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Prevalence of depression in patients with cardiovascular diseases

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Prevalence of Depression in Patients with Cardiovascular Diseases

By

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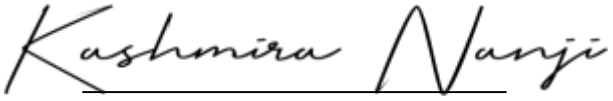

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Dedication

I dedicate this dissertation to my parents, whose priceless lesson on the lasting worth of education has had a profound impact on me. I want to dedicate this thesis to my loving nephew, Muhammad Hadeed, who is a continual source of inspiration for me.

Also, I'd like to recognize the important role that my dearest friend, Nabila Anwar, has played in defining the road that has led to this academic endeavor. Moreover, I would like to dedicate my thesis to my friend Ruqia, who was consistently by my side, offering unwavering love and support.

Abstract

Background

Approximately 17.3 million individuals across the globe lose their lives to cardiovascular diseases (CVD), with a majority of these cases occurring in low-to-middle-income countries. The incidence of cardiovascular disease in Pakistan is 918 cases per 100,000 individuals. Depression frequently impacts the health, expenses, and prognosis of patients with cardiovascular disease.

Purpose

This study aimed to determine the prevalence of depression among CVD patients at Aga Khan University Hospital, Karachi, and explore the influence of co-morbidities, marital status, age, and educational background on one's status, regarding depression.

Method

A quantitative descriptive cross-sectional study was conducted at the Aga Khan University Hospital, involving CVD patients admitted to the cardiology unit and those attending cardiac clinics.

Findings

The study included 234 participants, with a notable representation of individuals aged 60 to 70 years (34.2%), predominantly males (67.5%), and from the Sindh region (84.2%). Educational diversity was observed, with 29.9% holding graduate degrees and 17.5% holding master's degrees. Depression prevalence was 28 percent and was significantly higher among single participants. Moreover, the prevalence of depression showed a significant difference based on gender, with a higher prevalence among females ($p=0.025$). No significant differences were found regarding cardiovascular disease type, comorbid conditions, or residence location ($p>0.05$). However, a significance was observed in education level ($p=0.002$), indicating that primary education was a risk factor (OR=4.283, 95% CI: 1.434-12.798). Additionally, age showed varying

associations, with individuals below 40 years of age having higher odds of depression (OR: 1.179, CI: 0.351-3.955, p:0.022).

Conclusion

The study explores depression among patients with cardiovascular disease in Karachi, Pakistan, emphasizing the need for tailored interventions for high-risk groups like singles and those with lower education levels. It underscores the importance of managing depression to improve patient well-being and clinical outcomes, thereby enhancing the understanding of the complex relationship between cardiovascular diseases and depression.

List of Abbreviation / Acronyms

ACS	Acute Coronary Syndrome
ADL	The activity of daily living
AHA	American Heart Association
AKU	Aga Khan University
AKUADS	Aga Khan University Anxiety and Depression Scale
CAD	Coronary Artery Diseases
CBT	Cognitive Behavioral Therapy
CHD	Congenital Heart Disease
CHF	Congenital Heart Failure
CI	Confidence Interval
CRP	C-Reactive Protein
CVD	Cardiovascular Diseases
DM	Diabetes Mellitus
FMD	Flow Mediated Dilation
HTN	Hypertension
LIC	Low-Income countries
LMIC	Low and Middle income countries
MACE	Major Adverse Cardiac Events
MR	Medical Record
NICVD	National Institute of Cardiovascular Diseases
NSTEMI	Non-ST elevation Myocardial Infarction
OPD	Outpatient Department
PAD	Peripheral Artery Disease
PCI	Percutaneous Cardiac Intervention

ROS	Reactive Oxygen Specie
SAD	Social Anxiety Disorder
SPSS	Statistical Package for the Social Sciences
SSRI	Selective Serotonin Reuptake Inhibitor
STEMI	ST Elevation Myocardial Infarction
VHD	Valvular Heart Diseases
WHO	World Health Organization

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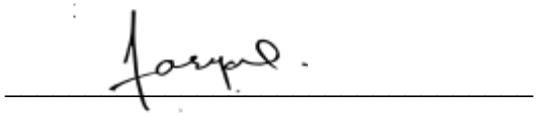
Declaration

I declare that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university and to the best of my knowledge it does not contain any material previously published or written by another person, except where due reference has been made in the text.

The editorial assistance provided to me has in no way added to the substance of my thesis which is the product of my research endeavours.



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Chapter One: Introduction

This chapter aims to discuss the background, burden of the issue and the pathophysiological association between depression and cardiovascular diseases. It also discusses the rationale, and the objective of the study, followed by research questions, and concludes with a chapter summary.

Background

Cardiovascular diseases include disorders of the heart and blood vessels, such as coronary artery disease, peripheral artery disease, heart failure, etc., which contribute to 17.3 million deaths per year globally (Vasileiou et al. (2022). It is the leading cause of death in low-to-middle-income countries (Barolia, 2017). In recent years, many research studies have been conducted that describe the bidirectional relationship between cardiovascular diseases and depression (Vasileiou et al., 2022). For instance, mental health issues, such as anxiety, depression, and stress, enhance the vulnerability of people to cardiovascular diseases (Khandaker et al., 2020).

Depression is one of the independent psychosomatic factors that leads to cardiovascular disorders (Nisar et al., 2019). Annually 3-9% of the general population is affected by major depression, which is a common mental health issue in primary care. Subsequently, patients who have coronary heart disease (CHD) are even more likely to experience major depression, with 12-month incidence rates varying between 10 and 20% (van Dijk et al., 2021). Particularly, the American Heart Association (AHA) has advised screening for depression in cardiac (Hasnain et al., 2011). Moreover, depression and anxiety have been recognized as intimidating and negatively affects prognosis in cardiac patients (AHA,2008).

A study conducted by Zheng et al. (2019) reported a relationship between somatic symptoms and, anxiety and depression in cardiac patients in the Chinese population. Somatic symptoms are physical symptoms such as chest pain, dizziness, fatigue, and abdominal discomfort that are caused by anxiety and depression and create discomfort, but they cannot be explained by the pathological disease process. Researcher highlighted that patient with lower

socio-economic status (lower education and employment) had the worst somatic symptoms. Further, he added that 30% of the patients with depression experience somatic symptoms but due to a lack of laboratory-assisted diagnostics, very few cardiologists identify the underlying cause of the issue.

In the context of Pakistan, people mostly neglect the biomedical aspect of depression and consider it as a normal response to stress-inducing scenarios (Nisar et al., 2019). Also, they state that Pakistan has the lowest psychiatrist-to-person ratio in the world. Pakistan has a concerning proportion of heart diseases. It is reported that 152 persons per one hundred thousand die due to cardiovascular diseases in Pakistan.

Cardiovascular diseases contribute 22.7% to the proportion of total deaths in Pakistan (Zhao, 2021). Most importantly, depression in patients with cardiovascular disease (CVD) mostly remains undiagnosed. The health care providers show little concern about the psychological aspects of cardiac patients in Pakistan. In addition, according to WHO's Mental Health, there are only four major psychiatric hospitals in Pakistan, along with 344 residential care facilities, and 654 psychiatric units in general hospitals. There are 2.1/10,000 beds for people in mental health facilities. And there are only 400 qualified psychiatrists at work (Javed et al., 2020). In terms of nurses, just three percent of a nurse's training programme in Pakistan is devoted to mental health education. In addition, only 5 percent of nurses have taken part in refresher courses that are at least 2 days long and that are devoted to mental health (WHO, 2018). Therefore, it is significant to conduct this study to assess the prevalence of depression in patients with cardiac diseases, and to see how the relationship between several factors, like marital status, education level, and socioeconomic status, affects patients with cardiac diseases, regarding developing depression.

Burden of Issue

One episode of depression enhances the risk of myocardial infarction fourfold (Piwoński et al., 2019). Additionally, the prevalence of depression in patients with cardiovascular diseases increases in old age. Uphoff et al. (2019) report that the prevalence of mental health issues in

South Asian countries, like India, Pakistan, and Bangladesh is less researched, and data and statistics results are taken from Western countries. In a meta-analysis of 83 studies from the South Asian region, the authors concluded that the prevalence of anxiety is 3 to 58% in patients with stroke, coronary artery disease, myocardial infarction, and unspecified heart diseases.

Khan et al. (2016) conducted a study at the Faisalabad Institute of Cardiology, in Pakistan, and reported that one in every five patients with coronary artery disease and heart failure was depressed. This situation is alarming, as the ratio is three times higher than the ratio in the general population. The authors further added that depression in patients with CVD not only enhances the socio-economic burden on the patients, families, and the health care system, but also most of the time, the mental and emotional aspect of patients in the cardiovascular departments remains neglected.

Another study conducted by Mujtaba et al. (2020) at the Larkana Satellite Center, National Institute of Cardiovascular Diseases (NICVD) reported that patients found it difficult to report about depression because the psychological aspects of diseases are not usually asked. Moreover, the questions regarding mental health issues are associated with taboos in society. To complain about being depressed or wanting to cry is forbidden, specifically in the rural culture of Pakistan. Nevertheless, Nisar et al. (2019) conducted a study using non-probability sampling to evaluate the attitudes of Karachi residents regarding depression. The findings revealed that the majority of participants did not view depression as a medical disease, but rather as a normal experience of feeling sad. Moreover, confounding variables such as smoking, physical inactivity, hypertension, obesity, and the severity of heart disease in patients with pre-existing cardiovascular disease also contribute independently to the development of depression. Furthermore, a study revealed that, even after accounting for confounding variables, the previously observed association between depression and cardiovascular outcomes did not persist (De Hert et al., 2022).

Pathophysiological Association between Depression and Cardiovascular Disorders

Exposure to acute and long-term stress can lead to changes in neurochemical processes, specifically in the synthesis or activity of norepinephrine, dopamine, or serotonin. These changes have the potential to impact both mood and cardiovascular risk (Vaccarino et al., 2020). Norepinephrine sensitivity increases when sympathetic nerve terminals discharge too many catecholamines into the systemic circulation. Dysregulation of stress-response pathways may also contribute to CVD in vulnerable individuals due to the pathophysiological relationship between stress and depression. Sympatho medullary and hypothalamus pituitary adrenal pathways are stress response pathways. The hypothalamus controls stress response modulates these pathways and alerts the pituitary gland and adrenal medulla for fight or flight. Depression has been linked to increased levels of inflammatory molecules, such as C-reactive protein and cytokines like TNF-, IL-1, and IL-6. These molecules have the potential to harm the heart and circulation. Oxidative stress is a condition characterized by an imbalance in reactive oxygen species (ROS) within cells and tissues, coupled with the failure of the antioxidant defense system to effectively eliminate them. This imbalance plays a significant role in the development, progression, and outcomes of atherosclerosis. Depression has been found to have a significant impact on platelet activation and thrombosis, which is another pathophysiological connection to coronary heart disease (CHD). The stress response system neurotransmitters, catecholamines, activate platelets through the stimulation of alpha and beta 2 adrenergic receptors. Depression has been found to elevate platelet activity and PAI-1, which is an anti-fibrinolytic factor (Vaccarino et al., 2020).

Rationale for Conducting this Study

Psychological illnesses are stigmatized more than physical health issues due to labelling, stereotyping, status loss, and discrimination. Depression is viewed differently by different cultures. Many believe psychiatric assistance is for “crazy people”. They also link mental illness to incompetence. Negative attitude due to social skills deficit, abnormal physical appearance with psychiatric symptoms, and categorization as mentally disturbed. Discussing emotionally traumatic

situations shames people, and stigma is the main reason they refuse psychological help (Husain & Waqar, 2020).

Depression is one of the major risk factors that deteriorates the cardiac condition of patients with CVD, and it has been linked to higher healthcare costs, disability, lower quality of life, and increased mortality (Khawaja et al., 2009). Patients with HF frequently suffer from psychiatric disorders, and previous studies reveal that these disorders further hurt patients' cardiovascular systems. Hence, depression plays a role in the onset and development of cardiovascular diseases (Celano et al., 2018). But a few studies have been conducted in Pakistan to assess the prevalence of depression in patients with cardiovascular diseases. This study was conducted in one of the tertiary health care settings the Aga Khan University Hospital, Karachi with the aim to assess the burden of the psychological issue-depression- in patients with cardio-vascular diseases. Thus, health care workers could consider attention to the psychological aspects of cardiac diseases and adopt strategies that can be fruitful for patients, to improve their quality of life.

Objective of the Study

The study aimed to determine the prevalence of depression among patients with cardiovascular disorders who came to the Aga Khan University Hospital, Karachi, a tertiary care hospital.

The study's findings can provide valuable insights for healthcare professionals to comprehend the intensity of the issue. An appropriate next phase of this study would involve identifying alternative approaches that may be implemented to enhance the mental well-being and overall quality of life of individuals suffering from cardiovascular diseases. While depression has been thoroughly studied, individuals with cardiac conditions have received comparatively less emphasis in Pakistan (Dogar et al., 2008).

Research Questions

1. What is the prevalence of depression in patients with cardiovascular diseases?

2. What is the effect of gender, age, marital status, and education status on the depression status of patients living with cardiovascular diseases?

Hypothesis

Null hypothesis. There is no link between cardiovascular diseases and depression in patients with CVD.

Alternative hypothesis. The development of depression is higher in patients with CVD than in the general population.

Summary of the Chapter

It is of interest to investigate the prevalence of depression in patients with CVD. However, there are complex and multiple factors that lead to the development of depression in patients with cardiac diseases that could be controlled to enhance their quality of life in them (Dhar & Barton, 2016). Hence, there is a need to find out the prevalence of depression in patients with cardiovascular diseases and to analyse the relationship between cardiovascular diseases and depression to improve the quality of life in patients.

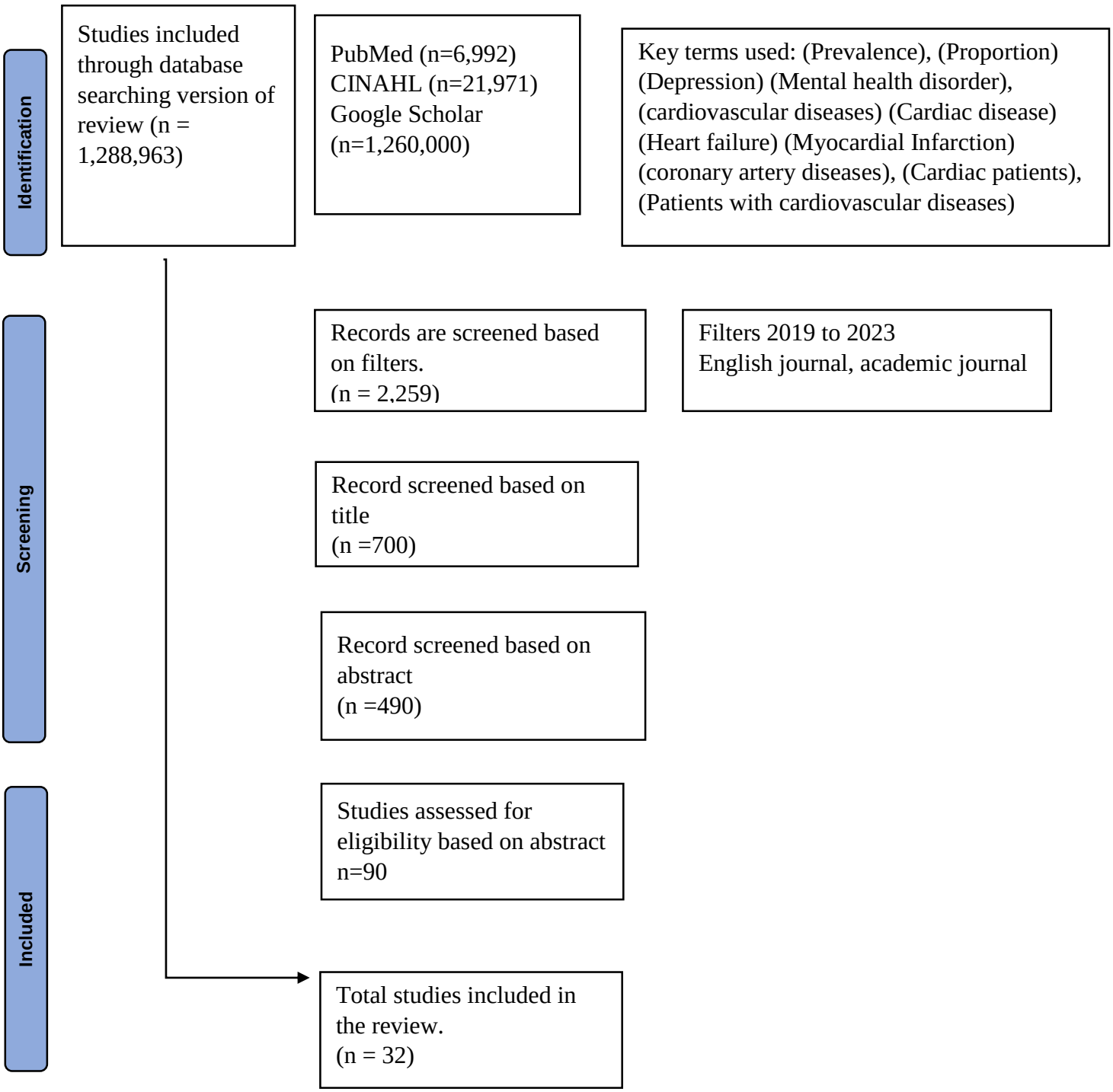
Chapter Two: Literature Review

This literature review aims to examine the relationship between cardiovascular disease (CVD) and depression. It presents the empirical literature that supports the current study. It is concluded with a brief gap analysis and summary.

Search Strategy

An extensive search was undertaken, and various databases, such as Google Scholar, CINAHL, and PubMed, were used. Key terms such as "prevalence," "depression," "cardiac patients," and "patients with cardiovascular diseases" were used to identify relevant research articles. A total of 32 articles out of 1,288,963 were selected based on their relevance to the topic and the quality of the research. Boolean operators (OR, AND) were used in the search strategy. Moreover, filters of the last 5 years 2019 to 2023, English language, and an academic journal were used.

Figure 1. *PRISMA Flow Diagram*



Globally, the most significant cause of death is cardiovascular disease, which includes peripheral artery disease, heart failure, coronary artery disease, and other disorders of the heart and blood vessels (Feng et al., 2019). Patients with CVD are reported to have a depression prevalence of 28.70% but the depression rates vary depending on country of origin, tools used to measure, study quality, sex, and race (Feng et al., 2019). Depression is a common mental disorder caused by social, psychological, and biological factors that cause chronic sadness, a loss of interest in previously enjoyable activities, and poor sleep and food, according to (WHO., 2023). A pooled analysis of two prospective studies found that baseline depressed symptoms are a risk factor for CVD (Harshfield et al., 2020). Likewise, according to Chichetto et al. (2021), depression is identified as a risk factor for cardiovascular disease. A lifetime prevalence of major depression among those undergoing severe cardiac events (comprising death, myocardial infarction, coronary revascularization, stroke, and hospitalization due to heart failure) is estimated to be around 40% (Choi et al., 2019; Piwoński et al., 2021). Moreover, anxiety, characterized by excessive fear and worry and related behavioural disturbances (WHO, 2023), is a common mental disorder linked to stroke, coronary artery diseases, myocardial infarction, and other heart diseases, with a prevalence of 3 to 58% in South Asian countries like Bangladesh, India, and Pakistan (E. P. Uphoff et al., 2019).

It was reported in the literature that atrial fibrillation doubles mortality risk in women and men. Depression preceding catheter ablation for Atrial fibrillation independently increases the incidence of recurrent Atrial fibrillation (Zhuo et al., 2020). Another study found that depression patients with percutaneous coronary intervention had 1.8 to 2.1 times higher rates of major adverse cardiac events (MACE) and all-cause mortality. Thus, pre-procedure depression is an independent risk factor for poor CVD clinical outcomes (Song et al., 2020).

Likewise, depressed patients have 57% more risk of poor clinical outcomes and a higher risk of death after PCI than non-depressed patients (W. Y. Zhang et al., 2019). However, Islam et al. (2019) report that depression in patients with coronary heart disease (CHD) mostly remains under-recognized and untreated; because, most of the time the mental and emotional aspects of

patients in cardiovascular departments remain neglected due to ignorance about the psychological aspects of health. However, patients with depression need effective treatment for both conditions (Khandaker et al., 2020a).

A significant body of literature has demonstrated a connection between heart failure and the presence of depression (Muhammad I. Husain et al., 2019; Liguori et al., 2018). Depression has been documented to affect 30% of patients with heart failure (Sbolli et al., 2020). Moreover, heart failure has a high mortality rate and 5% of the patients die within 5 years of diagnosis (Celano et al., 2018). Further, according to Ghaffari et al. (2019), patients with heart failure who also suffer from depression have a high death rate, and patients with anxiety and generalized anxiety disorder are more likely to experience severe morbidity. They discovered that 54% of patients experienced depression and 50% of patients experienced anxiety.

In a study on heart failure patients, Chialà et al. (2018), discovered that 48% of the patients exhibited severe cognitive impairment, high anxiety, and sadness. Furthermore, depression, along with potentially associated poor self-care, raises the risk of developing heart failure by 18% over the next seven years. In this regard, Y. Zhang et al. (2019), affirm that co-morbid depression has a detrimental effect on quality of life, finding that patients with chronic heart failure had a 21.5% prevalence of depression.

Quality of life is an individual's assessment of their position in life with respect to their dreams, plans, metrics, and reservations, in addition to the cultural and social context in which they reside (WHO, 2012). Multiple factors, according to Azim et al. (2021), contribute to the onset of anxiety and depression in patients. In the context of developing nations such as Pakistan, affordability and accessibility of healthcare facilities are two such factors. Husain et al. (2021) found that there are multiple factors that are responsible for developing depression in women, some of them include hardships in life, financial difficulties, emotional and physical abuse, and lack of social support.

It is also acknowledged that in developing countries like Pakistan screening for anxiety and depression is difficult due to lack of healthcare facilities, and the psychological aspects of diseases are not given much attention (Ghaffari et al., 2021). A recent study reported depression at 10.5% and anxiety at 7.5% in the admitted patients with CVD, in the National Institute of Cardiovascular Diseases, Larkana (NICVD) (Ghaffari et al., 2021; Mujtaba et al., 2020).

In order to address the issue of psychological well-being of patients suffering from cardiovascular diseases, numerous approaches have been evaluated. First, mental health and anxiety, depression, and cognitive impairment are all improved by exercise capacity; thus, exercise capacity influence's cognitive function and depression, anxiety, and depression (Chialà et al., 2018). Because depression has a negative impact on the autonomic and central nervous system, physical activities affect the nervous system and hormonal balance and thus help to reduce depression (Shaphe & Chahal, 2020).

During physical activity the muscles secrete myokines, which regulate the function of the hippocampus, and promote neurogenesis and memory formation (Pedersen, 2019). Kandola et al. (2019) report that high physical activity reduces the depression risk by 17%. Abdelbasset and Alqahtani (2019), evaluated the efficacy of aerobic exercises of moderate intensity on depression in middle-aged individuals who had heart failure through a clinical trial. After a duration of 12 weeks, a greater proportion of depressive symptoms were reduced.

A randomized control experiment demonstrated that cognitive behaviour therapy (CBT), a psychologically structured counselling therapy to modify negative behaviours, reduced depressive symptoms in heart failure patients (Freedland et al., 2022). Another study used four weekly text messages to educate and motivate nutrition, exercise, and cardiac education for six months. Compared to the control group, the intervention group had reduced depression scores (Islam et al., 2019).

Escitalopram, a selective serotonin reuptake inhibitor, effectively reduces anxiety in patients with coronary artery diseases. Exercise, compared to a placebo, is more beneficial. A

study found that exercise and escitalopram groups showed greater reductions in depression compared to patients who were taking placebo (Blumenthal et al., 2021). The results of the study by Kim et al. (2021), found escitalopram's benefits and supported the previous research. In a follow-up study over 8.4 years, escitalopram-treated individuals experienced fewer significant adverse cardiac events, including mortality, than placebo-treated patients. In escitalopram, placebo, and who are just treated for their disease, not for psychological aspects, 40.9%, 53.6%, and 59.6% respectively had MACE.

Further, virtual therapy to reduce anxiety and depression is effective in reducing social anxiety disorder and depression (Jóźwik et al., 2021). The virtual therapy used the virtual therapeutic garden, where patients were able to relax while coloring therapeutic mandalas. The results revealed a reduction in social anxiety disorder (SAD) and depression as compared to the control group. However, a study reveals that despite massive screening, and results of the screening conveyed to patients, there was no noticeable inclination of patients towards seeking help from psychotherapists and getting treatment for anxiety and depression (Kruse et al., 2022).

Risk Factors for Depression in Patients with Cardiovascular Diseases

Depression is linked to heart failure in patients with cardiovascular disorders due to chronic inflammation. Research indicates a connection between depression and higher levels of inflammatory markers, such as C-reactive protein and IL-6. Depression can cause behavioural and physiological changes that heighten the risk of heart failure. For example, depression can lead to reduced physical activity, increased obesity, and other cardiovascular risk factors. It can also affect the autonomic nervous system, leading to elevated heart rate and blood pressure, potentially causing arrhythmias and other cardiac problems. Additionally, depression is linked to elevated stress hormones, which can adversely affect the heart, contributing to hypertension, atherosclerosis, and other cardiovascular diseases.

Triglycerides are a form of fat present in the bloodstream that can build up in artery walls, resulting in atherosclerosis and potentially contributing to depression. C-reactive protein (CRP) is

a biomarker that indicates inflammation. It is synthesized by the liver as a response to infection or injury. Interleukin-6 (IL-6) is a crucial cytokine involved in the immune response. The development of depression may be influenced by various risk factors, which can impact inflammation and the immune system. However, the precise mechanisms underlying these connections are intricate and still not completely comprehended (Khandaker et al., 2020b). Secondly, age over 65 years old, being single, living alone, being widowed and having sedentary lifestyles were also found to be at higher risk of experiencing depression (Khan et al., 2021). Social support is crucial in the development of depression among cardiac patients. Individuals with limited social support are more susceptible to experiencing depression. Gender disparities play a significant role in the development of cardiovascular disease (CVD) and depression. There is a higher prevalence of depression among women compared to men. There is no difference in the occurrence of depressive disorders between males and females in childhood and early puberty. However, rates of depression in women rise during mid-puberty and later stages of life. Depression in women increases the risk of developing cardiovascular diseases, including heart failure and stroke (Bucciarelli et al., 2020). Financial status and educational status of patients also affects the psychological makeup of patients. Moreover, patients with higher levels of thyroid hormone are also at risk of developing depression.

Vitinius et al. (2019) found out that patients with CAD taking thyroid hormone substitute medicine are more inclined to depression. Hence, both hypo and hyperthyroidism in CAD increased the risk of depression in patients. The balance of specific brain chemicals, like serotonin and dopamine, which are involved in mood regulation, disturbed by low thyroid hormone level. The physical effects of hypothyroidism, such as weakness, weight gain, and low energy, may also play a role in the emergence of depression (Airaksinen et al., 2021). Additionally, stress related to hypothyroidism may be experienced by those who have it, and this stress may lead to depression (Nuguru et al., 2022).

Pathophysiology of Depression in Patients with CVD

Depression causes platelet hyper-reactivity, coagulation, endothelial dysfunction, inflammatory activation, and autonomic and neuro-endocrine dysregulation which consequently leads to the risk of cardiovascular diseases and negatively impacts the outcome (Vitinius et al., 2019). In a study by Borkowska et al. (2020), the authors investigated the relationship between inflammation and depression in patients with acute coronary syndrome. They measured levels of inflammatory markers, such as interleukin-6 (IL-6) and C-reactive protein (CRP) and found that patients with depression had significantly higher levels of these markers compared to those without depression. The authors suggest that inflammation may be a key factor in the development of depression in patients with cardiovascular disease. Moreover, in a systematic review and meta-analysis, Gao et al. (2021) investigated the relationship between autonomic dysfunction and depression in patients with heart failure. They found that patients with depression had significantly lower heart rate, which is a marker of autonomic dysfunction, compared to those without depression. The authors suggest that dysregulation of the autonomic nervous system may be a key mechanism linking depression and cardiovascular disease.

Furthermore, in a study by Giannitsi et al. (2019), the authors investigated the relationship between endothelial dysfunction and depression in patients with heart failure. They measured endothelial function using flow-mediated dilation (FMD) and found that patients with depression had significantly lower FMD. The authors suggest that endothelial dysfunction may be a key mechanism linking depression and cardiovascular disease.

Gap Analysis

Mental health is an important component for maintaining quality of life. Unfortunately, this important aspect of life remains neglected. In a thorough review of literature, it is evident that patients with CVD suffer from mental health issues that ultimately negatively affect their quality of life. However, the healthcare settings usually focus on the therapeutic management of the cardiovascular issue in patients and neglect their mental health needs.

There is a lack of Pakistani research exploring the relationship between depression and cardiovascular disease. There is a lack of studies that address the need for increased awareness of depression screening in patients with cardiovascular disease, culturally appropriate interventions to manage depression, and understanding the multiple risk factors for depression in these patients.

Summary of the Chapter

Multiple research projects have shown that patients with cardiovascular diseases (CVD) are at a high risk of developing depression. There is a bidirectional link between cardiovascular diseases and depression. Moreover, the presence of depression negatively affects the clinical outcomes and enhances the mortality rate in patients with cardiovascular diseases.

There are multiple risk factors that make patients with cardiovascular diseases more prone to developing depression. There are also multiple strategies that can effectively reduce depression in patients and positively influence the clinical outcome. But mental health remains neglected in healthcare settings, and there is a lack of awareness and understanding about the presence of depression in patients with CVD. Moreover, there is limited research on the prevalence of depression in patients with CVD in Pakistan and a lack of culturally appropriate interventions to manage depression in these patients. Therefore, there is a need for more research and attention to mental health in patients with CVD, to improve their quality of life and outcomes.

Chapter Three: Methodology

This chapter provides a comprehensive description of the methodology. It provides details about the study's design, location, participants, length of time, and number of participants. Additionally, the chapter describes the methods utilized to collect the data, the tools employed, and the analysis techniques employed. It ensures that ethical issues are addressed and ends with concluding remarks.

Study Design

This study aimed to assess the prevalence of depression in patients with cardiovascular diseases. The quantitative descriptive cross-sectional study design was used to conduct this study. Cross-sectional studies are observational studies that analyse data from a population at a specific moment in time, typically cost-effective and straightforward. They capture a collective of individuals without follow-up, and the researcher collects data to assess the connections between exposures and outcomes (Wang & Cheng, 2020).

Cross-sectional studies in clinical research focus on determining disease prevalence by analysing the percentage of individuals with a specific disease or characteristic at a specific point in time. There is a distinction made between incidence, which refers to the quantity of new cases, and prevalence. Researchers assess the occurrence of a disease or its association with a specific outcome, along with the distribution of variables within a community. They assist in generating initial data for future comprehensive studies (Setia, 2016).

Study Setting

This research was carried out at Karachi's renowned Aga Khan University Hospital (AKUHK), which is a tertiary care hospital founded in 1985. It is dedicated to providing top-notch, high-quality healthcare services and has earned accreditation from prestigious organizations like the Joint Commission International and the College of American Pathologists. Both the 16 bedded cardiology department of AKUH and the outpatient cardiac clinics provided data for this investigation.

Study Population

The study population was patients with cardiovascular diseases admitted to the cardiology unit of the AKUH, and patients who came to the outpatient cardiac clinics for follow-up.

Study Duration

The study was conducted from March to August 2023.

Eligibility Criteria

The following criteria are used to include and exclude the patients in the study.

Inclusion criteria.

- Male and female patients aged 18 years and above.
- Patients were admitted to the cardiology unit at the hospital.
- Patients visiting the cardiology outpatient department (OPD) at the hospital.
- Diagnosis includes coronary artery diseases (CAD), ST Elevation Myocardial Infarction (STEMI), Non-ST Elevation Myocardial Infarction (NSTEMI), Heart Failure (HF), Cardiac Arrhythmias, Valvular heart disease (VHD), Acute Coronary Syndrome (ACS), Atherosclerosis, Congenital Heart Disease (CHD), and Peripheral Artery Diseases (PAD).

Exclusion criteria.

- Patients with end-stage kidney diseases, liver cirrhosis, and organ failure.
- Patients with cognitive impairment.
- Patients with a history of drug abuse and alcohol abuse.
- Patients with unstable hemodynamic status.

Sample Size

To calculate the sample size, the study conducted at the Faisalabad Institute of Cardiology was used for reference values. The study's notable finding was that people with CVD had a depression level of 79.5%. This statistic contrasted with the depression level of 68.25% seen in

the group who were not exposed (Khan et al., 2016). These percentages were considered vital research referral levels because they suggested a possible link between CVD and depression. The software Open Epi Version 3 was used to calculate the sample size. The sample size included 237 study participants, at a 95 percent level of confidence and 80% power.

Sampling Strategy

Participants were chosen using the Non-Probability Purposive Sampling approach. This sampling strategy is employed in clinical research to recruit patients who match the inclusion criteria. This strategy takes into account the participants' convenience This method is less expensive and does not necessitate a list of every member of the population (Etikan, 2016).

Study Variables

This study had one dependent and one independent variable.

Dependent variable

Depression was the dependent variable in the study.

Conceptual definition of the dependent variable. Depression is a psychological state that reduces the self-worth, and ability of a person to function properly and affects emotional regulation, level of adaptation, and one’s quality of life (WHO, 2023).

Operational definitions of the dependent variable. A tool called the AKUADS (Aga Khan University Anxiety and Depression Scale) was used to evaluate depression in people. It is a validated self-reporting questionnaire that was created to precisely determine how severe the anxiety and depressive symptoms are. It comprises a number of questions that evaluate multiple aspects of depression, including depressive symptoms, interest loss, changes in eating or sleep habits, and general mental health. Using a Likert scale, or some comparable answer structure, participants are asked to assess the intensity and frequency of their symptoms during the previous two weeks. The results are added up to produce an overall score that represents the severity of depression symptoms. Higher scores represent a higher level of depression.

Independent variables

Cardiovascular diseases are the independent variable in the study.

Conceptual definition of the independent Variables. Patients with CVDs are those who are diagnosed with any cardiac morbidity, including stroke, congenital heart disease, Coronary Artery Diseases, STEMI, NSTEMI, HF, VHD, ACS, and Cardiac Arrhythmias.

Operational definition of the independent variable. Cardiovascular diseases are a class of illnesses that affect the heart and blood arteries and are defined by abnormal structural or functional changes. Diagnosis of any specific cardiovascular problem, as established by a licensed medical practitioner, including coronary artery disease, congestive heart failure, arrhythmias, valvular heart disease, peripheral arterial disease, and others included.

Data Collection Tool

A sociodemographic information questionnaire, with structured, closed-ended questions, was used. This questionnaire had questions about the age, gender, medical conditions, co-morbidities, place of residence, level of education, and marital status of participants, in order to gather pertinent information about their sociodemographic characteristics. Closed-ended questions provide uniform responses. By employing this method, the study sought to completely define the study population, facilitating a better understanding of the demographic characteristics of the participants.

The Aga Khan University Anxiety and Depression Scale (AKUDS), which is available in both English and Urdu, was used as per study participants choice, to gather data regarding depression. There are 25 items in this validated questionnaire, 12 of which examine somatic symptoms and 13 of which assess psychological symptoms of anxiety and depression.

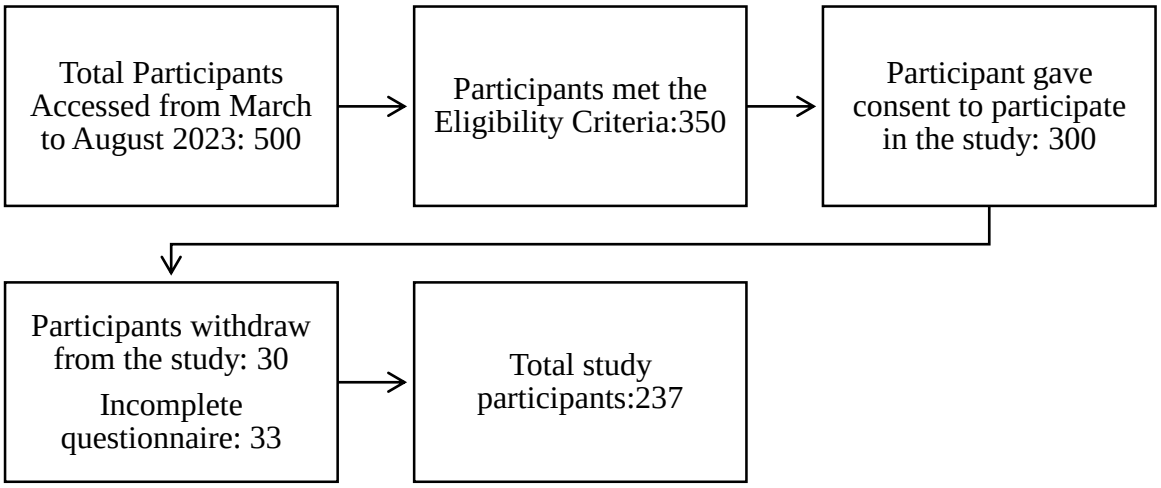
Each question on the survey has five Likert-scale response options: "Don't know", "Never", "Sometimes", "Mostly, and "Always". Participants were invited to offer answers on the basis of their experiences over the previous two weeks.

The AKUADS helped to properly identify those who were depressed, with a sensitivity of 66% at a score of 20. Its specificity was found to be 79%, indicating that it is capable of accurately identifying those who do not have depression. Additionally, it was discovered that the positive predictive value was 83%, showing the likelihood that a positive test would reveal actual depression, while the negative predictive value was 60%, indicating the probability that a negative test would reveal no evidence of depression. These characteristics highlight the AKUADS' validity and reliability in this study, in assessing the intensity of anxiety and depression symptoms (Ali et al., 1998).

Recruitment of Participants

The research participants were recruited at the Aga Khan University Hospital's Cardiology Unit and Outpatient Department. The hospital's Chief Medical Officer and the Ethical Review Board provided their institutional and the ethical approval, guaranteeing adherence to rules for conducting research and ethical concerns. The Floor In charge, who was in charge of supervising the relevant departments and ensuring proper study execution, was informed of the research's goal**.** A careful examination of patients' medical records was conducted to find those who met the specified qualifying requirements. Patients who met the requirements were contacted and given a thorough explanation of the study's goals, potential advantages, and related hazards. Following that, the patients' informed permission was obtained, to guarantee their willing participation and comprehension of their rights in the study. This methodical approach was intended to guarantee transparency, respect for ethical principles, and the participation of suitable volunteers who would aid in the accomplishment of the study's goals.

Figure 2. *Participants Recruitment*



Data Collection Process

All eligible participants were provided with a concise and clear explanation of the study's objectives, potential benefits, and associated risks. Each participant then gave their informed permission, confirming that they were willing to participate in the study and that they were aware of its conditions. The procedure for obtaining the data included interviewing the participants in two separate locations: the waiting room of the outpatient clinics and the bedside of patients in the inpatient cardiology unit. These places were selected for the convenience and comfort of the participants. To protect the anonymity and dignity of the participants, privacy concerns were rigorously followed during the data-obtaining procedure. Instead of utilizing the participants' real names and medical record (MR) numbers, special codes were issued to each participant to ensure participant confidentiality. This coding scheme was put in place to protect study participants' identities and lessen the possibility of any unintentional disclosure.

Data Analysis

A comprehensive analysis was conducted on the data collected from the study participants to determine the prevalence of depression in patients with cardiovascular illnesses. Multiple statistical tests were applied for this objective. In order to provide a comprehensive picture of the

research sample, descriptive analysis (percentages and frequency) was used to describe the traits and demographics of the participants. The inferential analysis included a Mann Whitney test, Chi-square test, and Logistic regression were employed. The mann whitney was used to compare depression mean scores between various subgroups, such as gender in order to analyze group differences. The existence of depression and the kind of cardiovascular disease are two categorical variables, and the chi-square test was used to analyze the relationships between them. Additionally, the logistic regression test was used to look at the association between variables, such as the depression and certain cardiovascular risk factors. SPSS version 23 was used to analyse the data.

Ethical Considerations

The Institutional Review Board gave its approval, and the study was conducted in conformity with ethical standards. The study's aims were clearly explained to the participants, and their informed permission was obtained to ensure their voluntary participation. To guarantee each participant's well-being during the study, their health state and feasibility were given due consideration. Moreover, their comfort and their availability were taken into consideration when conducting the interviews.

In order to protect the participants' privacy and dignity, confidentiality was strictly upheld throughout the interview process. To safeguard the information obtained, data security procedures were put in place. The data was maintained in password-protected computer files for the soft copies and the hard copies, and were kept in safe storage, under lock and key. Specific codes were issued to each participant to protect individual confidentiality and to ensure their anonymity in the research. To sustain ethical standards, protect participant privacy, and ensure the accuracy of the data gathered, these strict precautions were put into place.

Summary of the Chapter

This chapter provided an account of a quantitative descriptive cross-sectional study that examined the prevalence of depression among patients diagnosed with cardiovascular disorders. During the period of June to August 2023, a total of 237 individuals suffering with diverse cardiovascular diseases participated in the study at Aga Khan University Hospital. The adoption of the AKUADS data collection tool facilitated an accurate evaluation of depression. A comprehensive statistical methodology was employed in the study, which comprised descriptive analyses including percentages and frequencies, chi-square tests, and logistic regression. The investigation followed ethical guidelines. With the utmost regard for participant privacy and confidentiality, consent was obtained.

Chapter Four: Results

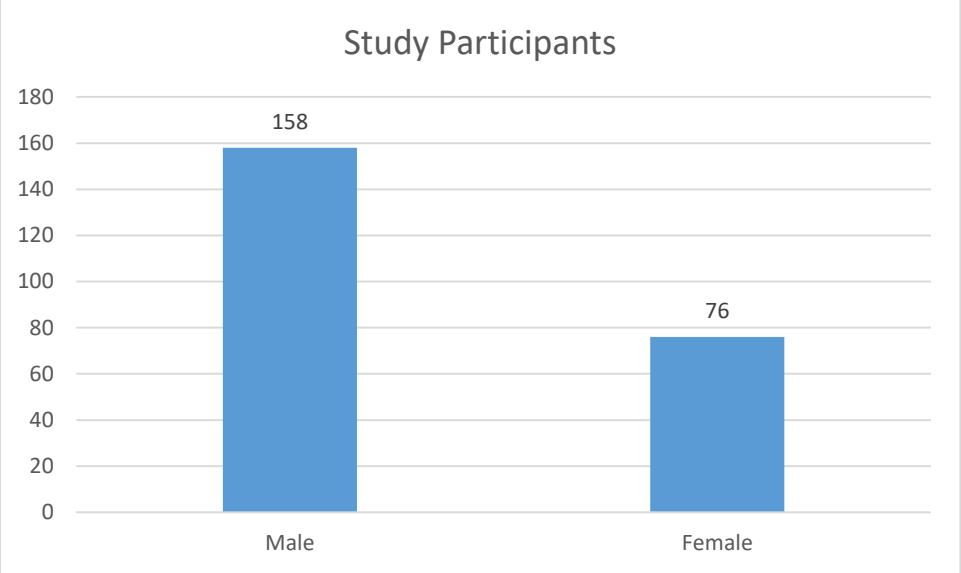
This chapter discusses the results of the prevalence of depression in patients with cardiovascular disease. This chapter is divided into three sections. The first chapter discusses the descriptive statistics of the socio-demographic factors. The second section includes inferential statistics on socio-demographic characteristics and depression in patients with cardiovascular disease. At the end, a regression model of depression is presented, followed by a chapter summary.

Statistical Analysis

The prevalence of depression was measured through the Aga Khan University Anxiety and Depression Scale (AKUADS). The AKUADS tool includes 25 items, and the scoring of this tool is measured through a 5-item Likert scale. The scoring range is from 0 to 75 and the cutoff value of 20 has been used to detect the presence of depression in patients with cardiovascular diseases (Farooq et al., 2019). The prevalence of depression was measured through descriptive statistics. Mann-Whitney U test was used to compare the prevalence of depression between males and females. The Chi-square test was used to assess the significance of the association between the sociodemographic characteristics of participants and the presence of depression in patients with cardiovascular diseases. Univariate and multivariate logistic regression is used to assess the strength of association between predictor variables and depression.

Figure 3

Study Participants (n=234)



Note. This table presented gender distribution of study participants.

Table 1

Socio-demographic Characteristics of the Study Participants (n=234)

Age	**n**	**%**
Below 40 years	13	5.6
40 to 50 years	27	11.5
>50 to 60 years	57	24.4
>60 to 70 years	80	34.2
>70 years and above	57	24.4

Residence	**n**	**%**
Punjab	6	2.6
Sindh	197	84.2
Balochistan	15	6.4
Khyber Pakhtunkhwa	8	3.4

Others*	8	3.4
Education level	**n**	**%**
Primary (grade 1-5)	36	15.4
Middle (grade 6-8)	15	6.4
Matric (grade 10)	39	16.7
Intermediate	33	14.1
Bachelors	70	29.9
Masters	41	17.5
Marital Status	**n**	**%**
Married	213	91
Single/Divorced	21	9

Note. This table presented an overview of the participants socio-demographics, *Residence (Others) includes Gilgit, Kashmir

Participant characteristics are detailed in Table 1 and Figure 1. A total of 234 participants, 67.5% males and 32.5% females, were enrolled in the study, from different backgrounds, based on residential area, age groups, educational level, and marital status. Most of the participants were residents of Karachi, Sindh (84.2%), majority were between >60 to 70 years of age (34.2%), most of the participants had bachelor's level qualification (29.9%), and the majority of the participants were married (91%).

Table 2

Clinical findings of Participants (n=234)

Diagnosis	**n**	**%**
IHD	171	73.1
Post-Surgery	63	26.9
Co-Morbids	**n**	**%**
Both DM, HTN	100	42.7
DM	38	16.2
HTN	66	28.2
None	30	12.8

Note. *HTN (hypertension), DM (Diabetes Mellitus), post-surgery (Coronary artery bypass grafting, Atrial septal defect closure)

The clinical characteristics of participants are presented in Table 2. Among the participants, 73.1% had ischemic heart disease (IHD). This category included patients with coronary artery diseases (CAD), Heart Failure (HF), ST-elevation myocardial infarction (STEMI), and non-ST elevation myocardial infarction (NSTEMI). The category of post-surgery (26.9%) included participants who had undergone coronary artery bypass grafting and Atrial septal defect closure. Most of the patients had co-morbid of both Hypertension and Diabetes Mellitus (42.7%); some had only Diabetes (16.2%) or only Hypertension (28.2%), and only 12.8% of participants had no co-morbid.

Table 3

Prevalence of Depression among Study Participants (n=234)

Variables	n	%	Median	Mean	Std. Deviation
AKUADS Score (0-75)	___	___	14	15.82	9.579
Depression	67	28.6	___		
Non-Depression	167	71.4	___	___	___

Note. This table presented the mean scores and prevalence of depression in study participants.

The prevalence of depression among the study participants(n=234) was 28.6%. The median score of AKUADS was found to be 14, with a mean score of 15.82, with a standard deviation of 9.579 (Table 3). The female participants had higher levels of depression (mean rank= 128.64, p=0.026) than the male study participants (Table 4).

Figure 4

Prevalence of Depression in Study Participants

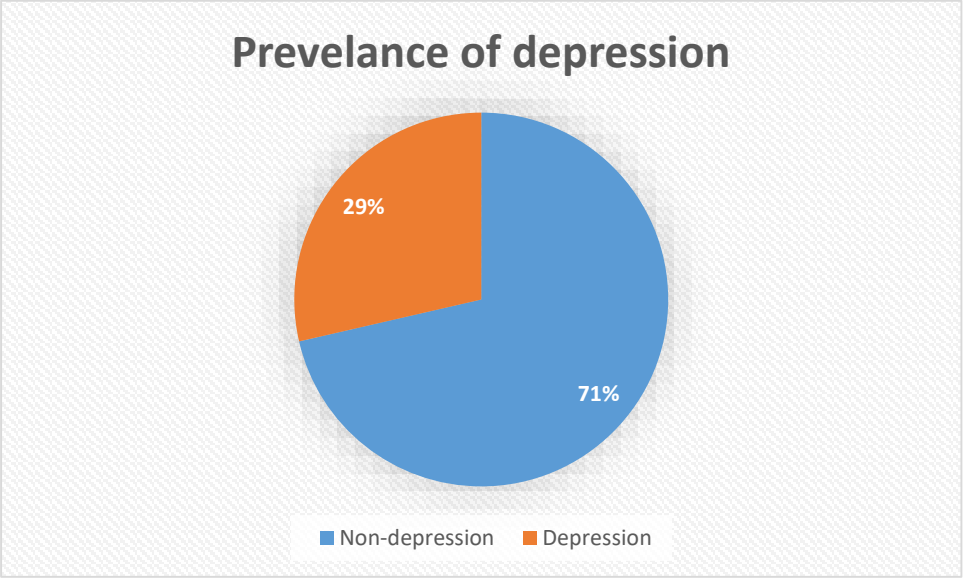


Table 4

Comparative Analysis of Depression Scores Across Genders in AKUADS Participants

Gender		n	Mean Rank	Sum of Ranks	Mann Whitney	p-value
AKUADS	Male	158	112.14	17718.00	5157	0.026
	Female	76	128.64	9777.00		
	Total	234				

Note. This table presented the difference in mean ranks of depression scores in males and females.

There are 25 items in the AKUADS tool in all; 13 of them evaluate psychological symptoms, and 12 evaluate the somatic symptoms of depression and anxiety. The score range of AKUADS is from 0 to 75. Somatic symptoms were more prevalent in the study participants as compared to psychological symptoms. Most participants reported sometimes and often for their experience of psychological and somatic symptoms. Among the participants, a substantial 38%, reported being anxious, 42.6% being unhappy, 37.1% being worried and 33.3% being cried for some time in the past two weeks. In the somatic symptom's category, 29.5% reported retrosternal burning, 25.7% reported indigestion, 20.3% reported nausea, 28.7% reported constipation, 29.1%

reported difficulty in breathing, 34.6% reported numbness of hands and feet, 30% reported a sensation of tension in their neck and shoulders, 32.1% reported having headaches, and 28.7% reported experiencing pain all over their body (Table 5).

Table 5

Individual Responses on the AKUADS Tool (n=234)

S/N	Question	Every- time (3)	Often (2)	Sometime (1)	Never (0)	Don't Know (9)
1	Have you been sleeping less?	15 (6.3%)	68 (28.7%)	50(21.1%)	104 (43.9%)	__
2	Have you had a lack of interest in your daily activities?	8(3.4%)	50(21.1%)	35(14.8%)	143(60.3%)	1(0.4%)
3	Have you lost interest in your daily hobbies?	6(2.5%)	29(12.2%)	26(11.0%)	176(74.3%)	__
4	Have you been anxious?	8(3.4%)	41(17.3%)	90(38.0%)	98(41.4%)	__
5	Have you had a sensation of impending doom?	2(0.8%)	46(19.4%)	57(24.1%)	131(55.3%)	1(0.4%)
6	Have you had difficulty in thinking clearly	3(1.3%)	25(10.5%)	30(12.7%)	179(75.5%)	__
7	Have you preferred to be alone?	14(5.9%)	38(16.0%)	33(13.9%)	152(64.1%)	__
8	Have you felt unhappy?	1(0.4%)	25(10.5%)	101(42.6%)	109(46.0%)	1(0.4%)
9	Have you felt hopeless?	1(0.4%)	18(7.6%)	36(15.2%)	180(75.9%)	2(0.8%)
10	Have you felt helpless?	2(0.8%)	22(9.3%)	46(19.4%)	165(69.6%)	2(0.8%)
11	Have you been worried?	2(0.8%)	42(17.7%)	88(37.1%)	105(44.3%)	__
12	Have you cried?	3(1.3%)	22(9.3%)	79(33.3%)	133(56.1%)	__

13	Have you thought of taking your life?		1(0.4%)	4(1.7%)	232(97.9%)	__
14	Have you had loss of appetite?	8(3.4%)	46(19.4%0	41(17.3%)	141(59.5%)	__
15	Have you had retrosternal burning?	7(3.0%)	36(15.2%)	70(29.5%)	124(52.3%)	__
16	Have you had indigestion?	4(1.7%)	38(16.0%)	61(25.7%)	133(56.1%)	1(0.4%)
17	Have you had nausea?	1(0.4%)	11(4.6%)	48(20.3%)	176(74.3%)	1(0.4%)
18	Have you had constipation?	19(8.0%)	56(23.6%)	68(28.7%)	94(39.7%)	__
19	Have you felt difficulty in breathing?	6(2.5%)	37(15.6%)	69(29.1%)	125(52.7%)	__
20	Have you felt tremulous?	7(3.0%)	20(8.4%)	45(19.0%)	165(69.6%)	__
21	Have you felt the numbness of hands and feet?	7(3.0%)	37(15.6%)	82(34.6%)	111(46.8%)	__
22	Have you felt a sensation of tension in your neck and shoulders?	6(2.5%)	45(19.0%)	71(30.0%)	115(48.5%)	__
23	Have you had a headache?	6(2.5%)	24(10.1%)	76(32.1%)	131(55.3%)	__
24	Have you felt pain all over your body?	5(2.1%)	44(18.6%)	68(28.7%)	117(49.4%)	3(1.3%)
25	Have you passed urine more frequently?	6(2.6)	67(28.6)	43(18.4)	117(50)	1(0.4)

There were significant associations of gender, age, and education level with the presence of depression in patients with cardiovascular diseases. In all, 56.7% of males and 43.3% of females (p=0.025) experienced depression. Most of the participants who experienced depression were from the age group of 70 years and above (35.8%, p= 0.018). Moreover, 28.4% of the

participants with primary education had experienced more depression as compared to those higher education levels (p=0.002). Other socio-demographic characteristics, residence, and marital status, diagnosis and co-morbids had insignificant relation (p=< 0.05) with the presence of depression (Table 6).

Table 6

Association between sociodemographic characteristics of participants and the presence of depression (n=234)

Variable	**Categories**	**f (%)**	**Depression**	**Non-Depression**	**P-value**
Gender	Male	158(67.5)	38(56.7%)	120(71.9%)	.025
	Female	76(32.5)	29(43.3%)	47(28.1%)	
Age	Below 40 years	13(5.6)	6(9%)	7(4.20%)	
	40 to 50 years	27(11.5)	9(13.40%)	18(10.80%)	
	50 to 60 years	57(24.4)	11(16.40%)	46(27.50%)	0.018
	60 to 70 years	80(34.2)	17(25.40%)	63(37.70%)	
	70 years and above	57(24.4)	24(35.80%)	33(19.80%)	
Diagnosis	IHD	171(73.1)	53(79.1%)	118(70.7%)	.188
	Post Surgery	63(26.9)	14(20.9%)	49(29.3%)	
Co-Morbids	Both DM, HTN	100(42.7)	32(47.8%)	68(40.7%)	.411
	DM	38(16.2)	7(10.4%)	31(18.6%)	
	HTN	66(28.2)	18(26.9%)	48(28.7%)	
	None	30(12.8)	10(14.9%)	20(12.0%)	
Residence	Punjab	6(2.6)	4(6%)	2(1.2%)	.146
	Sindh	197(84.2)	53(79.1%)	144(86.2%)	
	Balochistan	15(6.4)	6(9%)	9(5.4%)	

	KPK	8(3.4)	1(1.5%)	7(4.2%)	
	Others	8(3.4)	3(4.5%)	5(3%)	
Education	Primary	36(15.4)	19(28.4%)	17(10.2%)	.002
	Middle	15(6.4)	7(10.4%)	8(4.8%)	
	Matric	39(16.7)	11(16.4%)	28(16.8%)	
	Intermediate	33(14.1)	10(14.9%)	23(13.8%)	
	Bachelors	0.351	3.955	0.022	
	Masters	41(17.5)	8(11.9%)	33(19.8%)	
Marital Status	Married	213(91)	60(89.6%)	153(91.6%)	.801
	Single	21(9)	7(10.4%)	14(8.4%)	

Note. This table presented the univariate analysis between socio-demographics and CVD in study participants.

An intricate relationship was found between sociodemographic factors and the presence of depression. Firstly, concerning gender, females faced a statistically significant (OR = 1.948, p = 0.027) risk of depression. Single participants had an odds ratio of 1.275, as compared to married participants, but the results were insignificant (p=0.618). Participants below 40 years of age were found to be at higher risk of developing depression (OR:1.791, p:0.022) (Table 7). However, multivariate logistic regression revealed that study participants with primary education (OR=4.283, p=0.026), and middle education (OR 3.29, p= 0.026) were more inclined to develop depression and the risk of developing depression decreased with an increase in education level (Table 8).

Table 7

Association Between Sociodemographic Factors and Depression Risk

Variable	Categories	f (%)	OR	Lower CI	Upper CI	p-value
Gender	Male ®	158(67.5)	0.317			0.027
	Female	76(32.5)	1.948	1.081	3.513	
Education	Primary	36(15.4)	4.610	1.675	12.687	0.004
	Middle	15(6.4)	3.609	1.009	12.917	
	Matric	39(16.7)	1.621	0.572	4.588	
	Intermediate	33(14.1)	1.793	0.614	5.236	
	Graduation	70(29.9)	0.853	0.317	2.300	
	Master®	41(17.5)	0.242			
Marital	Married ®	213(91)	0.392			0.618
Status	Single	21(9)	1.275	0.491	3.314	
	Below 40years	13(5.6)	1.179	0.351	3.955	0.022
Age	40 to 50years	27(11.5)	0.687	0.264	1.791	
	>50 to 60years	57(24.4)	0.329	0.142	0.763	
	>60 to 70years	80(34.2)	0.371	0.175	0.768	
	>70years and above ®	57(24.4)	0.727			
Diagnosis	IHD	171(73.1)	1.572	0.799	3.093	0.190
	Post Surgery ®	63(26.9)	0.286			
Co-Morbids	Both DM and HTN	100(42.7)	0.941	0.395	2.241	0.422
	DM	38(16.2)	0.452	0.148	1.381	
	HTN	66(28.2)	0.750	0.295	1.906	
	None®	30(12.8)	0.500			

Residence	Punjab	6(2.6)	3.333	0.362	30.701	0.208
	Sindh	197(84.2)	0.613	0.142	2.656	
	Balochistan	15(6.4)	1.111	0.190	6.492	
	KPK	8(3.4)	0.238	0.019	3.011	
	Others	8(3.4)	0.600			

Note. This table presented the multivariate regression analysis between socio-demographics and CVD in study participants.

Table 8

Multi-variate Logistic Regression Model

Variable	Category	f (%)	OR	Lower CI	Higher CI	p-value
Education	**Primary**	36(15.4)	4.283	1.434	12.798	0.026
	Middle	15(6.4)	3.291	0.850	12.740	
	Matric	39(16.7)	1.625	0.547	4.832	
	Intermediate	33(14.1)	1.948	0.620	6.116	
	Graduation	70(29.9)	0.919	0.330	2.559	
	Master	41(17.5)				
Age	**Below 40years**	13(5.6)	1.077	0.290	3.994	0.043
	40 to 50years	27(11.5)	0.747	0.271	2.060	
	>50 to 60years	57(24.4)	0.334	0.138	0.807	
	>60 to 70years	80(34.2)	0.376	0.169	0.835	
	>70years and above	57(24.4)				
Gender	**Male**	158(67.5)				0.433
	Female	76(32.5)	1.310	0.667	2.570	

Summary of the Chapter

A comprehensive analysis of depression prevalence among cardiovascular disease patients was carried out, considering various socio-demographic factors. The dataset consisted of 234 participants, with a predominant age group of >60 to 70 years (34.2%). The majority were males (67.5%). Most of them were from Sindh, accounting for 84.2% of the participants. In terms of educational diversity, 29.9% of the individuals possessed bachelor's degrees, while 17.5% had obtained master's degrees.

The prevalence of depression showed a significant difference based on gender, with a higher prevalence among females (p=0.025). However, no significant differences were found regarding cardiovascular disease type, comorbid conditions, or residence location (p>0.05). However, a significance in education level was observed (p=0.002), indicating that primary education was a risk factor (OR=4.283, 95% CI: 1.434-12.798). Additionally, age showed varying associations, with individuals below 40 years of age having higher odds of depression (OR: 1.179, CI: 0.351-3.955, p:0.022). Logistic regression analysis revealed that gender (OR=1.948, 95% CI: 1.081-3.513, p=0.027) and education, specifically primary education (OR=4.283, 95% CI: 1.434-12.798, p=0.026), were significant predictors of depression. Age factors exhibited variability, wherein individuals below the age of 40 demonstrated an elevated risk (OR=1.077, 95% CI: 0.290-3.994, p=0.043). However, multivariate regression analysis revealed that increasing age and education levels neutralize the gender-specific effect on depression. This suggests that age and education play crucial roles in influencing depression rates, mitigating the gender-based disparity observed in the initial findings. It is worth noting that variables such as cardiovascular disease type, comorbid conditions, residence location, and marital status did not exhibit a statistically significant impact on the risk of depression within this study population.

Chapter Five: Discussion

This chapter discusses the study's critical findings considering the existing literature. The second section discusses the strengths, limitations, and recommendations. Finally, the chapter ends with a summary.

The current study reported a 28.6% prevalence of depression in patients with cardiovascular diseases, in the cardiology unit of Aga Khan University Hospital, Karachi. The AKUADS tool, with a specificity of 79%, reduces the risk of overreporting depression cases. However, the lower sensitivity (66%) implies potential underreporting, indicating the likelihood of missed cases.

There is multiple research that recognize the gravity of mental health issues (Alloh et al., 2018; Farooq et al., 2019; Yatham et al., 2018). According to recent statistics, around 14% of the population around the world struggles with some form of mental illness (Yatham et al., 2018). More than 80% of mental health illnesses and 85% of the world's population are in low- and middle-income countries (LMICs) (Alloh et al., 2018). Depression presently takes the fourth position in terms of its significant contribution to the overall disease burden globally (Farooq et al., 2019).

There are multiple factors that cause mental health issues in low-middle-income countries (LMIC). Low-income countries (LICs) experience increased mental health issues because of socioeconomic obstacles, limited access to resources during times of crisis, and discriminatory practices (Rathod et al., 2017). Abuse, intimate partner violence, and caring for a child with special needs are just a few of the factors that contribute to the high rate of mental health problems in poor and middle-income nations. Moreover, extreme depression in women is triggered by both biological factors and by temporary life stressors, such as illness in the family, financial difficulties, and lack of social support (Travasso et al., 2014). Furthermore, economic variables, such as material assets, unsecured debt, financial hardship, and financial stress

consistently show a strong and long-lasting relationship with depressive symptoms (Guan et al., 2022).

According to some research, this prevalence could be as high as thirty to forty percent of the population among those who have heart failure (Shiga, 2022). The results of a systematic review, in Low-and Middle Income Countries (LMIC), showed that the combined prevalence of depression among individuals diagnosed with heart failure was 51.5% (Mulugeta et al., 2023). Moreover, Seventy-five percent of all deaths from cardiovascular disease (CVD) occur in low- and middle-income countries (LMICs)(Ruan et al., 2018).

In terms of prevalence of depression in patients with CVD, the findings of the current study are consistent with the findings of several previous studies. For example, one meta-analysis, using a random effects model to assess the pooled prevalence of depression within the MI patient group, came up with an estimate of 28.70% for th patients who suffered from depression. North America had a pooled prevalence of 25.97%, Europe/UK had a prevalence of 23.50%, and Asia had a prevalence of 45.03% (Feng et al., 2019). The pooled prevalence of depression among patients with myocardial infarction (MI) varies significantly across areas and races. These regional disparities can be linked to a variety of factors, including socioeconomic status, socio-demographic traits, and social-cultural characteristics.

Similarly, Mbakwem et al. (2016), have reported that people who have chronic heart failure (HF) have a prevalence of significant depression that typically falls within the range of 20-40%, which is roughly 4-5% greater than the prevalence reported in the general population. The overall point prevalence of depression in heart failure patients is approximately 21%, while it is important to note that reported rates in different research differ significantly, ranging from 9% to as high as 60% (Rutledge et al., 2006). The reason that patients with heart failure develop depression is their compromised quality of life. For instance, individuals with congestive heart failure (CHF) are more likely to develop depression due to symptoms like fatigue, dyspnea, as well as the use of commonly prescribed medications. These medications can cause adverse

effects, such as increased urinary frequency, gynecomastia, and body dysmorphia (Liguori et al., 2018).

However, contrary to the findings of the current study, one study has demonstrated different findings. This study conducted at the Larkana (city in Pakistan) satellite centre of NICVD revealed a lower prevalence of depression (10.5%) among its patients, which is inconsistent with the findings of the current study (S. F. Mujtaba et al., 2020). Moreover, some studies have reported a higher prevalence of depression in patients with CVD (Bahall, 2019; Khan et al., 2016). A study was conducted at the Faisalabad Institute of Cardiology, Pakistan, reported 79.5% prevalence of depression in patients with CVD (Khan et al., 2016). Likewise, Bahall (2019), conducted a study in Trinidad and Tobago and reported that the prevalence of clinically significant depression in hospitalized patients with cardiac disease was 40.0%. This indicates that depression in patients with cardiovascular disease, is prevalent in diverse geographical contexts.

The current study identified female gender, younger age and lower education as a risk factor for developing depression in patients with CVD. These findings are supported by Ni et al. (2022), who reported several independent risk factors that develop depression, including gender, residential address location, alterations in health status, physical disabilities, chronic pain, childhood health status, and activity of daily living (ADL).

The current study had more male participants (67.5%) as compared to female (32.5%), with CVD, as there were more male patients admitted and came for follow-up in the cardiology unit of the Aga Khan University Hospital. A study by van der Laan et al. (2019) also supported this fact and stated that most of the men presented with cardiovascular diseases. Moreover, a study conducted in Jordan had gender distribution that aligned with the current study where, 75.2% study participants with CVD were male and their mean age was 57.5 years. Moreover, this study reported higher prevalence of depression, with 34% having moderate to severe depressive symptoms, 45.1% experiencing mild depression, and 20.9% falling within the normal range. Another similarity in both the studies is the significance of sociodemographic factors in predicting

depression, female gender, and low educational level were identified as significant independent predictors of depression in both studies (Rawashdeh et al., 2021).

Regarding the age of the participants, in the current study, most participants (58.6%) with CVD were above 60 years of age, which shows that cardiovascular diseases are more prevalent in old age. The age factor of patients in the current study is aligned with a study conducted in China, where the mean age of the study participants was 63.25 years (SD: 9.76), and being single was an independent risk factor for both anxiety and depression. But, contrary to the sample distribution in the present study, their study had a total sample of 435 participants, with a gender distribution that leaned towards female participants, comprising 67.82%, while male participants represented 32.18%. Moreover, the depression was lower than reported in the current study, as categorized by the HADS-D score, which were 9.20% participants in the Chinese study (Wu et al., 2022).

Despite of having more old age study participants > 60years of age (58.6%), the current study reported that patients with young age were more likely to develop depression. In contrast to these findings, in a study conducted in Greater Kumasi of the Ashanti region, with a sample size of 428 respondents, the prevalence of depression was reported at 42.1%. The mean age of participants was 69.9 ($SD = 8.8$), and the distribution was balanced for both sexes ($p = 0.25$). Notably, the prevalence of depression was particularly high among females, older adults aged over 80 years, and respondents from lower economic classes.

With regard to difference in the prevalence of depression between males and females, the results of the current study demonstrated a higher mean rank of depression in females, as compared to men. A similar pattern of results has been found in previous studies where females with CVD have been found to be more prone to experience depression. A study evaluated the global burden of diseases estimates for 12 mental disorders, across 23 age groups, and 204 countries and territories, from 1990 to 2019. The results showed that gender-based disparities in the prevalence of mental diseases persist, with females exhibiting higher rates of depression and anxiety (GBD, 2019).

A consistent finding from the literature is that women are more prone to experiencing depression compared to men (Feng et al., 2019). The results of a cross-sectional study, conducted in Jordan, showed that females, were significant predictors of PHQ-9 scores after controlling for the other variables in the model and concluded that being female was a risk factor in the development of depression in CVD. Similarly, Bahall (2019) conducted a study in Trinidad and Tobago, the results of which are aligned to the current study, that prevalence of depression is higher in women (83.1%) as compared to men (72.9%). Likewise, Lee et al. (2023) reported that an association between cardiovascular disease (CVD) risk and the frequency of depressive symptoms exhibited gender-specific difference ; the impact of CVD risk on depression was more prominent in females, with CVD risk being 2.25 times higher, while in males, it was 1.81 times higher.

It is important to note that the gender disparity goes beyond just the occurrence of depressive symptoms. The reason behind the higher ratio of females experiencing depression is that they are independently linked to lower levels of physical activity. This association may be driven by factors like reduced perceived self-efficacy and self-management capabilities among women. Additionally, women tend to experience cardiovascular disease (CVD) at a later stage in life than men, which leads to a higher likelihood of comorbidity and, consequently, lower levels of physical activity (Achttien et al., 2019).

As per education level, the results of the current study demonstrated that the study participants with primary education experienced depression more than participants with higher education. Similar findings were observed in a study conducted in a public hospital in Karachi, out of the total number of 1,015 participants, 66% (670) of them, exhibited symptoms of depression, lower educational attainment with higher scores on the BDI scale (M. I. Husain et al., 2019). Similarly, in a study conducted in Gulshan-e-Iqbal, Karachi, with 2,867 individuals participating, 27.4% reported experiencing symptoms of anxiety and depression. Moreover, illiteracy was associated with a 51% increase in the odds of experiencing anxiety and depression. Gender also emerged as a noteworthy contributor, with women having 2.4 times higher odds of

reporting these symptoms, as compared to men (Farooq et al., 2019). A prospective cohort study conducted in Karachi also supports the fact that lower income and lower education is associated with developing depression in patients with CVD (M. I. Husain et al., 2019).

In terms of marital status, in the current study being single had more risk to develop depression as compared to being married but the results were insignificant. The insignificant results could be due to the non-normally distributed data set as 91% of the study participants were married and 9% were single.

The current study reported that most of married participants did not have depression. A meta-analysis also supports the fact that Individuals who were not in a marital relationship, either because they were single or because they were no longer married, had poorer prognoses from depression than those who were. This was demonstrated by a 9.25% difference for single people and an 8.02% difference for participants who were no longer married. Even after correcting for depressive disorder characteristics and other relevant confounding variables, the observed gap remained statistically significant (Buckman et al., 2021).

A similar conclusion was reached by a study, conducted in Islamabad, which showed that affection had a negative and statistically significant association with depression among married nonworking women. Furthermore, it was also found that social support had a significant negative connection with depression in this group. The interaction between attachment and social support was also found to be a significant predictor of depression among married nonworking women (Abbas et al., 2019).

Strengths of the Study

The study addresses an important and clinically relevant issue, the prevalence of depression in a patient population with cardiovascular diseases, an area that has received limited attention in the health care system of Pakistan.

The diverse sample, collected from both the indoor cardiology unit and the outdoor patient department, enhances the external validity of the findings, providing insights into the wider population of cardiovascular disease patients observed in a hospital environment.

The application of the validated AKUADS (Aga Khan University Anxiety and Depression Scale) tool for data collection further emphasises the accuracy and thoroughness of the results.

Lastly, the study's location at the Aga Khan University Hospital, is a renowned institution, where factors that can lead to developing depression in patients with CVD were highlighted.

Limitations of the Study

One of the major limitations is that the data was collected from one well known private institution, and most of the study participants belonged to the upper class, which limits the generalizability of the findings to a larger population.

Furthermore, because of probable gender differences in CVD prevalence, the gender distribution in the study was inclined towards a higher number of males, which could impair the representativeness of the results.

Another limitation derives from the assumption about the patients' financial situation. Data regarding income could not be included because of the assumption that people seeking care at AKUH are mostly financially stable. However, this assumption may not be true, as the hospital has many welfare patients, and financial status can be a factor in moderating other predictive factors.

The study used a cross-sectional methodology, was very short in duration, and did not capture the potential changes in depression prevalence over longer time periods. Several possible risk variables, such as a family history of psychiatric problems, marital dissatisfaction, domestic violence, maladaptive coping methods, continuous life stressors, and the loss of a loved one, were outside the scope of the current study and hence, were not addressed.

The results demonstrated insignificant association of CVD and co-morbids with the prevalence of depression. This area can be covered in future research to assess the association between CVD and depression, specifically in the context to Pakistan, to observe whether CVD and co-morbids independently cause depression or the associated socio-demographic factors are responsible for causing depression.

Recommendations

Practice Level

Given the relatively high prevalence of depression among patients with cardiovascular diseases, healthcare practitioners need to consider instituting routine depression screening in both inpatient and outpatient settings, using validated measures, such as the AKUADS scale. This has the potential to improve patient outcomes by assisting in the early detection and management of depression.

Because the current study found gender disparities in depression prevalence, it is critical to customise therapies to the distinct needs of male and female patients. Provision of more effective care can be considered by implementing gender-sensitive support programmes and treatment options.

Integrate mental health education into nursing curricula, offering specialized training programs for identifying and managing mental health issues in cardiovascular patients. Provide continuous professional development for nurses.

Research Level

Future research should focus on undertaking longitudinal studies, with extended observation periods, to better understand the dynamics of depression in cardiovascular disease patients. This will aid in determining how depression evolves over time, as well as its impact on the evolution of cardiovascular disorders. Moreover, it is recommended that measures of socioeconomic position, including income, be incorporated into the study methodologies. This

will allow for a more comprehensive study of the association between patients' financial position and depression.

Modify the AKUADS tool for context relevance, collaborating with mental health professionals, researchers, and developers to improve sensitivity and specificity.

Investigation of the numerous factors that lead to depression in individuals with cardiovascular disease is required, including lifestyle, comorbidities, and psychosocial factors. A multifaceted approach will aid in the development of therapies that address the complexities of depression in this population.

Moreover, there is need to conduct correlational studies to assess the association between cardio-vascular diseases, co-morbids and depression to assess the relative risk factors in developing depression in various cardio-vascular diseases, separately. So that specific management of related psychological issues could be managed effectively.

Policy Level

Patient education programmes need to be initiated to raise awareness about psychological impact of cardiovascular disease and the risk of depression. It might also be good to educate patients about accessible support resources and self-management options.

It is important to encourage collaboration between cardiology and mental health experts to provide complete care to patients with cardiovascular diseases. An integrated approach can address both their physical and psychological health concerns. Moreover, there is a need to advocate for policies and funding to support mental health treatments in cardiovascular care settings; this includes ensuring that mental health specialists and mental health support programmes are available. Furthermore, the complex association between depression and cardiovascular disease needs to be further investigated.

Conclusion

This research addresses the prevalence of depression among participants diagnosed with cardiovascular diseases, providing valuable perspectives on this frequently disregarded area of healthcare. The results of this study indicated that there was a high prevalence of depression among the study participants with CVD, with a statistically significant rate of 28.6%. An obvious gender differences was observed, as women exhibited elevated rates of depression. Additionally, factors such as age, marital status, and education seemed to contribute to the emergence of depressive symptoms.

The presence of depression in patients with cardiovascular conditions is a multidimensional matter that involves a complex interaction of sociodemographic and clinical factors. The findings presented in this study are consistent with some prior research, highlighting the significance of geographical and sample-specific characteristics as key drivers of observed variability. The significant incidence of depression and its consequential effects on the overall health and well-being of individuals with cardiovascular conditions necessitates the implementation of regular screening procedures and the adoption of gender-sensitive techniques within therapeutic practise. Moreover, the research indicates the necessity for further extensive and longitudinal inquiries in order to have a thorough understanding of the intricacies surrounding depression within this particular demographic. Furthermore, the limitations that have been noted highlight the need for further studies to investigate and resolve these limitations.

Overall, this study's findings highlight the importance of holistic healthcare, which takes into account both physical and psychological well-being, and sheds light on the complexities surrounding depression in people with cardiovascular diseases. This will help in improving patient care.

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List of Appendices

Appendices A. *Permission Letter from the Chief Medical Officer*

آغا خان یونیورسٹی
THE AGA KHAN UNIVERSITY

Dated: October 18, 2022

Title: Prevalence of depression in patients living with Cardiac diseases

Principal Investigator: Dr. Salma Rattani
Assistant Professor, School of Nursing
Aga Khan Hospital
Karachi

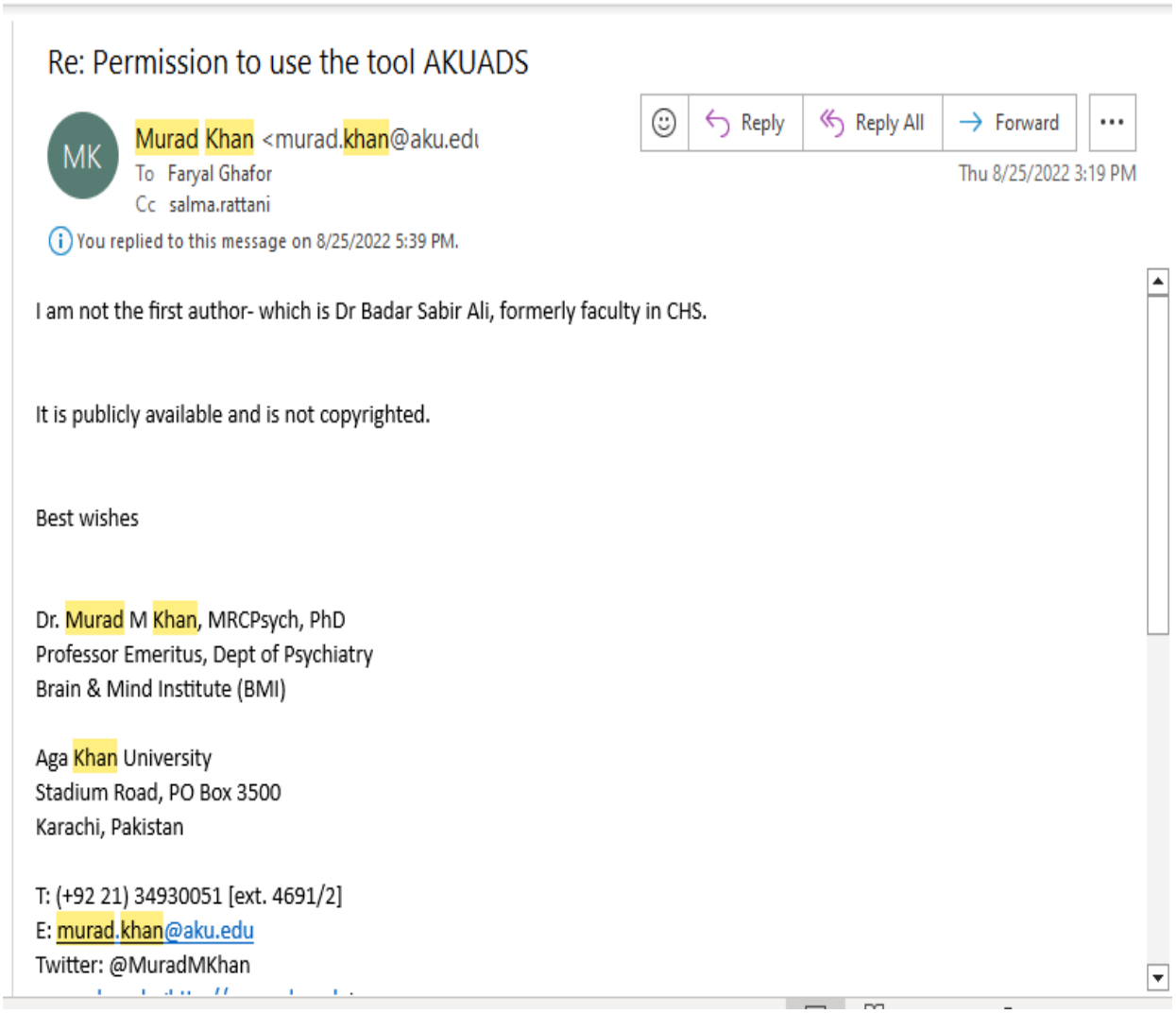
The above-entitled study is a descriptive Cross-Sectional study in the Aga Khan University Hospital, Karachi.

As Chief Medical Officer at the Aga Khan University Hospital, Karachi, I approve the above named study to be conducted within the Hospital, following required approvals and maintaining compliance with all Institutional ethical and regulatory requirements

Asim F. Belgaumi,
Professor, Pediatric Hematology & Oncology,
Department of Oncology.
Chief Medical Officer,
Associate Dean for Clinical Affairs
Aga Khan University Hospital.

Stadium Road, P. O. Box 3500, Karachi 74800, Pakistan
Telephone: +92 21 3493 0051, Fax: +92 21 3493 4294 / 3493 2095, Website: www.aku.edu

Appendices B. *Tool Permission*



Re: Permission to use the tool AKUADS

MK

Murad Khan <murad.khan@aku.edu

To Faryal Ghafor

Cc salma.rattani

Reply | Reply All | Forward | ...

Thu 8/25/2022 3:19 PM

You replied to this message on 8/25/2022 5:39 PM.

I am not the first author- which is Dr Badar Sabir Ali, formerly faculty in CHS.

It is publicly available and is not copyrighted.

Best wishes

Dr. Murad M Khan, MRCPsych, PhD
Professor Emeritus, Dept of Psychiatry
Brain & Mind Institute (BMI)

Aga Khan University
Stadium Road, PO Box 3500
Karachi, Pakistan

T: (+92 21) 34930051 [ext. 4691/2]
E: murad.khan@aku.edu
Twitter: @MuradMKhan

Appendices C. Approval Letter from the Ethical Review Committee

آغا خان یونیورسٹی
THE AGA KHAN UNIVERSITY

08-Feb-2023

Dr. Salma Rattani
Department of School of Nursing and Midwifery
Aga Khan University
Karachi

Dear Dr. Salma Rattani,

2023-8092-24049, Salma Rattani: Prevalence of depression in cardiac patients: A cross-sectional descriptive study

Thank you for submitting your application for ethical approval regarding the above mentioned study.

Your study was reviewed and discussed in ERC meeting. There were no major ethical issues. The study was given an approval for a period of one year with effect from 08-Feb-2023. For further extension a request must be submitted along with the annual report.

List of document(s) approved with this submission.

Submission Document Name	Submission Document Date	Submission Document Version
AKUADS(Eng) Apndx B version 1	07-Oct-2022	1.7
AKUADS(Urdu) Apndx C version 1	04-Sep-2012	1.5
Faryal Certificate	31-May-2022	1.4
Rumin Jiwani Ethics certificate 696858_42268894	11-Aug-2022	1.4
Salma Rattani cerificate valid till 26 January 2025	01-Jan-2022	1.4
Zahra Tharani	08-Aug-2021	1.4
Approval letter	19-Oct-2022	1.7
Affidavit for translation (1)	19-Oct-2022	1.7
consent (eng) Apndx E	26-Jan-2023	1.7
Consent(Urdu) Apndx F	26-Jan-2023	1.7
Demographic details Apndx A version 1	06-Feb-2023	1.7
Study protocol version (1)	07-Feb-2023	1.7
ERC Response sheet	07-Feb-2023	1.7

Any changes in the protocol or extension in the period of study should be notified to the Committee for prior approval. All informed consents should be retained for future reference.

Please ensure that all the national and institutional requirements are met.

Thank you.

Sincerely,

Dr. Hammad Ather

Chairperson
Ethics Review Committee

Appendices D. *Approval of Amendment from the Ethical Review Committee*

آغا خان یونیورسٹی
THE AGA KHAN UNIVERSITY

15-Jun-2023

Dr. Salma Rattani
Department of School of Nursing and Midwifery
The Aga Khan University
Karachi

Dear Dr. Salma Rattani,

Re: 2023-8092-25328, Salma Rattani: Prevalence of depression in patients with cardio-vascular diseases: A cross-sectional descriptive study

Thank you for your submission.

The proposed amendments have been reviewed and approved. Please note that this only constitutes an approval to your requested amendment(s) till the current validity period of your ERC approval. If any further extension is required, then kindly apply for an extension separately by creating a subform.

List of amended document(s) approved with this submission.

Submission Document Name	Submission Document Date	Submission Document Version
Research Proposal version 1	06-Jun-2023	2

Any changes in the protocol or extension in the period of study should be notified to the committee for prior approval. All informed consents should be retained for future reference.

Thank you.

Sincerely,

Dr. Bushra Moiz

Chairperson

Ethics Review Committee

Appendices E. *Literature Synthesis*

Author (s) Name **Year of Publication**	**Purpose of study**	**Design** **Sample Size**	**Key Findings**
Abdelbasset, W. K., & Alqahtani, B. A./ 2019	The purpose of this study was to evaluate the impact of moderate-intensity continuous aerobic exercise on the depression status of middle-aged patients with congestive heart failure.	RCT/ The study included 50 middle-aged patients with congestive heart failure. The participants were randomly assigned to an exercise group (n=25) or a control group (n=25)	The study found that moderate-intensity continuous aerobic exercise significantly improved depression status, physical function, and quality of life in middle-aged patients with congestive heart failure, suggesting it as an effective intervention.
Blumenthal, J. A., Smith, P. J., Jiang, W., Hinderliter, A., Watkins, L. L., Hoffman, B. M., . . . Sherwood, A. 2021	The purpose of the study was to investigate the effects of exercise, escitalopram (an antidepressant medication), and placebo on anxiety in patients with coronary heart disease (CHD)	RCT/The study included a total of 366 patients with CHD who were randomized into three groups: exercise (n=121), escitalopram (n=122), and placebo (n=123).	In a study comparing exercise, escitalopram, and placebo interventions for anxiety symptoms in patients with, all three interventions were found to significantly reduce anxiety symptoms over 16 weeks.

			However, there were no significant differences in the magnitude of reduction between the groups. Both exercise and escitalopram were also associated with significant improvements in physical functioning and quality of life. These findings suggest that exercise and escitalopram may be effective treatments for anxiety in patients with CHD.
Bucciarelli, V., Caterino, A. L., Bianco, F., Caputi, C. G., Salerni, S., Sciomer, S., Maffei, S., & Gallina, S. (2020).	The study aim is to summarize the current knowledge about depression and CVD relationship in women, highlighting the sex differences in physiopathology, clinical presentation and treatments.	Literature Summarization	In high-income countries, cardiovascular disease (CVD) and depressive disorders (DD) are major causes of disability. Cardiac patients, especially women, have a higher risk of developing DD due to unique neuroendocrine factors. Depression can worsen cardiovascular morbidity and mortality, particularly in conditions like coronary artery disease (CAD), heart failure (HF), and stroke. Interestingly,

			treatments for DD also seem to benefit cardiovascular health. While guidelines suggest screening for DD in cardiac patients, the effectiveness of routine psychosocial risk factor screening remains debated. It's crucial to raise awareness among healthcare practitioners, considering gender-specific issues when treating CVD patients. Further research is needed to better understand the gender-specific mechanisms linking depression and CVD, particularly regarding antidepressant therapy metabolism and its impact on cardiovascular outcomes.

Celano, M., C., Villegas, C., A., Albanese, A.,C., J. 2018	The purpose of the review was to provide an overview of the prevalence, diagnosis, and treatment of depression and anxiety in patients with heart failure.	Literature Review/ Not applicable	The review found that depression and anxiety are prevalent in patients with heart failure, with rates ranging from 20% to 40%. These conditions are linked to negative outcomes such as higher mortality, hospitalizations, and reduced quality of life. Diagnosing depression and anxiety in heart failure patients is challenging due to symptom overlap. Treatment options include medication, psychotherapy, and exercise-based interventions, with a multimodal approach potentially being the most effective.
Chialà, O., Vellone, E., Klompstra, L., Ortali, G. A., Strömberg, A., & Jaarsma, T. 2018	The purpose of the study was to investigate the relationships between exercise capacity and anxiety, depression, and cognition in patients with heart failure.	Cross-sectional study/ The study included a total of 83 patients with heart failure.	A study found that patients with heart failure who had higher levels of exercise capacity had lower levels of anxiety and depression. However, there was no significant relationship between exercise capacity and cognitive function.

			These findings suggest that exercise may have a positive impact on mental health outcomes in patients with heart failure, specifically in managing anxiety and depression. The authors recommend considering exercise as a potential therapy for these patients.
Chichetto, N. E., Kundu, S., Freiberg, M. S., Koethe, J. R., Butt, A. A., Crystal, S., Tindle, H. A. 2021	The purpose of the study was to examine the association between syndemic unhealthy alcohol use, smoking, and depressive symptoms on incident cardiovascular disease (CVD) among veterans with and without HIV-infection.	Cohort Study, The study included a total of 119,246 veterans, including 32,485 with HIV-infection and 86,761 without HIV-infection.	The study found that veterans with a syndemic of unhealthy alcohol use, smoking, and depressive symptoms had a higher incidence of cardiovascular disease (CVD) compared to those without a syndemic. This association was stronger among veterans with HIV infection. The findings suggest that the syndemic may be an important risk factor for CVD, especially among those with HIV infection. The

			authors recommend interventions targeting the syndemic to reduce the risk of CVD in these populations.
Choi, B. G., Rha, S. W., Yoon, S. G., Choi, C. U., Lee, M. W., & Kim, S. W. (2019). Association of Major Adverse Cardiac Events up to 5 Years in Patients With Chest Pain Without Significant Coronary Artery Disease in the Korean Population. *Journal of the American Heart Association*, *8*(12), e010541. https://doi.org/10.1161/JAHA.118.010541	The aim is to evaluate its association with long-term major adverse clinical events (MACE) up to 5 years in patients who presented with chest pain without significant coronary artery disease.	Prospective cohort study/A total of 5890 subjects with chest pain without significant coronary artery disease were prospectively enrolled in this study.	In patients without significant CAD, aging and insignificant coronary stenosis have a strong association with future long-term MACE. Also, aging, dyslipidemia, insignificant coronary stenosis, coronary artery spasm, and myocardial bridge are strongly associated with future angina pectoris.
Ghaffari, A. S., Bajwa, R. S., Hussain, M., Tahir, M., Bibi, S., & Khalid, A. 2019	The purpose of this study was to determine the prevalence and factors associated with anxiety and depression in patients with heart failure in South Punjab, Pakistan.	Sectional survey study. The study included a total of 194 patients with heart failure	According to the study, the prevalence of anxiety and depression in patients with heart failure was 62.4% and 58.2% respectively. Female gender, lower education level, and lower income were associated with a higher risk of anxiety and depression.

			Patients with NYHA class III or IV heart failure had a higher risk of depression compared to those with NYHA class I or II heart failure. The study suggests that anxiety and depression are common comorbidities in patients with heart failure in South Punjab, Pakistan, and screening and management of these conditions should be included in routine care for these patients.
Harshfield, E. L., Pennells, L., Schwartz, J. E., Willeit, P., Kaptoge, S., Bell, S., . . . Davidson, K. W. 2020	The purpose of this study was to investigate the association between depressive symptoms and incident cardiovascular disease (CVD) events, including coronary heart disease, stroke, and heart failure.	This is a prospective cohort study that included individual participant data from 21 cohort studies. The study included a total of 162,248 participants without a history of CVD at baseline.	The study found that depressive symptoms were independently associated with a higher risk of developing cardiovascular disease (CVD) events, such as coronary heart disease, stroke, and heart failure. This association was observed even after accounting for traditional cardiovascular risk factors like

			smoking, diabetes, and hypertension. The study also revealed that the link between depressive symptoms and CVD events was stronger in younger individuals and those without a history of CVD. These findings suggest that depressive symptoms may play a significant role as a risk factor for CVD events, especially in younger individuals.
Islam, S. M. S., Chow, C. K., Redfern, J., Kok, C., Rådholm, K., Stepien, S., . . . Hackett, M. L. 2019	To evaluate the effect of text messaging on depression in patients with coronary heart disease.	Sub-study analysis from a randomized controlled trial. 710 patients with coronary heart disease	The study found that text messaging had a significant impact on reducing depression in patients with coronary heart disease. After 6 months, the group that received the intervention showed a statistically significant decrease in depression scores compared to the control group. These findings indicate that text messaging could be an effective and cost-efficient method for managing depression in patients with coronary heart

Feng, L., Li, L., Liu, W., Yang, J., Wang, Q., Shi, L., & Luo, M. 2019	The purpose of the study was to determine the prevalence of depression in patients with myocardial infarction (MI).	Meta analysis The study included a total of 30 studies with a combined sample size of 30,931 patients.	The study found that 32.8% of patients with MI had depression, but there was significant variation across studies. Depression was more prevalent in female patients, those with a history of depression, and those with a more severe MI. These findings indicate that depression is a common comorbidity in MI patients and may impact their prognosis and quality of life. The authors suggest that routine screening and management of depression should be included in the standard care for MI patients.
Jha M, Qamar A, Vaduganathan M, et al. Screening and Management of Depression in Patients with Cardiovascular Disease. J Am Coll Cardiol. 2019 Apr, 73 (14) 1827–1845. https://doi.org/10.1016/j.jacc.2019.01.041	In this review, the authors discuss a practical approach for the screening and management of depression in patients with CVD.	Literature Review	Depression is a common comorbidity in patients with cardiovascular conditions, posing a risk for adverse events, excess healthcare costs, and poor quality of life. Screening for depression using questionnaires can be

			integrated into cardiovascular practices. SSRIs are considered safe first-line treatment, but nonpharmacological approaches may be more suitable for heart failure patients. Future studies should evaluate patient-centered outcomes and randomized clinical trials to develop personalized care plans. Cardiologists play a crucial role in managing depression in a multidisciplinary care model.
Jóźwik, S., Cieślik, B., Gajda, R., & Szczepańska-Gieracha, J. 2021	To investigate the effectiveness of virtual therapy in cardiac rehabilitation of female patients with heart disease	Prospective, randomized controlled trial 60 female patients with heart disease	A study was conducted to assess the effectiveness of virtual therapy in female patients with heart disease. The results showed that virtual therapy was successful in reducing anxiety and depression symptoms and enhancing quality of life. The group that received virtual therapy demonstrated significant

			improvements in anxiety and depression scores compared to the control group. Furthermore, the virtual therapy group experienced enhancements in various aspects of quality of life.
Khan, Z., Musa, K., Abumedian, M., & Ibekwe, M. (2021). Prevalence of Depression in Patients With Post-Acute Coronary Syndrome and the Role of Cardiac Rehabilitation in Reducing the Risk of Depression	This systematic review aims to identify the various risk factors and the role of cardiac rehabilitation in reducing the risk of depression in patients after AMI.	Systematic Review/included data on the prevalence of depression in patients post-AMI for the years 2016-2017 from a cardiac rehabilitation unit at Morriston Hospital, Swansea, a primary coronary angioplasty center.	A meta-analysis of seven studies found that post-acute coronary syndrome (ACS), the prevalence of depression ranged from 20-35% depending on the screening method used. Risk factors for post-ACS depression included being female, over 65 years old, single, living alone or widowed, and having a sedentary lifestyle. Post-myocardial infarction depression was linked to higher mortality, morbidity, hospital readmissions, and future cardiac events. However, the analysis revealed publication bias, data heterogeneity, and a pooled depression estimate of 1.78 (95% CI = 1.58-

			2.01) using a random-effects model.
Khandaker, G. M., Zuber, V., Rees, J. M. B., Carvalho, L., Mason, A. M., Foley, C. N., Gkatzionis, A., Jones, P. B., & Burgess, S. (2020). Shared mechanisms between coronary heart disease and depression: findings from a large UK general population-based cohort. *Molecular psychiatry*, *25*(7), 1477–1486. https://doi.org/10.1038/s41380-019-0395-3	The aim of the study is to assess whether comorbidity between depression and cardiovascular risk factors, specifically coronary heart disease (CHD), is primarily due to genetic or environmental factors. Additionally, the study aims to investigate whether cardiovascular risk factors and CHD have a causal relationship with depression using Mendelian randomization, a method that utilizes genetic variants as instrumental variables to explore causality in observational data.	a population-based cohort study,/We performed a range of analyses in 367,703 unrelated middle-aged participants of European ancestry from UK Biobank.	The findings showed that while a family history of heart disease was associated with a 20% increased risk of depression, a genetic risk score strongly associated with CHD did not affect depression risk. Mendelian randomization analyses suggested that triglycerides, interleukin-6 (IL-6), and C-reactive protein (CRP) are likely causal risk factors for depression, with each standard deviation increase in genetically-predicted levels showing significant associations. Overall, the study suggests that the comorbidity between depression and CHD is primarily due to shared environmental factors, and it highlights triglycerides, IL-6, and CRP as potential targets for the treatment and prevention of depression.

Kim, J. M., Stewart, R., Kang, H. J., Kim, S. Y., Kim, J. W., Lee, H. J., . . . Yoon, J. S. 2021	To investigate the long-term cardiac outcomes of depression screening, diagnosis, and treatment in patients with acute coronary syndrome.	The study was a prospective observational study The study included 537 patients with acute coronary syndrome	A study found that depression screening, diagnosis, and treatment were linked to lower risks of cardiovascular mortality and composite cardiovascular events. The impact of treatment was particularly significant for patients with major depressive disorder. Additionally, the positive effects of treatment were observed for a duration of up to 10 years after acute coronary syndrome.
Kruse, M., Laudicella, M., Olsen, K. R., Zwisler, A. D. O., Helmark, C., & Pedersen, S. S. 2022	To evaluate the effects of screening for anxiety and depression in patients with ischaemic heart disease in Denmark	Nationwide Danish register study 57,137 patients with ischaemic heart disease	A study found that screening for anxiety and depression in patients with ischaemic heart disease led to positive outcomes. These included reduced mortality and risk of recurrent myocardial infarction, increased use of antidepressant medication, and referral to psychological treatment. The results suggest that routine screening for

			anxiety and depression in these patients can improve their outcomes.
Mujtaba, Fayaz, S., Sial, Akbar, J., Karim, & Musa. 2020	To investigate the prevalence of depression and anxiety in patients undergoing percutaneous coronary intervention for acute coronary syndrome.	Cross-sectional Study	The study found a high prevalence of depression and anxiety among patients undergoing percutaneous coronary intervention for acute coronary syndrome. Depressive symptoms were reported in 58% of patients,while 52% of patients had anxiety symptoms. The study also found that depression and anxiety were associated with poor health-related quality of life and increased mortality risk.
Minallah, A., Azam, N., & Merani, I. 2019	To determine the frequency of depression and associated risk factors among elderly patients in two tertiary care hospitals in Rawalpindi, Pakistan.	Cross-sectional Study, Not specified	The study found a high frequency of depression among elderly patients in the two hospitals. Factors associated with depression included female gender, chronic medical conditions, and limited physical activity.

Piwoński, J., Piwońska, A. M., Zdrojewski, T., Cicha-Mikołajczyk, A., Rutkowski, M., Bandosz, P., Kozakiewicz, K. 2021	To investigate the association between cardiovascular diseases and depressive symptoms in adults	Pooled analysis of population-based surveys (WOBASZ, NATPOL 2011, and WOBASZ II), Sample size 28018	The study found a significant association between cardiovascular diseases and depressive symptoms in adults. Participants with a history of cardiovascular diseases had a higher prevalence of depressive symptoms compared to those without. The association remained significant after adjusting for age, sex, education level, and other confounding factors. The study highlights the importance of considering the psychological well-being of patients with cardiovascular diseases in clinical practice.
Sbolli, M., Fiuzat, M., Cani, D., M. 2020	To evaluate the relationship between depression and heart failure.	Mata Analysis, 28 studies including 172,617 patients with heart failure	Depression is a common comorbidity in patients with heart failure, with a prevalence of up to 40%. Depression is associated with an increased risk of hospitalizations and mortality in patients with heart failure.

			Depression screening and treatment should be considered an integral part of the management of patients with heart failure.
Song, X., Song, J., Shao, M., Gao, X., Ji, F., Tian, H., Zhuo, C. 2020	To investigate the relationship between depression and the risk of adverse events after percutaneous coronary intervention (PCI) by conducting a meta-analysis	Meta Analysis Data from 12 studies including 3,782 patients were analyzed	Patients with depression had a higher risk of major adverse cardiac events (MACE) after PCI than those without depression (OR=1.58, 95% CI 1.24-2.02, p<0.001). Furthermore, patients with depression were also more likely to experience all-cause mortality (OR=1.79, 95% CI 1.37-2.34, p<0.001) and target vessel revascularization (OR=1.51, 95% CI 1.21-1.88, p<0.001) after PCI.
Uphoff, E. P., Newbould, L., Walker, I., Ashraf, N., Chaturvedi, S., Kandasamy, A., Churchill, R. 2019	To estimate the prevalence of common mental disorders (CMDs) in people with non-communicable diseases (NCDs) in Bangladesh, India, and Pakistan	systematic review and meta-analysis 40 studies included in the meta-analysis	The pooled prevalence of CMDs among people with NCDs was 34.2%, with depression being the most common disorder. The prevalence of CMDs was higher among

			people with cardiovascular diseases and diabetes compared to other NCDs. Women, people with lower income and education levels, and those living in rural areas had a higher prevalence of CMDs. The authors highlight the need for integrated mental health services for people with NCDs in South Asia.
Vitinius, F., Escherich, S., Deter, H. C., Hellmich, M., Jünger, J., Petrowski, K., Albus, C. 2019	To identify somatic and sociodemographic predictors of depression outcome among depressed patients with coronary artery disease	Secondary analysis of the SPIRR-CAD study 166 depressed patients with coronary artery disease	The study found that patients with a lower level of education, comorbidities, and high baseline depressive symptom severity were more likely to have a poorer depression outcome. Moreover, age, sex, and severity of coronary artery disease were not significant predictors of depression outcome. The study also highlighted the importance of appropriate treatment

			for comorbidities and baseline depressive symptom severity to improve depression outcomes in depressed patients with coronary artery disease.
Zhang, W. Y., Nan, N., Song, X. T., Tian, J. F., & Yang, X. Y. 2019	To investigate the impact of depression on clinical outcomes following percutaneous coronary intervention (PCI).	Systematic review and meta-analysis The study included a total of 16 studies with 6312 participants	The study found that depression was associated with an increased risk of major adverse cardiovascular events (MACE), all-cause mortality, cardiac mortality, and target lesion revascularization (TLR) following PCI. The risk of MACE was increased by 42% in patients with depression compared to those without depression.
Zhang, Y., Lv, X., Jiang, W., Zhu, Y., Xu, W., Hu, Y., Liang, Y. 2019	To evaluate the effectiveness of a telephone-delivered psycho-behavioural intervention on depression in elderly patients with chronic heart failure	RCT	The study is ongoing and therefore, there are no published key findings at the moment.
Zhuo, C., Ji, F., Lin, X., Jiang, D., Wang, L., Tian, H., Chen, C.	To determine the association between	Meta-analysis of cohort studies	The meta-analysis found that patients with

2020	depression and the recurrence of atrial fibrillation after catheter ablation	Not Applicable	depression had a significantly higher risk of atrial fibrillation recurrence after catheter ablation than those without depression. The association remained significant even after adjusting for potential confounding factors.