

## LATENT MODIFIABLE RISK FACTORS FOR CORONARY ARTERY DISEASE: QUALITY AND QUANTITY OF SLEEP?

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DOI: <https://doi.org/10.5281/zenodo.20459071>

### Keywords

### Article History

Received: 03 April 2026

Accepted: 12 May 2026

Published: 30 May 2026

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### Abstract

#### **Objective:**

Earlier research has indicated that insufficient sleep has harmful impacts on multiple systems, with observable alterations in metabolic, endocrine, and immune processes. Both brief and extended sleep durations are linked to a higher risk of diabetes and hypertension. Nevertheless, the connection between sleep duration, sleep quality, and Coronary Artery Disease (CAD) remains unclear among the Pakistani population. We investigated the notion that sleep length (relative to <6 h) and sleep quality (PSQI > 5) are contributors to CAD risk.

#### **Methods:**

A controlled and retrospective study was performed involving 354 adults (>18 yrs) participants (177 controls and 177 cases, 60% male, average age M = 51 ± 9.38). The quality and duration of sleep were assessed using the Pittsburgh Sleep Quality Index (PSQI). Low sleep quality and inadequate sleep duration were characterized as PSQI >5 and total sleep time <6.0 h, respectively. Patients with OSA were not included in the study. The primary outcome of interest was the occurrence of any CAD (n = 177), which included MI, angina, and stroke. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were determined through Multivariate Logistic Regression analysis.

#### **Results:**

We identified that both inadequate sleep quality and reduced sleep duration were independently linked to CAD. In comparison to a total sleep duration of 6.0 hours, the multivariate odds ratio (95% confidence interval) for CAD was 3.81 (1.69 to 8.58), while for poor sleep quality (PSQI > 5), it was found to be 16.62 (9.13 to 30.28).

#### **Conclusion:**

A positive correlation was found between both brief sleep duration and inadequate sleep quality with CAD in a chosen group of Pakistani adults. These findings indicate that inadequate sleep quality and limited sleep duration could be significant changeable CAD risk factors within the Pakistani population.

### INTRODUCTION:

Sleep is an innate behavior in living organisms that occurs spontaneously and aligns with the daily cycle. However, it has turned into an issue for humans. Past research has demonstrated that insufficient sleep has harmful impacts on various systems, resulting in noticeable alterations in

metabolic, endocrine, and immune pathways. Short and long sleep durations are associated with a higher risk of diabetes and hypertension. Recent decades of epidemiological studies have shown that sleep disturbances are associated with mortality from cardiac issues and other causes. Multiple epidemiological studies indicate a

significant link between sleep issues or reduced sleep durations and heart-related diseases. A recent review presents compelling evidence that those who sleep little (>5 h of sleep/night) face a greater risk of coronary incidents. Nevertheless, insomnia, the most prevalent sleep issue among cardiac patients, has remained overlooked. There is a significant deficiency of published research regarding the connection between sleep duration, sleep quality, and Coronary Artery Disease (CAD) in developing nations. It was suggested that brief sleep duration and low sleep quality might contribute to CAD. The purpose of the research was to examine sleep length and sleep quality in individuals with CAD.

#### **METHOD:**

##### **Study population:**

We performed a retrospective and controlled analysis. A total of 354 participants were recruited for this study from July to November 2020. At the time of enrollment, participants or their relatives provided either written or verbal informed consent.

A total of 177 consecutive cases from the CCU of a tertiary care facility with a recent diagnosis of CAD, which includes myocardial infarction, angina, and stroke, were included. 177 controls were gathered from the general population. Patients were excluded if they had sleep disorders such as OSA and/or any other major medical condition leading to inadequate sleep. To eliminate any potential sleep disorder such as OSA, a comprehensive sleep history was obtained with the bed partner present. Individuals who reported persistent, loud snoring, gasping, experiencing a dry mouth or sore throat upon waking, daytime headaches, or excessive drowsiness, including struggling against sleepiness during the day, at work, or while driving were excluded. Additionally, individuals with cognitive and social challenges, such as memory issues, learning struggles, lack of focus, attention deficits, irritability, depression, mood fluctuations, or personality alterations were not included. Poor sleep quality was characterized by “feeling tired upon waking” and/or indicating “unrefreshing mornings,” while short sleep duration was defined

as total sleep time being less than 6.0 hours. Sleep quality and total sleep time (TST) were assessed using the Pittsburgh Sleep Quality Index (PSQI) developed by Buysse in 1989.

The PSQI is a 19-question survey that requires respondents to describe their usual sleep patterns over the last month. In the current research, the duration of one month was altered to one year to acquire data regarding the pre-morbid condition. Every question in the PSQI receives a score ranging from 0 to 3, with some relating to other questions in the survey, while others have an individual score. The PSQI evaluates sleep length, time taken to fall asleep, daytime impairment from drowsiness, sleep efficiency, general sleep quality, and reliance on medication for sleep assistance. The total PSQI score is the sum of all individual measure scores [from 0 to 21], where scores below 5 indicating improved sleep quality and values exceeding 5 indicating inadequate sleep quality (Buysse DJ, 1989).

Short sleep duration was defined as less than 6.0 hours of sleep (reference group).

Data regarding demographic profile and medical history was gathered via direct interview. The variables comprised age, gender, marital status, hypertension, and diabetes. Statistical analyses were performed utilizing SAS statistical software version 9.2 (SAS Institute, INC., Cary, NC). The characteristics of participants are shown as mean  $\pm$  SD/Median for continuous variables or as percentages for categorical variables. Multivariate Logistic regression analysis was employed to calculate Odds ratios (ORs) and 95% confidence intervals (95% CIs) for CAD across sleep categories. Participants with a regular sleep duration of 6 hours were regarded as the reference group for limited sleep duration.

#### **RESULTS:**

The research included 354 patients, among whom 177 had recently been diagnosed with CAD, while the rest were healthy controls from the general population. All participants completed a questionnaire to gather demographic, medical, and information regarding sleep quality and duration. Most of the total participants were male (60.5%) with an average age of 49.9 years.

Table 1 presents the demographic and medical characteristics of the participants.

Among them, the majority were men (60.5%), 29.8% had hypertension, and 23% had DM. Table 2 presents a comparison of demographic variables and sleep quality (poor) and sleep duration (short) categorized by individuals with and without CAD.

68.8% of patients with CAD experienced poor sleep quality, whereas 10.2% of those without CAD did ( $p = 0.001$ ).

17% of CAD patients reported sleeping for under 6 hours per day, while only 6.3% of participants without CAD indicated sleeping less than 6 hours ( $p = 0.001$ ).

The control group's median PSQI score was 2, while the cases had a median score of 7 ( $p = 0.001$ ).

The median total sleep time (TST) for individuals without CAD was 7.16, while for those diagnosed with CAD it was 7 ( $p = 0.001$ ).

Seventy-nine CAD participants confirmed snoring (44.9%), while 29.5% of the control group reported it as well ( $p = 0.003$ ).

In subjects with CAD, those sleeping less than 6 hours had a higher OR (3.81) of CAD events compared to subjects without CAD. Low sleep quality characterized by restless or disturbed nights and unrefreshing mornings was linked to a higher OR (16.62) of CAD (Table 3).

**TABLE 1: DEMOGRAPHIC AND MEDICAL CHARACTERISTICS OF THE PARTICIPANTS**

	N=354
AGE (IN YEARS)	49.9
HTN	29.80%
DM	23%
MALE	60.50%
FEMALE	39.50%

**TABLE 2: COMPARISON OF DEMOGRAPHIC VARIABLES CATEGORIZED BY INDIVIDUALS WITH AND WITHOUT CAD**

	CONTROLS (N=177)		CASES (N=177)		P VALUE
AGE	50.19 ± 6.42	42-77	51.51 ± 11.58	20-85	0.190
FEMALE	61	34.7%	78	44.3%	0.064
MARRIED	167	94.9%	142	80.7%	<0.001
PSQI>5	18	10.2%	121	68.8%	<0.001
TST<6	11	6.3%	30	17.0%	0.002

**TABLE 3: MULTIVARIATE LOGISTIC REGRESSION ANALYSIS.**

Variables	P VALUE	ODD RATIO	95% CI
Unmarried	0.004	3.00	1.00-9.00
PSQI > 5	<0.001	16.62	9.13-30.28
TST < 6	0.001	3.81	1.69-8.58

**DISCUSSION:**

To our understanding, this is the initial research that investigated the relationship between sleep duration and sleep quality in Pakistani patients with CAD. Past research identified a notable link between short (under 6 h) and long sleep duration

(over 8 h) and CHD, DM, and HTN in the general population.

Earlier research involving Americans or Europeans backs up our conclusions.

The Nurses' Health Study involving 71,617 women aged 40 to 65 found that, in comparison

to 8 hours of sleep, shorter sleep duration of 5 hours or less correlated with a 1.4-fold higher risk of coronary heart disease. This research indicates a favorable link between the occurrence of CAD and inadequate sleep quality along with reduced sleep duration. Multivariate logistic analysis shows that individuals who sleep less than 6 hours per day have a higher risk of developing CAD compared to those who sleep more than 6 hours per day. Additionally, inadequate sleep quality demonstrates a heightened risk for these occurrences, reaffirming the existence of a U-shaped relationship. Research indicates that both short and long sleep durations are independently linked to a higher risk of coronary events. Both short sleeper groups (those sleeping 5 hours and 6 hours) and individuals who sleep extremely long hours showed heightened unadjusted CHD risk. (10 h) for both sexes when compared to midrange (7-8 h) sleepers.

A different research conducted by Amagai, Y. et al, demonstrated that short sleep duration (<6 h) is a notable risk factor for coronary events among a working male population in Japan. The likelihood of CHD events was not influenced by significant cardiovascular risk factors or occupational elements. Reduced sleep duration in a cohort of healthy individuals heightened sympathetic nervous system activity and led to increased blood pressure. Consequently, prolonged short sleep duration may result in negative cardiovascular effects. The connection between limited sleep duration and the occurrence of CVD may result from short sleep impacting intermediate biological risk factors for CVD.

Epidemiological research indicated that limited sleep duration correlated with increased rates of overweight, obesity, and hypertension, along with elevated blood pressure, total cholesterol, hemoglobin A(1c), and triglyceride levels. Additionally, blood pressure reaches its minimum levels during nighttime rest when parasympathetic activity is at its peak. As a result, individuals with shorter sleep duration experience the smallest benefit in their arteries from this positive effect. Additionally, sleep quality could influence the relationship between sleep duration and

cardiovascular disease. The quality of sleep plays a crucial role in the body's physiological recovery during rest, and maintaining good sleep quality can help prevent cardiovascular disease (CVD). Chandola et al discovered in the Whitehall II cohort that the link between short sleep (6h) and CHD risk was strongest for those who indicated experiencing some sleep disturbance. These results bolster the idea that for certain individuals, a sleep duration of 6 hours or less might suffice for the restorative biological functions linked to sleep, while for others, it may not.

#### LIMITATIONS:

The current research faced certain limitations. The study's primary limitations were a small sample size, which restricted the ability to adjust for potential confounders in the analysis. As a result, interpreting the causality of our results is challenging. We lacked information on other confounders such as hyperlipidemia, alcohol consumption, and exercise frequency, and thus could not account for these factors in the analysis. Regrettably, we could not evaluate the impact of overweight, obesity, and hypertension alongside elevated blood pressure, total cholesterol, hemoglobin A (1c), and triglycerides on our findings. Our study had another limitation due to the absence of objective measurements for sleep duration, blood pressure, and glucose.

#### CONCLUSION:

Acknowledgment of brief sleep length and inadequate sleep quality is a novel research domain that could influence the treatment of individuals with CVD. It remains to be investigated in properly designed studies whether enhancing sleep quality and duration can reverse the chronic cardiovascular and metabolic effects of sleep disorders, especially in comparison to standard approaches.

#### CONFLICTS OF INTEREST:

All authors have none to declare.

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