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# INVESTIGATING THE LINK BETWEEN SLEEP APNEA AND CARDIOVASCULAR DISEASE PROGRESSION: A LONGITUDINAL STUDY

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## ABSTRACT

***Background:*** *Obstructive sleep apnea (OSA) is increasingly acknowledged as an independent risk factor for cardiovascular disease (CVD), mainly due to intermittent hypoxia, systemic inflammation, and sympathetic overactivity. Despite its clinical significance, there is a scarcity of longitudinal data from South Asia, particularly Pakistan, assessing CVD progression about OSA severity.* ***Objective:*** *To investigate the relationship between the severity and progression of obstructive sleep apnea (OSA) and cardiovascular disease.* ***Study Design:*** *Prospective longitudinal study.* ***Setting:*** *This study was conducted at a tertiary care hospital in Pakistan.* ***Duration of Study:*** April 2023 to October 2023, *(enrollment), with a 12-month follow-up period for each participant.* ***Methods:*** *A total of 78 adults with newly diagnosed moderate to severe obstructive sleep apnea (Apnea-Hypopnea Index [AHI] ≥15), confirmed through polysomnography, were enrolled. Participants were followed for 12 months, during which cardiovascular parameters—including systolic and diastolic blood pressure, lipid profile, high-sensitivity C-reactive protein (hs-CRP), and cardiovascular events (such as myocardial infarction and angina)—were monitored. Data were analyzed using SPSS version 26. Statistical tests included paired t-tests, chi-square tests, and logistic regression; p-values less than 0.05 were considered statistically significant.* ***Results:*** *Over the 12-month follow-up, there were statistically significant increases in: Systolic blood pressure (mean +6.7 mmHg, p = 0.01), Diastolic blood pressure (mean +4.2 mmHg, p = 0.03), LDL cholesterol levels (p = 0.04), hs-CRP levels (p < 0.01), Cardiovascular events occurred more frequently in the severe OSA group (8 events) than in the moderate OSA group (3 events). Severe OSA and elevated hs-CRP levels (≥5 mg/L) were identified as independent predictors of cardiovascular events with odds ratios (OR) of 3.8 and 4.1, respectively.* ***Conclusion:*** *Severe obstructive sleep apnea significantly contributes to cardiovascular disease progression in the Pakistani population, likely mediated through inflammatory and hypertensive mechanisms. Early detection and management of OSA may offer a strategic opportunity to mitigate long-term cardiovascular risks.*

**Keywords:** Sleep apnea, Cardiovascular disease, Pakistan, Inflammation, Hypertension, Longitudinal study, hs-CRP

## INTRODUCTION

Obstructive sleep apnea (OSA) is a chronic sleep-related breathing disorder characterized by repeated episodes of upper airway obstruction during sleep, leading to intermittent hypoxia, sleep fragmentation, and sympathetic overactivity. Globally, OSA has been recognized as a major independent risk factor for cardiovascular diseases (CVD), including hypertension, coronary artery disease, stroke, and heart failure (1). In Pakistan, the burden of OSA remains under-recognized despite its increasing prevalence due to urbanization, rising obesity, and high rates of undiagnosed diabetes and hypertension (2,3).

Recent studies indicate that a significant portion of the Pakistani population may be at risk for sleep apnea, particularly among middle-aged males with metabolic syndrome and cardiovascular risk factors (4). The rising prevalence of obesity, affecting over 27% of adults, and undiagnosed type 2 diabetes has created a fertile ground for OSA and its cardiovascular consequences (5,6). However, clinical awareness and screening for sleep disorders remain limited in Pakistan, especially in cardiology and primary care settings.

The pathophysiological link between obstructive sleep apnea (OSA) and cardiovascular disease progression is multifactorial, involving intermittent hypoxemia, oxidative stress, systemic inflammation, endothelial dysfunction, and sympathetic nervous system activation (7). These mechanisms collectively accelerate atherosclerosis and exacerbate existing cardiovascular conditions. High-sensitivity C-reactive protein (hs-CRP), a marker of systemic inflammation, has been shown to increase significantly in patients with moderate to severe obstructive sleep apnea (OSA) and is predictive of cardiovascular events (8). Despite this evidence, local data on the longitudinal impact of OSA on cardiovascular health remains scarce.

A few regional studies from Pakistan have reported high proportions of undiagnosed OSA among patients with ischemic heart disease and resistant hypertension, suggesting a silent but significant contributor to poor cardiovascular outcomes (9,10). However, most of these investigations are cross-sectional and lack long-term follow-up. There is a clear need for longitudinal research to understand the progression of cardiovascular disease among patients with sleep apnea in the Pakistani population.

This study aims to address this gap by evaluating the association between sleep apnea severity and the progression of cardiovascular disease over 12 months in a cohort of Pakistani adults. The findings are expected to highlight the importance of early diagnosis and intervention for OSA in preventing cardiovascular complications in high-risk populations.

## METHODOLOGY

This prospective longitudinal study was conducted at a tertiary care hospital in Pakistan over a six-month period, from April 2023 to October 2023, to evaluate the association between sleep apnea severity and the progression of cardiovascular disease. The study included adult patients aged 35 to 65 years who were newly diagnosed with moderate to severe obstructive sleep apnea (OSA), confirmed by

overnight polysomnography with an Apnea-Hypopnea Index (AHI) of ≥15 events per hour. Patients with a prior history of cardiovascular disease (including myocardial infarction, heart failure, or stroke), chronic kidney disease, central sleep apnea, or other primary sleep disorders were excluded to reduce confounding.

Participants were recruited consecutively from the sleep and cardiology outpatient departments through non-probability purposive sampling. After obtaining written informed consent, baseline data were collected, including demographic details, body mass index (BMI), smoking status, comorbidities (hypertension, diabetes), lipid profile, blood pressure measurements, and inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP). All patients underwent a comprehensive cardiovascular evaluation, which included resting electrocardiography, echocardiography, and assessment of cardiac biomarkers. Sleep apnea severity was categorized as moderate (AHI 15–29.9) or severe (AHI ≥30), and patients were followed for 12 months to assess the progression of cardiovascular parameters.

During the follow-up period, patients continued their usual care and were monitored quarterly. Data on incident cardiovascular events (such as myocardial infarction, new-onset angina, or hospitalization for heart failure) were recorded. Repeat assessments of blood pressure, lipid profiles, and hs-CRP levels were performed at 12 months. Standardized clinical protocols were employed to ensure consistency in data collection, and any cardiovascular events were confirmed through review of clinical records and diagnostic investigations.

All data were entered and analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Paired t-tests were used to compare baseline and follow-up data. Independent t-tests and chi-square tests were applied to compare outcomes between moderate and severe OSA groups. Multivariate logistic regression analysis was conducted to identify independent predictors of cardiovascular event occurrence, adjusting for baseline comorbidities and inflammatory markers. A p-value of less than 0.05 was considered statistically significant. Ethical approval was obtained from the institutional review board of the participating hospital, and the study adhered to the principles of the Declaration of Helsinki.

## RESULTS

A total of 78 participants with newly diagnosed moderate to severe sleep apnea were enrolled and monitored for cardiovascular outcomes through clinical evaluations and diagnostic assessments. Most participants were middle-aged males, with a high prevalence of obesity (mean BMI 30.4) and cardiometabolic comorbidities, including hypertension and diabetes. More than 45% had severe sleep apnea based on Apnea-Hypopnea Index (AHI). (Table 1).

There was a statistically significant increase in blood pressure, LDL cholesterol, and high-sensitivity C-reactive protein (hs-CRP) levels over a 12-month period, indicating inflammatory progression and heightened cardiovascular risk. The number of cardiac events more than doubled during follow-up. (Table 2).

Patients with severe sleep apnea experienced significantly more significant increases in blood pressure and inflammatory markers. They had a higher incidence of cardiac events compared to those with moderate sleep apnea, suggesting a dose-response relationship. (Table 3)

**Table 1: Baseline Demographic and Clinical Characteristics of Participants (n = 78)**

| Variable | Value / Frequency | (%) |
|---|---|---|
| Mean Age (years ± SD) | 52.3 ± 8.7 | – |
| **Gender** | | |
| - Male | 52 | 66.7 |
| - Female | 26 | 33.3 |
| Body Mass Index (BMI ± SD) | 30.4 ± 3.9 | – |
| Hypertension | 49 | 62.8 |
| Type 2 Diabetes Mellitus | 37 | 47.4 |
| Smoking History | 29 | 37.2 |
| **Sleep Apnea Severity (AHI)** | | |
| - Moderate (15–29.9) | 42 | 53.8 |
| - Severe (≥30) | 36 | 46.2 |

**Table 2: Cardiovascular Events and Biomarker Progression Over 12 Months**

| Outcome | Baseline | 12 Months | p-value |
|---|---|---|---|
| Systolic BP (mmHg ± SD) | 138.2 ± 14.1 | 144.9 ± 16.2 | 0.01* |
| Diastolic BP (mmHg ± SD) | 84.5 ± 9.2 | 88.7 ± 10.4 | 0.03* |
| LDL Cholesterol (mg/dL ± SD) | 132.1 ± 24.5 | 139.4 ± 27.3 | 0.04* |
| hs-CRP (mg/L ± SD) | 4.1 ± 1.2 | 5.3 ± 1.6 | <0.01* |
| Cardiac Events (MI/Angina) | 5 | 11 | – |

**Table 3: Association Between Sleep Apnea Severity and Cardiovascular Outcomes**

| Sleep Apnea Severity | Mean BP Rise (mmHg) | hs-CRP Increase (mg/L) | New Cardiac Events (n) |
|---|---|---|---|
| Moderate (n = 42) | +4.6 / +2.7 | +0.7 | 3 |
| Severe (n = 36) | +8.3 / +4.6 | +1.6 | 8 |
| p-value | <0.05 | <0.01 | 0.02 |

**Table 4: Multivariate Regression Analysis Predicting Cardiovascular Event Risk**

| Predictor Variable | Odds Ratio (OR) | 95% Confidence Interval (CI) | p-value |
|---|---|---|---|
| Severe Sleep Apnea | 3.8 | 1.4–10.2 | 0.008* |
| BMI ≥30 | 2.2 | 0.9–5.4 | 0.07 |
| hs-CRP ≥5 mg/L | 4.1 | 1.6–10.3 | 0.004* |
| Hypertension at Baseline | 2.7 | 1.1–6.7 | 0.03* |

Multivariate analysis showed that severe sleep apnea and elevated hs-CRP levels were independent predictors of cardiovascular event risk, highlighting the inflammatory link between sleep apnea and CVD progression. (Table 4) Sleep apnea, particularly in its severe form, was associated with worsening cardiovascular profiles over a 12-month follow-up period. Significant increases in blood pressure, LDL cholesterol, and hs-CRP levels were observed. The number of cardiovascular events, including angina and myocardial infarction, more than doubled. Severe sleep apnea and elevated inflammation (hs-CRP ≥ 5 mg/L) were strong, independent predictors of adverse cardiovascular outcomes. These findings emphasize the need for routine cardiovascular risk screening and early intervention in sleep apnea patients, especially in high-risk populations such as those in Pakistan.

## DISCUSSION

This longitudinal study demonstrated a significant association between the severity of obstructive sleep apnea (OSA) and the progression of cardiovascular disease (CVD) markers and events in a Pakistani population. Over a 12-month follow-up period, patients with severe OSA experienced more significant increases in systolic and

diastolic blood pressure, LDL cholesterol, and high-sensitivity C-reactive protein (hs-CRP), along with a higher incidence of cardiovascular events such as myocardial infarction and angina. These findings are consistent with international and regional studies that highlight the pathophysiological link between OSA and CVD through mechanisms involving systemic inflammation, endothelial dysfunction, and sympathetic activation.

In our study, patients with severe sleep apnea (AHI ≥30) had nearly twice the rate of cardiovascular events compared to those with moderate OSA, indicating a dose-response relationship. This aligns with the findings of Yaggi et al., who showed that untreated severe OSA significantly increases the risk of incident cardiovascular disease and stroke (11). Similarly, Shah et al. reported that patients with higher AHI levels had a 2.5-fold greater risk of coronary artery disease progression within a 2-year follow-up (12).

One of the key findings in our study was the significant rise in hs-CRP levels in patients with severe OSA, which independently predicted cardiovascular events in the multivariate analysis. This observation supports prior evidence that hs-CRP is a sensitive biomarker linking chronic inflammation in OSA to atherosclerotic progression. Jelic et al. and Mehra et al. also identified elevated inflammatory markers as predictive of future cardiac complications in sleep apnea patients, especially when comorbid with obesity or metabolic syndrome (13,14).

The increase in both systolic and diastolic blood pressure among participants is in line with studies suggesting that OSA contributes to the development and worsening of hypertension due to persistent sympathetic activation and nocturnal hypoxia. A study by Marin et al. demonstrated that severe OSA was associated with a significant rise in 24-hour blood pressure and a higher likelihood of developing resistant hypertension (15). This phenomenon was also observed in our study, where patients with severe OSA experienced a mean systolic blood pressure increase of over eight mmHg at follow-up.

Interestingly, our findings also revealed that LDL cholesterol levels increased significantly over the 12 months, particularly in patients with severe OSA. This reinforces the idea that OSA not only promotes an inflammatory state but may also alter lipid metabolism, thereby compounding cardiovascular risk. Previous studies by Tasali et al. and Borel et al. have identified disrupted sleep and intermittent hypoxia as contributors to dyslipidemia and impaired glucose metabolism (16,17).

In the context of Pakistan, where obesity, metabolic syndrome, and poorly controlled hypertension are highly prevalent, these results are particularly relevant. Regional studies have confirmed that OSA remains vastly underdiagnosed in high-risk cardiovascular populations due to a lack of awareness, screening, and diagnostic facilities (18). Our findings underscore the need for integrating sleep assessments into routine cardiovascular risk evaluations in Pakistani clinical settings.

Despite the robust findings, this study has some limitations. The sample size was modest, and the study was conducted in a single tertiary care center, limiting the generalizability of the results. Moreover, adherence to continuous positive airway pressure (CPAP) therapy was not evaluated, which could have influenced cardiovascular outcomes. Future multicenter studies with extended follow-up periods and compliance tracking for CPAP are warranted to strengthen the evidence.

## CONCLUSION

In conclusion, our study confirms that severe OSA is independently associated with adverse cardiovascular progression in Pakistani adults. These findings support early identification and management of OSA in high-risk populations to prevent cardiovascular morbidity and mortality.

## DECLARATIONS

**Data Availability Statement**

All data generated or analysed during the study are included in the manuscript.

**Ethics approval and consent to participate**

Approved by the department Concerned. (IRBEC-24)

**Consent for publication**

Approved

**Funding**

Not applicable

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHOR CONTRIBUTION

***ALINA MUNEEB (****Consultant Physician)*
*Conception of the Study, Development of Research Methodology Design, Study Design, Review of the manuscript, and final approval of the manuscript.*
*Manuscript manuscript drafting.*
***SARROSH KHAN (****Specialist Internal Medicine)*
*Manuscript drafting.*
*Conception of Study, Final approval of manuscript.*
*Data entry, data analysis, and drafting the article.*
***WARDA TAJAMMAL (Resident Medical Officer )***
*Revisions, critical input. Study Design, Review of Literature.*

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