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Respiratory Physiology and Clinical Manifestations of Obstructive Sleep Apnea: Pathophysiological Mechanisms and Cardiovascular Consequences

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is a highly prevalent sleep-related breathing disorder characterized by recurrent upper airway collapse, intermittent hypoxemia, and sleep fragmentation. Beyond sleep disruption, OSA is increasingly recognized as a systemic condition with strong associations with cardiovascular morbidity and mortality.

Objectives: The purpose of this study was to examine the link between OSA severity, respiratory physiology, clinical symptoms, and cardiovascular implications in adult patients with suspected OSA.

Methods: A prospective study was carried out at two tertiary care hospital in Lahore, Pakistan, between March 2023 and March 2024. Ninety patients aged 30-70 years performed a standardized clinical examination, including the Epworth Sleepiness Scale (ESS), anthropometry, nighttime polysomnography (PSG), arterial blood gas measurement, and cardiovascular evaluations such as blood pressure, electrocardiography, echocardiography, and biomarker testing. The severity of OSA was determined using the apnea-hypopnea index (AHI). The data was analyzed using SPSS v26.0, with a significance level of $p < 0.05$.

Results: The average age was 49.6 ± 10.8 years, and 64.4% were men. Patients with severe OSA exhibited substantially greater BMI, neck circumference, and ESS ratings compared to moderate OSA ($p < 0.001$). PSG results showed a decline in mean nocturnal SpO_2 (92.4% in moderate vs. 87.2% in severe, $p < 0.001$), oxygen desaturation index, and alertness index. Severe OSA was associated with higher rates of cardiovascular problems, including as hypertension (78.1%), resistant hypertension (21.9%), atrial fibrillation (18.8%), diastolic dysfunction (46.9%), pulmonary hypertension (28.1%), and increased hs-CRP (6.9 ± 2.2 mg/L).

Conclusion: OSA severity strongly correlates with respiratory impairment, systemic inflammation, and cardiovascular dysfunction. Early recognition and comprehensive management are essential to reduce long-term cardiovascular risk and improve patient outcomes.

Keywords: Obstructive sleep apnea, respiratory physiology, intermittent hypoxemia, cardiovascular risk, hypertension, arrhythmias

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INTRODUCTION

Obstructive sleep apnea (OSA) has been identified as a world-wide health issue that has significant medical, social and economic implications [1]. It falls under the category of a sleep-related breathing disorder where frequent instances of partial or complete occlusion of the upper airway during sleep are experienced causing intermittent hypoxemia, recurrent arousals, and changes in intrathoracic pressure [2]. OSA has long been considered a sleep disorder characterized by snoring and daytime sleepiness, but it has now been determined to be a systemic disease with adverse impacts on respiratory physiology, cardiovascular performance, metabolic homeostasis and neurological integrity [3]. Its clinical importance as a disease is high prevalence and strong and independent correlation with cardiovascular morbidity, metabolic syndrome, neurocognitive impairment and all-cause mortality [4].

According to epidemiological studies, OSA is observed in about 9-38 percent of the general adult adult population with the highest prevalence in men, older persons and obese people. Recent estimates indicate that approximately 1 billion people all over the world could be impacted and the prevalence among the population has been increasing with obesity and aging populations [5]. The burden is likely to be high especially in the South Asian region including Pakistan because of the increasing prevalence of obesity, diabetes mellitus, sedentary life style and access or lack of awareness about the diagnostic facilities. Despite its widespread occurrence, OSA remains underdiagnosed, with nearly 80% of moderate to severe cases left unrecognized [6]. This diagnostic gap underscores the importance of understanding the fundamental respiratory physiology and systemic manifestations of OSA to enable timely recognition and intervention [7].

From a respiratory physiology perspective, OSA represents a pathological exaggeration of normal sleep-related reductions in upper airway tone [8]. During sleep, especially in rapid eye movement (REM) sleep, relaxation of pharyngeal dilator muscles predisposes the airway to collapse [9]. In healthy individuals, airway patency is maintained by neural reflexes and negative intrathoracic pressure, but in susceptible individuals—due to obesity-related pharyngeal fat deposition, craniofacial structural abnormalities, or neuromuscular dysfunction—the airway becomes collapsible [10]. This collapse results in apnea or hypopnea, accompanied by significant oxygen desaturation and hypercapnia, which trigger arousal responses mediated by chemoreceptor stimulation. Repeated cycles of collapse and arousal fragment sleep architecture, impair restorative slow-wave and REM sleep, and generate a cascade of systemic effects [11].

The pathophysiological consequences of OSA extend well beyond disordered breathing. Intermittent hypoxemia initiates oxidative stress and systemic inflammation, processes that impair endothelial function and accelerate atherosclerosis [12]. Negative intrathoracic pressure swings increase cardiac afterload, impair left ventricular filling, and predispose to atrial enlargement, contributing to arrhythmogenesis. Furthermore, heightened sympathetic nervous system activity—resulting from recurrent arousals and chemoreflex activation—induces sustained hypertension and metabolic dysregulation. Endothelial dysfunction, vascular stiffness, and platelet activation further contribute to cardiovascular injury, linking OSA with coronary artery disease, heart failure, arrhythmias, pulmonary hypertension, and stroke [13]. Thus, OSA provides a unifying mechanistic model for the

intersection of respiratory instability, cardiovascular dysfunction, and metabolic disease.

Clinically, OSA presents with a wide spectrum of manifestations. Nocturnal symptoms include habitual loud snoring, witnessed apneas, choking or gasping during sleep, nocturnal awakenings, and nocturia [14]. Daytime symptoms often dominate the clinical picture, including excessive daytime sleepiness, morning headaches, reduced concentration, irritability, and mood disturbances, which significantly impair occupational performance and quality of life. Over time, untreated OSA leads to major long-term sequelae such as motor vehicle accidents due to drowsiness, neurocognitive decline, and cardiovascular morbidity. Importantly, many patients with OSA remain asymptomatic or attribute their symptoms to aging, stress, or lifestyle, delaying diagnosis until complications such as resistant hypertension or ischemic heart disease emerge [15].

The global recognition of OSA as a critical cardiovascular risk factor has shifted the paradigm from viewing it as a benign sleep disturbance to appreciating it as a chronic systemic disorder [16]. The pathophysiological links between respiratory physiology and cardiovascular outcomes highlight the importance of integrated, multidisciplinary approaches to screening, diagnosis, and management. Standard diagnostic tools such as polysomnography remain the gold standard, while therapeutic interventions including continuous positive airway pressure (CPAP), weight reduction, positional therapy, oral appliances, and surgical modalities have demonstrated significant benefits in reducing symptoms and mitigating cardiovascular risk [17,18].

This study aims to provide a comprehensive overview of the respiratory physiology underlying OSA, the mechanisms that drive its clinical and cardiovascular consequences, and the spectrum of its clinical manifestations. It is through the combination of physiological knowledge and clinical experience that we would like to point out the systemic nature of OSA, the significance of early diagnosis, and the fact that it is a risk factor that can be modified in the prevention of cardiovascular disease [19].

MATERIALS AND METHODS

This prospective study was carried out over a period of twelve months, between March 2023 and March 2024, in two tertiary care hospitals of, Lahore, Pakistan. The main aim was to assess the cardiovascular outcomes, clinical signs, and pulmonary physiology of obstructive sleep apnea (OSA) in adult patients with the symptoms of sleep disordered breathing. Upon passing the inclusion criteria, 90 patients aged between 30 and 70 were obtained.

Those individuals who accepted to carry out nightly polysomnography (PSG), and portrayed clinical signs including persistent loud snoring, reported apneas, intense daytime somnambulism, or unaccounted resistant hypertension were regarded as eligible. All the participants provided informed consent, which was written. Patients who had undergone uninterrupted positive airway pressure (CPAP) therapy in the previous treatment of OSA, neuromuscular disorders, unstable cardiovascular sickness, or central sleep apnea were eliminated. The study did not include people with major mental conditions, and the pregnant women were excluded as well. The sample size was determined through the use of the single population proportion technique with a 10 per cent margin of error and 95 per cent confidence interval and an estimated prevalence of OSA of about 20 per cent amongst the high-risk population. The data sample of 90 patients was selected to include

the dropouts and missing data as this figure would give a minimum of 82 cases.

Every participant received a thorough clinical assessment that involved a detailed medical history that included excessive sleepiness, fatigue, headache in the morning and apneas, snoring, choking incidents, frequent awakenings and nocturia. The Epworth Drowsiness Scale was created to determine the daytime drowsiness. Age, gender, body mass index (BMI), neck circumference, waist-hip ratio, and other anthropometric and demographic characteristics were recorded, along with comorbidities such as smoking, diabetes, hypertension, and dyslipidemia.

Overnight attended polysomnography was used in a specialist sleep lab to measure respiratory function. Parameters recorded were electroencephalography, electro-oculography, electromyography, electrocardiography, thoracoabdominal movements, nasal and oral airflow, pulse oximetry, and snoring episodes. The apnea-hypopnea index (AHI) was calculated by counting the number of apneas and hypopneas per hour of sleep. OSA was classified as mild if the AHI was between 5 and 14 events per hour, moderate if it was between 15 and 29 events per hour, and severe if it was more than 30 events per hour. Following polysomnography, an arterial blood gas analysis was done in the morning to assess hypoxemia and hypercapnia.

The cardiovascular examination included standardized blood pressure measurements; resistant hypertension is defined as blood pressure that remains uncontrolled after taking three or more antihypertensive medications. Every patient had a twelve-lead ECG obtained at rest, and a few were followed for cardiac arrhythmias using Holter monitors for 24 hours. Transthoracic echocardiography was utilized to evaluate diastolic function, pulmonary arterial pressures, left ventricular mass, and ejection percent. Laboratory tests were performed to assess metabolic and inflammatory status, including high-sensitivity C-reactive protein (hs-CRP), lipid profiles, fasting blood glucose, and glycated hemoglobin (HbA1c).

The major outcome of interest was to establish a link between respiratory physiology metrics such as oxygen desaturation index, mean nocturnal oxygen saturation, and arousal index, as well as clinical symptomatology and OSA severity, as measured by AHI. One of the secondary outcomes examined the link between OSA severity and cardiovascular events such as systemic hypertension, arrhythmias, left ventricular failure, and increased inflammatory markers.

The data was analyzed using SPSS version 26.0 (IBM, USA). Categorical data were reported as frequencies and percentages, whereas continuous variables were expressed as mean ± standard deviation. Individuals with mild, moderate, and severe OSA were compared using the Chi-square test for categorical data and analysis of variance for continuous data, respectively. To identify independent determinants of cardiovascular effects in OSA patients, multivariate logistic regression analysis was employed. P-values below 0.05 were considered statistically significant. The Institutional Review Boards of both participating hospitals approved the study. Prior to enrollment, all participants gave written informed permission. Throughout the study, patient confidentiality and anonymity were strictly maintained, and all procedures were carried out in accordance with the Declaration of Helsinki's principles.

RESULTS

The study included ninety individuals who all underwent clinical assessments, nocturnal polysomnography, and cardiovascular examination. The demographic and baseline

clinical features of the study cohort are shown in Table 1. The average age of participants was 49.6 ± 10.8 years, with 64.4% being male. The average body mass index (BMI) was 31.2 ± 4.5 kg/m², indicating a largely obese sample. A considerable majority of patients (72.2%) had a neck circumference more than 40 cm, and 68.9% were classified as centrally obese based on waist-hip ratio. Hypertension was the most common comorbidity, affecting 61.1% of patients, followed by diabetes mellitus (42.2%) and dyslipidemia (38.9%). Smoking history was found in 31.1% of patients. The average Epworth drowsiness Scale (ESS) score was 12.6 ± 4.2, indicating a significant frequency of excessive daytime drowsiness among the subjects.

Table-1: Baseline demographic and clinical characteristics of study participants (n = 90)

Variable	Total (n=90)	Mild OSA (n=28)	Moderate OSA (n=30)	Severe OSA (n=32)	p-value
Age (years, mean ± SD)	49.6 ± 10.8	46.2 ± 9.4	50.1 ± 11.2	52.3 ± 11.1	0.08
Male sex (%)	58 (64.4)	16 (57.1)	18 (60.0)	24 (75.0)	0.21
BMI (kg/m², mean ± SD)	31.2 ± 4.5	28.6 ± 3.2	31.5 ± 4.1	33.7 ± 4.8	<0.001
Neck circumference >40 cm (%)	65 (72.2)	14 (50.0)	21 (70.0)	30 (93.8)	<0.001
Hypertension (%)	55 (61.1)	11 (39.3)	19 (63.3)	25 (78.1)	0.002
Diabetes mellitus (%)	38 (42.2)	7 (25.0)	13 (43.3)	18 (56.3)	0.01
Dyslipidemia (%)	35 (38.9)	7 (25.0)	12 (40.0)	16 (50.0)	0.07
Smoking history (%)	28 (31.1)	6 (21.4)	9 (30.0)	13 (40.6)	0.19
Epworth Sleepiness Scale (ESS)	12.6 ± 4.2	9.1 ± 3.1	12.8 ± 3.7	15.4 ± 4.1	<0.001

As shown in Table 1, patients with severe OSA were more likely to be obese, have higher neck circumference, and suffer from hypertension and diabetes compared to those with mild disease. A stepwise rise in the Epworth Sleepiness Scale score across the three groups further highlighted the clinical burden of disease severity.

The polysomnography findings are summarized in Table 2. The mean apnea–hypopnea index (AHI) for the entire cohort was 27.8 ± 13.5 events per hour. Patients with severe OSA had significantly higher AHI values (41.5 ± 8.7) compared with moderate (23.4 ± 6.9) and mild (9.8 ± 3.2) disease ($p < 0.001$). Mean nocturnal oxygen saturation (SpO_2) declined progressively with OSA severity, with severe cases demonstrating an average SpO_2 of 87.2 ± 4.3% compared to 92.4 ± 3.1% in mild cases. The oxygen desaturation index (ODI) also increased substantially in moderate and severe OSA. Arousal index, reflecting sleep fragmentation, was significantly higher in severe OSA (28.6 ± 7.9 arousals/hour) compared to mild disease (11.4 ± 4.5; $p < 0.001$). Morning arterial blood gas analysis revealed mild hypoxemia and elevated $PaCO_2$ among severe OSA patients, consistent with chronic nocturnal hypoventilation.

Table-2: Polysomnography findings according to OSA severity

Parameter	Mild OSA (n=28)	Moderate OSA (n=30)	Severe OSA (n=32)	p-value
AHI (events/hour)	9.8 ± 3.2	23.4 ± 6.9	41.5 ± 8.7	<0.001
Mean nocturnal SpO_2 (%)	92.4 ± 3.1	89.5 ± 3.7	87.2 ± 4.3	<0.001
ODI (events/hour)	12.6 ± 4.7	26.8 ± 8.4	44.2 ± 9.1	<0.001
Arousal Index (events/hour)	11.4 ± 4.5	20.2 ± 6.1	28.6 ± 7.9	<0.001
Morning PaO_2 (mmHg)	87.3 ± 5.2	83.6 ± 6.8	78.5 ± 7.4	<0.001
Morning $PaCO_2$ (mmHg)	38.1 ± 3.4	40.6 ± 3.9	44.2 ± 4.7	<0.001

The cardiovascular evaluation results are presented in Table 3. Hypertension was most prevalent in severe OSA patients (78.1%), compared to 63.3% in moderate and 39.3% in mild OSA. Resistant hypertension was documented in 21.9% of severe OSA patients. Arrhythmias were significantly associated with disease severity; atrial fibrillation was observed in 18.8% of severe cases compared to 3.6% of mild cases. Ventricular premature complexes were also more frequent in moderate to severe OSA. Echocardiography demonstrated progressive increases in left ventricular mass index and impaired diastolic function across groups. Pulmonary hypertension, defined as systolic pulmonary artery pressure >35 mmHg, was detected in 28.1% of severe OSA patients, whereas it was absent in mild OSA. Inflammatory marker hs-CRP was significantly elevated in moderate and severe cases, indicating systemic inflammation.

Table-3: Cardiovascular findings in study participants

Parameter	Mild OSA (n=28)	Moderate OSA (n=30)	Severe OSA (n=32)	p-value
Hypertension (%)	39.3	63.3	78.1	0.002
Resistant hypertension (%)	3.6	10.0	21.9	0.01
Atrial fibrillation (%)	3.6	6.7	18.8	0.03
Ventricular ectopy (%)	7.1	13.3	21.9	0.04
LV mass index (g/m^2, mean ± SD)	88.2 ± 14.6	103.5 ± 18.3	118.7 ± 20.4	<0.001
LV diastolic dysfunction (%)	10.7	26.7	46.9	<0.001
Pulmonary hypertension (%)	0.0	6.7	28.1	<0.001
hs-CRP (mg/L, mean ± SD)	2.8 ± 1.1	4.6 ± 1.7	6.9 ± 2.2	<0.001

As summarized in Table 3, cardiovascular complications increased markedly with OSA severity. Severe OSA patients exhibited the highest burden of hypertension, arrhythmias, left ventricular hypertrophy, diastolic dysfunction, and pulmonary hypertension. The progressive rise in hs-CRP across groups confirmed that systemic inflammation correlated with disease severity.

Overall, the findings of the current study indicate that there is a close correlation

between the severity of OSA and respiratory and cardiovascular dysfunction. The severely obese patients had a higher OSA and were found to have a high level of structural risks including increased neck circumference, and they displayed higher levels of sleep fragmentation and nocturnal desaturation. These abnormalities were converted to the increased occurrence of systemic hypertension, arrhythmias, left ventricular dysfunction, and pulmonary hypertension. The results highlight that the pathophysiological processes of OSA such as intermittent hypoxemia, sympathetic overactivity and intrathoracic pressure variations are clinically manifested in the continuum of cardiovascular effects, which become more severe as the disease advances.

DISCUSSION

In this prospective study of 90 participants with the obstructive sleep apnea (OSA) there is clear evidence that the severity of the disease is closely linked with a remarkable respiratory and cardiovascular derangements [15]. The results show that the apnea-hypopnea index (AHI) showed an inverse relationship with the pathophysiologic mechanisms of a deeper nocturnal hypoxemia, increased sleep fragmentation, and increased sympathetic response, which were reflected in a significantly greater proportion of hypertension, arrhythmias, left ventricular dysfunction, pulmonary hypertension, and systemic inflammation. These findings support the idea that OSA is more than a nocturnal breathing disorder but a systemic ailment with far clinical and pathophysiological implications [16].

Our patients are well assured of the epidemiology of OSA due to their demographic profile. The average age of about 50 and the male dominance fall in line with the previous study like Sleep Heart Health Study which reported a higher prevalence in middle-aged and old men [17]. Obesity, particularly central obesity and increased neck circumference, emerged as strong predictors of OSA severity in our cohort, consistent with existing literature demonstrating that fat deposition in the pharyngeal region increases airway collapsibility. These findings highlight the critical role of weight and body habitus in OSA pathogenesis, suggesting that lifestyle and weight management remain key preventive strategies [18].

Our polysomnography data showed a progressive decline in mean nocturnal oxygen saturation and a substantial increase in oxygen desaturation index and arousal index with increasing OSA severity. These findings are physiologically significant because intermittent hypoxemia and repeated arousals generate a “two-hit” mechanism of injury [19]. Hypoxia–reoxygenation cycles mimic ischemia–reperfusion injury, leading to oxidative stress, endothelial dysfunction, and systemic inflammation. Simultaneously, recurrent arousals activate the sympathetic nervous system, resulting in sustained elevations in blood pressure and heart rate even during wakefulness. This dual pathway of injury explains why OSA is such a potent risk factor for cardiovascular disease [20].

The cardiovascular consequences observed in this study are striking. Hypertension was the most prevalent comorbidity and its frequency increased stepwise with OSA severity, reaching 78.1% in severe cases [21]. Importantly, resistant hypertension was documented in over one-fifth of patients with severe OSA, underscoring the robust association between disordered breathing and blood pressure dysregulation. This observation is supported by large-scale epidemiological studies, including the Wisconsin Sleep Cohort and the HIPARCO trial, which identified OSA as an independent and modifiable risk factor for resistant

hypertension. Our findings therefore strengthen the argument that screening for OSA should be an integral component of hypertension management, particularly in patients with poor blood pressure control despite multidrug therapy [22].

Arrhythmias were also significantly more common in severe OSA, with atrial fibrillation being the most frequent [23]. The pathophysiological basis for this link includes atrial stretch from negative intrathoracic pressures, intermittent hypoxemia-induced electrophysiological instability, and sympathetic overdrive. Previous studies, such as those by Gami et al. and the Sleep Heart Health Study, have shown that OSA increases the risk of new-onset atrial fibrillation and impairs success rates of cardioversion and ablation. Our findings align with these observations and suggest that aggressive diagnosis and treatment of OSA may improve rhythm control strategies in atrial fibrillation patients [24].

Echocardiographic abnormalities, including increased left ventricular mass index, diastolic dysfunction, and pulmonary hypertension, were strongly associated with OSA severity. The chronic hemodynamic stress induced by large intrathoracic pressure swings and sympathetic activation provides a plausible mechanism for left ventricular remodeling and impaired relaxation [25]. Pulmonary hypertension, detected in nearly 30% of patients with severe OSA, reflects a combined effect of hypoxic pulmonary vasoconstriction, endothelial dysfunction, and concomitant left heart disease. These findings are in line with prior study indicating that untreated OSA accelerates the development of heart failure and worsens outcomes in existing heart failure patients [26].

Inflammatory status, as measured by hs-CRP, also demonstrated a stepwise increase with disease severity. Elevated hs-CRP reflects systemic inflammation and is a recognized marker of cardiovascular risk [27]. The association between OSA and systemic inflammation supports the hypothesis that OSA contributes to a pro-inflammatory milieu, thereby accelerating atherosclerosis. This finding corroborates reports from Drager et al. and others, who have shown that OSA patients exhibit increased circulating cytokines, oxidative stress markers, and endothelial dysfunction even in the absence of overt cardiovascular disease [28].

Taken together, the results of this study emphasize that OSA operates as a “silent cardiovascular risk amplifier.” It not only worsens existing risk factors such as obesity, hypertension, and diabetes but also independently contributes to adverse cardiovascular outcomes through pathophysiological mechanisms unique to sleep-disordered breathing [29]. Importantly, many of these pathways are reversible with effective treatment. Continuous positive airway pressure (CPAP) therapy has been shown to improve blood pressure control, reduce arrhythmia burden, and attenuate markers of systemic inflammation. While CPAP compliance remains a challenge, our data add to the growing body of evidence underscoring the necessity of integrating OSA diagnosis and treatment into cardiovascular risk management [30].

This study has several strengths, including its prospective design, use of full polysomnography, and comprehensive cardiovascular assessment. However, limitations should be acknowledged. The study was conducted at two tertiary care centers in Pakistan, which may limit generalizability to the broader community population [31]. The sample size, although adequate for statistical analysis, may not capture less frequent cardiovascular outcomes. Longitudinal follow-up was not included, and thus causal

relationships between OSA and cardiovascular events could not be directly established. Nevertheless, the strong associations observed provide a compelling rationale for larger, multicenter studies and interventional trials in South Asian populations, where the burden of both OSA and cardiovascular disease is rapidly rising [32].

CONCLUSION

This study demonstrates that obstructive sleep apnea is a major contributor to both respiratory and cardiovascular dysfunction. Increasing severity of OSA was associated with greater obesity, nocturnal hypoxemia, and sleep fragmentation, which in turn translated into higher rates of hypertension, arrhythmias, left ventricular remodeling, pulmonary hypertension, and systemic inflammation. These findings reinforce the need for early recognition and management of OSA as part of comprehensive cardiovascular risk reduction strategies. Timely intervention through CPAP therapy, weight reduction, and lifestyle modification has the potential to mitigate the systemic impact of OSA and improve long-term outcomes.

Conflict of Interest:

The authors report no conflicts of interest.

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Authors' contributions:

UT: Conceptualization, drafting.
MSL: Data collection, analysis.
AZ: Literature review, editing.
NT: Statistics, data acquisition.
SK: Clinical evaluation.
MA: Investigation support.
FAR: Revision, final approval.

Data Availability Statement:

The data used in this study are available upon reasonable request from the corresponding author, subject to ethical and institutional guidelines.

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