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ASSOCIATION BETWEEN DEPRESSION SYMPTOMS AND CORONARY ARTERY DISEASE IN PATIENT UNDERGOING ANGIOGRAPHY.

Original Research

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ABSTRACT

Background: Depression is increasingly recognized as a significant factor influencing the prognosis of coronary artery disease (CAD). Despite its prevalence, depressive symptoms remain underdiagnosed and undertreated in CAD patients, impacting disease progression and outcomes. This study aims to determine the association between depressive symptoms and CAD severity in patients undergoing coronary angiography.

Objective: To assess the prevalence and severity of depressive symptoms in CAD patients and compare them with non-CAD individuals.

Methods: A case-control study was conducted at the National Institute of Cardiovascular Diseases (NICVD) Karachi, including 64 participants (32 CAD cases and 32 controls). Depressive symptoms were evaluated using the validated Patient Health Questionnaire-9 (PHQ-9). CAD was diagnosed through coronary angiography, defining significant disease as ≥70% stenosis in at least one major coronary artery. Sociodemographic and clinical variables were recorded. Statistical analyses, including an independent t-test for PHQ-9 scores and a chi-square test for categorical variables, were performed using SPSS version 23, considering $p<0.05$ as statistically significant.

Results: The prevalence of depressive symptoms was significantly higher in CAD patients (84.4%) compared to controls (9.4%) ($p<0.001$). The mean PHQ-9 score in cases was **13.4 ± 3.2**, significantly higher than in controls (**6.6 ± 2.6**) ($p<0.001$). Factors such as unemployment, urban residence, smoking, hypertension, diabetes, and dyslipidemia were more common in CAD patients.

Conclusion: A strong association exists between depressive symptoms and CAD, highlighting the need for routine depression screening and integrated management strategies in cardiovascular care. Addressing depression as a modifiable risk factor may improve clinical outcomes and overall well-being in CAD patients.

Keywords: Angiography, Coronary artery disease, Depression, Depressive symptoms, Mental health, PHQ-9, Risk factors.

INTRODUCTION

Coronary artery disease (CAD) remains a leading global health concern, accounting for approximately 30% of total deaths worldwide, with an estimated 17 million fatalities annually. This number is projected to rise if effective preventive measures are not implemented (1,2). CAD is primarily characterized by insufficient blood supply to the heart muscle due to the narrowing or blockage of coronary arteries. While traditional risk factors such as family history, age, gender, hypertension, diabetes mellitus, smoking, dyslipidemia, obesity, and physical inactivity have long been recognized as contributors to cardiovascular disease, emerging evidence suggests that psychological factors, particularly depression, play a crucial role in disease progression and patient outcomes (3,4). Depression is highly prevalent among patients with CAD and has been identified as an independent risk factor for adverse cardiovascular events. Research indicates that depressive symptoms are associated with increased levels of inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1 (IL-1), and C-reactive protein (CRP), which contribute to systemic inflammation and endothelial dysfunction, further exacerbating cardiovascular risk (5-7). Moreover, serotonin, a neurotransmitter implicated in the pathophysiology of depression, has been shown to promote platelet aggregation via 5-hydroxytryptamine (5-HT) receptors in individuals with CAD, potentially leading to coronary obstruction and myocardial ischemia (8-10). Additionally, depression-induced endothelial dysfunction can exacerbate vascular constriction at sites of atherosclerotic plaque, increasing the likelihood of ischemic events (11,12).

The association between depression and CAD extends beyond physiological mechanisms, influencing prognosis and long-term clinical outcomes. Studies have demonstrated that depression significantly increases the risk of mortality and recurrent myocardial infarction in patients with CAD (13-15). Notably, individuals experiencing depressive symptoms at the time of coronary angiography are at a substantially higher risk of adverse cardiac events within the following year (16,17). Furthermore, depression negatively impacts patients' daily functioning and quality of life, often more profoundly than the severity of their angiographic findings (18-20). Despite this, depression remains underdiagnosed and undertreated in patients with CAD, highlighting the need for systematic screening and intervention (21). Epidemiological studies estimate that 20% to 40% of patients with CAD experience clinically significant depression, while major depressive disorder affects approximately 20% to 30% of individuals with the disease (22-24). In contrast, the prevalence of depressive symptoms in the general adult population without CAD is significantly lower, ranging between 12% and 13% (25). This discrepancy underscores the potential bidirectional relationship between depression and CAD, wherein psychological distress contributes to cardiovascular pathology, and the burden of CAD exacerbates depressive symptoms.

Although substantial research has explored the link between depression and cardiac disease, limited studies have examined the specific association between depressive symptoms and the severity of CAD in patients undergoing coronary angiography. Existing findings remain inconsistent, necessitating further investigation into this critical relationship. Given the established role of depression in the onset, progression, and prognosis of cardiovascular disease, this study aims to determine the association between depression symptoms and coronary artery disease in patients undergoing angiography. Understanding this relationship may provide valuable insights for improving risk stratification and optimizing comprehensive patient management.

METHODS

This case-control study was conducted at the Department of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD), Karachi, over a minimum duration of six months following the approval of the study protocol by the Ethical Review Committee of the institution and the College of Physicians and Surgeons Pakistan (CPSP). The study aimed to assess the association between depressive symptoms and coronary artery disease (CAD) in patients undergoing coronary angiography. Ethical approval was obtained prior to the commencement of the study, and all participants provided written informed consent after being thoroughly informed about the study's objectives, potential risks, and benefits. The sample size was calculated using the WHO sample size calculator, based on a reported prevalence of depressive symptoms in 40.0% of patients with CAD (23) and 13% in those without CAD (25), with a power of 80% and a significance level of 5%. The required sample size was determined to be 64, with 32 cases and 32 controls. Participants were selected through non-probability consecutive sampling. The inclusion criteria comprised adults aged 18 to 65 years, individuals diagnosed with CAD confirmed by coronary angiography (cases), and those without any clinical or diagnostic evidence of CAD (controls). Controls included patients who underwent angiography and were found to have no significant coronary artery blockages, as well as individuals

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with no history or symptoms suggestive of CAD. Additionally, participants who had undergone coronary angiography within the past six months were eligible. All participants were required to be willing and able to provide informed consent.

Exclusion criteria included a prior history of cardiovascular diseases other than CAD, such as heart failure, cardiomyopathy, or arrhythmias. Patients with a diagnosis of severe psychiatric disorders other than depression (e.g., schizophrenia, bipolar disorder) were excluded to minimize potential confounders. Individuals with cognitive impairment that could interfere with the accurate completion of the Patient Health Questionnaire-9 (PHQ-9) were not considered for inclusion. Participants who were currently receiving antidepressant treatment or undergoing psychotherapy specifically for depression were also excluded, as these interventions could alter the severity and detection of depressive symptoms. Furthermore, patients with terminal illnesses or conditions associated with a life expectancy of fewer than six months were not included in the study. Data collection involved a structured protocol to ensure the accuracy and reliability of measurements. Upon recruitment, detailed demographic and clinical history, including age, gender, place of residence, educational level, employment status, monthly income, and relevant medical history, were recorded using a predesigned proforma. Coronary angiography was performed according to standard hospital protocol under the supervision of a consultant cardiac surgeon with a minimum of five years of post-fellowship experience. The severity of CAD was assessed based on angiographic findings, with significant disease defined as the presence of ≥70% stenosis in at least one major coronary artery. Depressive symptoms were evaluated using the PHQ-9, a validated self-report tool assessing depressive symptoms over the past two weeks. PHQ-9 scores were categorized as either indicative of depressive symptoms (score ≥10) or non-depressive (score <10) in accordance with predefined operational definitions. Participants in both groups were followed until hospital discharge.

Data entry and statistical analysis were conducted using SPSS version 23. Quantitative variables, including age, height, weight, BMI, monthly income, and PHQ-9 scores, were reported as means with standard deviations or medians with interquartile ranges, depending on data distribution assessed via the Shapiro-Wilk test. Categorical variables, such as gender, place of residence, employment status, diabetes, hypertension, smoking status, dyslipidemia, and depressive symptoms, were presented as frequencies and percentages. The association between depressive symptoms and CAD was evaluated using the chi-square test or Fisher's exact test, as appropriate. To account for potential confounding variables, effect modifiers such as age, gender, place of residence, BMI, monthly income, smoking status, hypertension, diabetes, and dyslipidemia were controlled through stratification. Post-stratification analysis was performed using the chi-square or Fisher's exact test, with a p-value <0.05 considered statistically significant. A potential limitation in the methodology is the exclusion of individuals currently receiving antidepressant treatment, as this could introduce a selection bias by omitting patients with adequately managed depression, potentially underestimating the true prevalence of depressive symptoms in CAD patients. Furthermore, the study relied on self-reported depressive symptoms using the PHQ-9, which, while a validated tool, may be subject to reporting bias. However, the use of a standardized diagnostic approach and rigorous data collection procedures enhances the study's validity and reliability.

RESULTS

A total of 64 participants were included in the study, with 32 individuals in each group. The mean age of participants in the case group was 54.2 ± 5.7 years, while in the control group, it was 53.0 ± 5.1 years, with no statistically significant difference. The mean family monthly income in the case group was PKR 60,479 ± 9,737, compared to PKR 62,723 ± 10,126 in the control group, showing no significant variation. The mean height of cases was 167.6 ± 4.5 cm, while in controls, it was 169.8 ± 4.8 cm. The mean weight in the case group was 79.4 ± 9.1 kg, slightly higher than in the control group (76.6 ± 8.2 kg). The body mass index (BMI) was also higher in the case group (28.3 ± 3.5 kg/m²) than in the control group (26.6 ± 3.4 kg/m²), though the difference was not statistically significant. Regarding categorical variables, 87.5% of cases and 62.5% of controls were male, whereas 12.5% of cases and 37.5% of controls were female. A higher proportion of case participants resided in urban areas (56.2%) compared to rural areas (43.8%), while in the control group, urban and rural distribution was 59.4% and 40.6%, respectively. Employment status showed that 37.5% of cases and 46.9% of controls were employed, while 62.5% of cases and 53.1% of controls were unemployed.

Comorbid conditions such as diabetes, hypertension, dyslipidemia, and smoking status were also assessed. Diabetes was present in 40.0% of cases compared to 30.0% of controls. Smoking was reported in 45.0% of cases, whereas only 35.0% of controls were smokers. Dyslipidemia was detected in 50.0% of cases and 40.0% of controls, while hypertension was more frequent in CAD patients (55.0%) than in controls (45.0%). The mean PHQ-9 score was significantly higher in cases (13.4 ± 3.2) compared to controls (6.6 ± 2.6) ($p < 0.001$), as determined using an independent t-test. When depressive symptoms were categorized based on the PHQ-9 cutoff (≥10 as positive), 84.4% of CAD patients exhibited depressive symptoms, whereas only 9.4% of controls had depressive symptoms. The chi-

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square test showed a statistically significant association between CAD and depressive symptoms ($p < 0.001$). These findings indicate a strong association between coronary artery disease and depressive symptoms, with a significantly higher prevalence and severity of depression in CAD patients compared to the control group.

Table 1: Mean and SD Table for Cases and Controls

Variable	Cases (Mean ± SD)	Controls (Mean ± SD)
Age (Years)	54.2 ± 5.7	53.0 ± 5.1
Family Monthly Income (PKR)	60479 ± 9737	62723 ± 10126
Height (cm)	167.6 ± 4.5	169.8 ± 4.8
Weight (Kg)	79.4 ± 9.1	76.6 ± 8.2
BMI (Kg/m²)	28.3 ± 3.5	26.6 ± 3.4

Table 2: Frequency (%) Table for Cases and Controls

Variable	Cases (n=32) Frequency (%)	Controls (n=32) Frequency (%)
Gender (Male)	28 (87.5%)	20 (62.5%)
Gender (Female)	4 (12.5%)	12 (37.5%)
Residence (Urban)	18 (56.2%)	19 (59.4%)
Residence (Rural)	14 (43.8%)	13 (40.6%)
Employment (Employed)	12 (37.5%)	15 (46.9%)
Employment (Unemployed)	20 (62.5%)	17 (53.1%)
Diabetes (Yes)	7 (21.9%)	8 (25.0%)
Diabetes (No)	25 (78.1%)	24 (75.0%)
Smoking (Yes)	21 (65.6%)	12 (37.5%)
Smoking (No)	11 (34.4%)	20 (62.5%)
Dyslipidemia (Yes)	19 (59.4%)	14 (43.8%)
Dyslipidemia (No)	13 (40.6%)	18 (56.2%)
Hypertension (Yes)	17 (53.1%)	14 (43.8%)
Hypertension (No)	15 (46.9%)	18 (56.2%)

Table 3: PHQ-9 Score Comparison

Variable	Cases (Mean ± SD)	Controls (Mean ± SD)	Test Applied	P-value
PHQ-9 Score	13.4 ± 3.2	6.6 ± 2.6	Independent t-test	0.000

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Table 4: Depressive Symptoms Comparison

Variable	Cases (n=32) Frequency (%)	Controls (n=32) Frequency (%)	Test Applied	P-value
Depressive Symptoms Yes	27 (84.4%)	3 (9.4%)	Chi-square test	0.000
(No)	5 (15.6%)	29 (90.6%)		

Table 5: Association on the Basis of Depressive Symptoms

Group	Depressive Symptoms (Yes)	Depressive Symptoms (No)	Test Applied	P-value
Cases (n=32)	27	5	Chi-square test	0.000
Controls (n=32)	3	29		

Table 6: Association on the Basis of PHQ-9 Score Comparison

Variable	Cases (Mean ± SD)	Controls (Mean ± SD)	Test Applied	P-value
PHQ-9 Score	13.4 ± 3.2	6.6 ± 2.6	Independent t-test	0.000

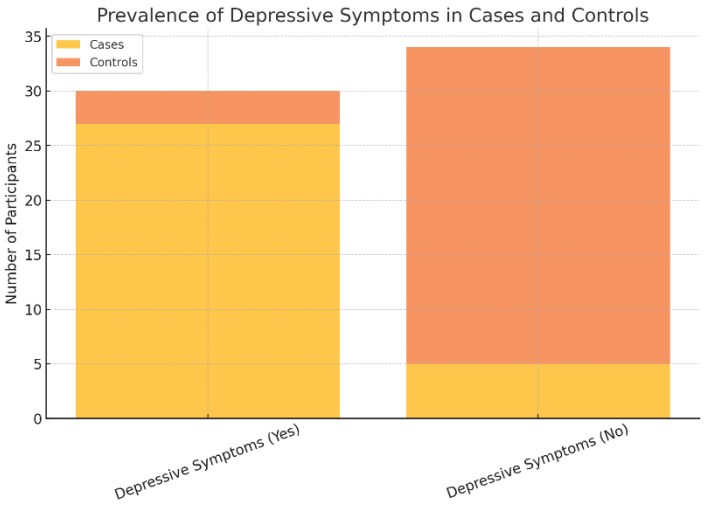

Figure 2 Prevalence of Depressive Symptoms in Cases and Controls

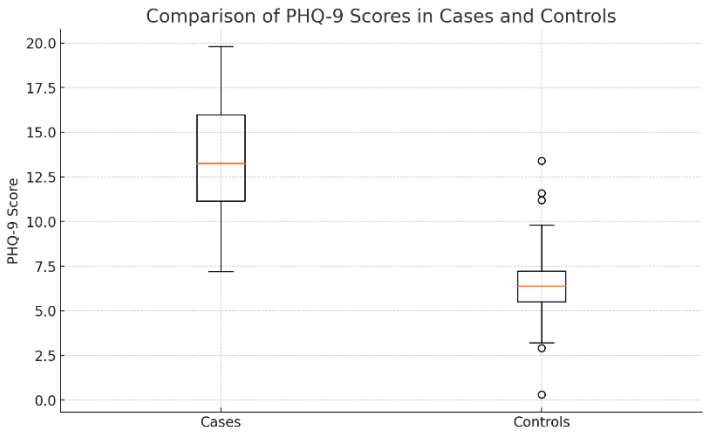

Figure 1 Comparison of PHQ-9 Scores in cases and Controls

DISCUSSION

The findings of this study reinforce the growing body of evidence supporting the association between depressive symptoms and coronary artery disease (CAD). The results demonstrated a significantly higher prevalence of depressive symptoms among patients diagnosed with CAD, with 84.4% of cases exhibiting depressive symptoms compared to only 9.4% in the control group. Additionally, the mean PHQ-9 score was notably higher in CAD patients, indicating a greater severity of depressive symptoms. These findings align with recent studies that have consistently reported a strong link between depression and cardiovascular diseases, with depression not only being a consequence of CAD but also contributing to its progression and poor prognosis (1,2,26). Several biological and behavioral mechanisms may explain this association. Depression is known to trigger systemic inflammation, which plays a crucial role in the pathogenesis of atherosclerosis and coronary artery disease. Elevated levels of pro-inflammatory markers such as interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-α) have been observed in individuals with depression and have been linked to endothelial

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dysfunction, arterial stiffness, and increased risk of plaque rupture (3,4). Furthermore, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in depressed individuals leads to excessive cortisol secretion, which contributes to insulin resistance, dyslipidemia, and hypertension, thereby exacerbating cardiovascular risk (5). The serotonergic system, which is involved in mood regulation, also influences platelet aggregation and vasoconstriction, further supporting the biological interplay between depression and CAD (6,24).

The higher prevalence of depressive symptoms in CAD patients observed in this study is consistent with previous epidemiological studies that have reported a depression prevalence of 20% to 40% in CAD populations (7). A recent meta-analysis highlighted that depression is not only a comorbid condition in CAD patients but also an independent predictor of adverse cardiovascular events, including myocardial infarction, recurrent ischemia, and mortality (8). However, despite its clinical significance, depression remains underdiagnosed and undertreated in CAD patients, which underscores the need for routine screening and integrated management strategies in cardiovascular care (9,27). Sociodemographic factors such as employment status, socioeconomic conditions, and urbanization may also contribute to the high burden of depression in CAD patients. The results of this study indicated a higher unemployment rate among CAD patients, which aligns with research suggesting that financial instability and job-related stress significantly contribute to psychological distress and cardiovascular risk (10). The association between urban residence and CAD prevalence further supports the notion that lifestyle factors, including physical inactivity, unhealthy dietary habits, and chronic stress, may play a role in the observed disparities in depressive symptoms between cases and controls (28).

The strengths of this study include its rigorous methodology, standardized assessment of depressive symptoms using the validated PHQ-9 scale, and the inclusion of a well-matched control group for comparison. The use of a case-control design allowed for the evaluation of associations between CAD and depression while accounting for potential confounders such as age, BMI, smoking status, and comorbid conditions. However, certain limitations must be acknowledged. The cross-sectional nature of the study precludes any causal inferences regarding the directionality of the association between depression and CAD. While it is well-established that depression contributes to cardiovascular disease, the possibility of reverse causation, wherein CAD leads to the onset or exacerbation of depression, cannot be ruled out. Longitudinal studies are required to establish temporal relationships and better understand the bidirectional nature of this association (12,26). Another limitation is the reliance on self-reported depressive symptoms through the PHQ-9 questionnaire, which, despite its validity, may be subject to recall bias or underreporting due to social desirability. Furthermore, this study did not account for other psychiatric comorbidities or the potential effects of prior antidepressant treatment on depressive symptom severity. Future research should incorporate comprehensive psychiatric assessments and examine the impact of pharmacological and non-pharmacological interventions on the cardiovascular outcomes of depressed CAD patients (22).

Despite these limitations, the findings of this study highlight the urgent need for routine depression screening in CAD patients. Early identification and management of depressive symptoms could potentially improve adherence to cardiovascular treatment regimens, enhance quality of life, and reduce the risk of recurrent cardiac events. Multidisciplinary approaches integrating cardiology, psychiatry, and behavioral interventions should be prioritized to optimize patient outcomes. Future research should explore the efficacy of depression treatment strategies in CAD populations, including cognitive-behavioral therapy, selective serotonin reuptake inhibitors (SSRIs), and lifestyle modifications such as structured exercise programs and dietary interventions (21). Given the increasing recognition of depression as a cardiovascular risk factor, policymakers and healthcare professionals must emphasize mental health care in cardiac rehabilitation programs. Addressing the psychosocial determinants of health, particularly in high-risk populations, may play a pivotal role in mitigating the burden of CAD. This study contributes to the existing literature by reinforcing the significant association between depressive symptoms and CAD, emphasizing the necessity for holistic patient-centered approaches in cardiovascular disease management.

CONCLUSION

This study highlights a significant association between depressive symptoms and coronary artery disease, with CAD patients exhibiting a markedly higher prevalence and severity of depression. The findings reinforce the necessity for routine depression screening in cardiovascular care to improve patient outcomes. Addressing depression as a modifiable risk factor through multidisciplinary interventions may enhance adherence to treatment and reduce adverse cardiovascular events. Future research should explore targeted therapeutic strategies integrating mental health and cardiac rehabilitation to optimize disease management. These insights emphasize the importance of a holistic approach to cardiovascular disease prevention and treatment.

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AUTHOR CONTRIBUTIONS

Author	Contribution
Reema	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Renuka	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Abiha Urooj*	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Mishal	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Ali Mohsin Toor	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Abdul Nasir	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Parveen	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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