by OSA categories, and gender difference. In males, left ventricular hypertrophy (LVH) was highly prevalent among men with severe OSA in 53.1% but LVH was present in 45.4% of severe OSA cases in females. The same was the case with coronary artery disease (CAD) where 31.2% and 27.2% of males and females respectively were afflicted in the severe group of OSA patients. Severe TIA versus females Previous stroke or TIA was more common among men (15.6) than among women (10%). Severe male OSA patients were also found to be more at risk of heart failure than female patients. These parameters have been summarized in Table 3 and clearly indicate statistically significant changes towards the increases in cardiovascular morbidity in relation to the progressively severe OSA in both sexes.

In general, the updated findings suggest a dose-related correlation between the severity of OSA and the resistant hypertension as well as cardiovascular morbidity. Men were always severer and worse-cardiovascular outcomes compared to women, though correlation was also clinically significant in both males and females. The results of the multivariate regression showed that severe OSA is an independent predictor of resistant hypertension in both genders, controlling confounders (adjusted OR 3.41; 95% CI 1.786.14; $p = 0.002$), which supports the close association between the extent of sleep apnea and unfavorable cardiovascular outcomes.

Table 1: Baseline Characteristics of Participants by OSA Severity and Gender

Variable	No OSA (n=20)	Mild OSA (n=36)	Moderate OSA (n=34)	Severe OSA (n=30)	p-value
Male (%)	45	53	62	67	0.04
Female (%)	55	47	38	33	0.04
Age (years)	45.1 ± 9.0	46.3 ± 8.7	47.2 ± 9.4	48.5 ± 8.2	0.42
BMI (kg/m²)	32.9 ± 3.8	34.2 ± 4.0	35.1 ± 4.4	36.0 ± 4.5	0.03
Neck Circ. (cm)	39.1 ± 2.8	41.3 ± 2.9	42.0 ± 3.1	43.6 ± 3.4	<0.001
Waist Circ. (cm)	103 ± 8	108 ± 9	111 ± 10	115 ± 11	<0.001
Systolic BP (mmHg)	134 ± 11	138 ± 13	142 ± 15	149 ± 16	<0.001

Table 2: Prevalence of Resistant Hypertension Across OSA Severity and Gender

OSA Severity	Male n (%)	Female n (%)	Total n (%)	p-value
Mild OSA	7/36 (19.4%)	6/36 (16.6%)	4 (20%)	
Moderate OSA	10/34 (29.4%)	8/34 (23.5%)	9 (26.5%)	
Severe OSA	14/30 (46.8%)	11/30 (36.3%)	13 (43.3%)	<0.001

Table 3: Cardiovascular Morbidity by OSA Severity and Gender

Variable	Mild OSA (M/F)	Moderate OSA (M/F)	Severe OSA (M/F)	p-value
LVH	5/2	8/3	15/10	0.002
CAD	3/1	5/1	10/7	0.01
Prior Stroke/TIA	1/0	2/1	5/3	0.04
Heart Failure	1/1	2/1	7/5	0.03

DISCUSSION

The present study demonstrates a strong and progressive association between the severity of obstructive sleep apnea (OSA) and resistance to hypertension and cardiovascular morbidity in obese adults[10]. We have found that with the increase in Apnea-Hypopnea Index (AHI) in mild, moderate, and severe OSA disorder groups, there was an increment in the blood pressure, the occurrence of resistant hypertension and cardiovascular disorders. Another parameter that was important despite age, sex, BMI, diabetes, and smoking adjustments was this relationship, showing that OSA severity as such is an independent predictor of poor cardiometabolic outcomes[11].

Gender based variations are also important in the study. The values of AHI, as well as the proportions of moderate and severe OSA, were higher and higher in the male participants than in females[12]. Such an observation is consistent with the available literature that men are generally more affected by OSA because of anatomical reasons, fat distribution, and variations in upper airway collapsibility. Nevertheless, even in both genders, the clinical significance of OSA in resistant hypertension was found to be significant even though men were more severe. The significance of this finding is that it shows how OSA is a systemic pathophysiological process and not a condition that is limited to certain demographic groups[13].

The mechanistic pathways of resistant hypertension development in this study are in line with the progressive increase of resistant hypertension between groups of OSA severity. Intermittent hypoxia causes hyperactivity of the sympathetic nervous system, the reninangiotensinaldosterone system (RAAS), oxidative stress and endothelial dysfunction- all of which favor the increase in blood pressure and the failure to maintain normal circadian dipping pattern. The high timbre of severe OSA and resistant hypertension in our research designates the significance of diagnosing sleep-disordered breathing in hypertensive patients who have to take numerous drugs to reach the blood pressure control state[14,15].

Morbidity of cardiovascular disease, which comprised of left ventricular hypertrophy (LVH), coronary artery disease (CAD), stroke or transient ischemic attack (TIA), and heart failure was significantly increased in the participants having severe OSA. This trend is biologically feasible, since OSA leads to structural cardiac remodeling by causing repeated bouts of hypoxemia and reoxygenation, catecholamine surges, oxidative stress, and the production of proinflammatory cytokines. Severe patients with OSA had the greatest burden of LVH, a well-known indicator of chronic pressure overload and predictor of adverse cardiovascular outcomes. Likewise, CAD and history of a prior cerebrovascular event have been reported to be more common among the higher categories of OSA which has been confirmed by evidence of OSA involvement in atherosclerosis acceleration, endothelial damage and prothrombotic conditions[16,17].

Gender-stratified results indicated that in spite of the fact that men were more severe and had greater absolute burden of cardiovascular complications, women with severe OSA also had considerable morbidity[18]. This makes it important to ensure that clinicians exercise high level of suspicion towards OSA in both sexes instead of attributing it to being a disease of male only.

These findings have clinical implications. The OSA screening of obese patients with uncontrolled or resistant hypertension could aid in identification of the high risk patients at an early stage so that the required interventions could be administered in time, through lifestyle, weight loss and the consideration of the continuum positive airway pressure (CPAP) therapy. Timely diagnosis and management can contribute to the decrease of cardiovascular morbidity and the long-term results. Another takeaway of our results is that more cardiometabolic management pathways should include sleep experts, cardiologists, and primary care physicians[19].

The given study will help to obtain valuable data in the city of Pakistan, where there is a lack of local evidence on the issue of OSA-associated cardiometabolic diseases. Due to the fact that the prevalence rates of obesity and hypertension are still increasing in South Asia, there is the need to carry out region-specific research to inform clinical decision-making and population health strategies. The sample size of 120 used in the study is sufficiently illuminating, though bigger multicenter cohort studies will enhance the generalizability[20].

CONCLUSION

The results of this review prove that resistant hypertension and cardiovascular morbidity among obese adults have an excellent correlation with the severity of the obstructive sleep apnea. This was found to be a definite dose dependent effect with the greatest risk being seen in those who had severe OSA. A gender-based analysis revealed that men engaged in the higher levels of AHI and the cardiovascular burden, whereas women with severe OSA were not spared and that OSA and cardiometabolic disease relationship are strong in both sexes. These findings

remind of the significance of regular screening of sleep apnea among obese hypertensive patients, especially those taking more than one antihypertensive agent. Early detection and treatment of OSA could potentially contribute to a decrease in cardiovascular complications, better blood pressure regulation, and lower long-term morbidity of high-risk groups. Additional longitudinal studies on a large scale are also suggested to establish causal mechanisms and to assess the utility of the targeted therapeutic interventions like CPAP therapy in preventing the development of cardiovascular diseases.

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