Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Naz et al., 2026

GENDER BASED PREVALENCE OF DIABETES MELLITUS IN HEART FAILURE PATIENTS IN A TERTIARY MEDICAL HOSPITAL IN PESHAWAR

Naima Naz
Department of Health and Biological Sciences Abasyn University Peshawar . naimanaz175@gmail.com
Muhammad Abad
Department of Health and Biological Sciences Abasyn University Peshawar
Adnan Khadim
Coordinator Cardiology Abasyn University Peshawar. adnan.khadim@abasyn.edu.pk
Qandeel Hira
Department of Health and Biological Sciences Abasyn University Peshawar
Shah Fahad Khalid
Cardiology Lecturer at Department of Health and Biological Sciences Abasyn University Peshawar
Saba Gul
Department of Health and Biological Sciences Abasyn University Peshawar
Kanwal Khalid
Department of Health and Biological Sciences Abasyn University Peshawar
Wasif Khan*
Lecturer Cardiology Abasyn University Peshawar. Corresponding Author Email: imwk48335@gmail.com

Author Details

Received on 04 March, 2026

Accepted on 21 March, 2026

Published on 24 March, 2026

Corresponding E-mails & Authors*:
Wasif Khan
imwk48335@gmail.com

Abstract

Background: Diabetes mellitus and heart failure are closely interrelated cardiovascular conditions that significantly contribute to morbidity and mortality worldwide. Gender-based differences in the prevalence of diabetes mellitus among heart failure patients remain an important yet insufficiently explored area, particularly in developing regions. **Objective:** The objective of this study was to determine the gender-based prevalence of diabetes mellitus in patients with heart failure at a tertiary care hospital in Peshawar. **Methods:** This cross-sectional study was conducted among 246 patients diagnosed with heart failure at a tertiary medical hospital in Peshawar. Data

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about
Online ISSN 3007-2387
Print ISSN 3007-2379

were collected using echocardiographic findings and clinical records to assess heart failure status and the presence and type of diabetes mellitus. Statistical analysis was performed to determine the distribution of diabetes mellitus across gender groups and related clinical characteristics. **Results:** Among the 246 participants, 128 (52%) were male and 117 (47.6%) were female. Heart failure was diagnosed in 71.1% of patients based on echocardiography, with HFmrEF being the most common subtype (36.6%). Regarding diabetes mellitus, 100 (41%) had no diabetes, while 80 (33%) had type 1 diabetes mellitus and 65 (26%) had type 2 diabetes mellitus. A substantial proportion of patients also had hypertension (52%) and a positive family history of cardiovascular disease or diabetes (51%), indicating a high burden of associated risk factors. **Conclusion:** The study highlights a considerable prevalence of diabetes mellitus among patients with heart failure, along with a high burden of hypertension and other cardiovascular risk factors. These findings emphasize the importance of early screening, integrated management of diabetes and heart failure, and gender-sensitive preventive strategies to reduce disease progression and improve clinical outcomes.

Keywords: Diabetes mellitus, heart failure, gender-based prevalence, echocardiography, hypertension, cardiovascular disease.

1. Introduction

1.1. Background

1.1.1. Human Cardiac Anatomy

The human heart is the central organ of the cardiovascular system, designed to sustain life by continuously receiving, pumping, and distributing blood throughout the body. Its structure reflects a highly coordinated relationship between muscular chambers, valves, vessels, electrical pathways, and supporting tissues, allowing the heart to function as both a pulmonary and systemic pump. The epicardium, myocardium, and endocardium are the three primary layers that make up the heart's wall. Each layer assists in internal blood flow, contraction, and protection. After Blood is ejected into the pulmonary artery and aorta, the semilunar valves, such as the aortic and pulmonary valves, keep it from going back to the ventricles. The structural basis for comprehending both the development of heart disease and normal circulatory function is provided by human cardiac anatomy. (Anderson et al., 2004).

In the human body, the heart is situated in the middle mediastinum, between the lungs, posterior to the sternum, and superior to the diaphragm, with its apex directed downward, forward, and toward the left side of the thoracic cavity. The outer surface of the heart is enclosed by the Pericardium, a protective Fibro serous sac that anchors the Heart within the thoracic cavity and reduces friction during cardiac movement. For

oxygenation in the lungs, this blood flows by the tricuspid valve into the right ventricle, which subsequently pumps it through the pulmonary valve into the pulmonary trunk and pulmonary arteries. The tricuspid and mitral valves, which make up the Atrioventricular valves, control blood flow among the ventricles and atria. Due to their primary function of receiving blood and transferring it into the ventricles, the atria have comparatively thin walls. The cardiac veins are primarily responsible for collecting venous blood from the myocardial, which then drains into the coronary sinus before opening into the right atrium. (Moore et al., 2023)[1].

This anatomical position enables the heart to connect efficiently with the major vessels of circulation, including the venae cava pulmonary arteries, pulmonary veins and aorta. Through the coronary sinus, inferior vena cava, and superior vena cava, the right atrium receives deoxygenated blood from the systemic circulation. The cardiac valves maintain one-way measure of blood through the heart and prevent backward flow during contraction and relaxation. Since the left ventricle must produce high pressure in order to pump blood through the systemic circulation, it has the thickest myocardial wall. The right and left coronary arteries arise from the ascending aorta and branch ended the surface of the heart to supply different myocardial areas. The heart's ability to sustain constant blood flow throughout life is made possible by the coordinated arrangement of its chambers, valves, myocardial layers, coronary veins, and conduction pathways. (Standring, 2020).

The endocardium lines the interior chambers and valves to enable effective heart function, while the myocardium forms a thick muscular middle layer and is in responsible of the heart's pumping circulation. The aortic valve allows the left ventricle to pump oxygen rich blood into the aorta, where it is supplied to the body's tissues. Depending on their functional demand, the heart chambers' thickness changes. The rhythmic activity of the heart is controlled by a specialized electrical conduction system that coordinates atrial and ventricular contraction. Effective circulation, cardiac output, and heart rhythm all depend on proper conduction. (Hall, 2021).

The heart is divided into four chambers: the right atrium, right ventricle, left atrium, and left ventricle. The pulmonary veins carry oxygenated blood back from the lungs to the left atrium, where it delivers via the mitral valve and into the left ventricle. Papillary muscles and chordae tendineae keep these valves, preventing valve prolapse into the atria during ventricular contraction. The right ventricle has a relatively thick wall because it pumps blood to the lungs through the low-pressure pulmonary circulation. To create coordinated ventricular contraction, these impulses first move through the

atria to the atrioventricular node. From there, they go through the atrioventricular bundle, bundle branches, and Purkinje fibers. (Drake et al., 2020).

Changes in left ventricular size, thickness, or function are closely associated with cardiovascular conditions such hypertension, cardiomyopathy, and heart failure, making this anatomical variation therapeutically significant. Therefore, studying cardiovascular physiology, interpreting clinical results, and investigating problems like coronary artery disease, arrhythmias, valve disease, cardiomyopathy, and heart failure all require a thorough grasp of cardiac anatomy. (Jia et al., 2018).

The coronary circulation supplies the heart with its own blood supply, which supplies the myocardium nourishment and oxygen. The left coronary artery usually divides into the left anterior descending artery and the circumflex artery, while the right coronary artery carries the majority of the right heart and in many cases, a portion of the inferior left ventricle and interventricular septum (Loukas et al., 2009). By producing electrical impulses that start each heartbeat, the right atrium's sinoatrial node functions as the body's natural pacemaker. (Kawashima, 2005).

1.1.2. Human Heart Physiology

The ability of the heart to produce rhythmic electrical impulses, synchronize atrial and ventricular contraction, sustain cardiac output, and control blood pressure in accordance with the body's metabolic requirements is the core of its physiology. The pulmonary circulation, which transports blood from the heart to the lungs and the systemic circulation, which distributes oxygenated blood throughout the body, are the two main circulatory pathways that the heart uses to function. (Klabunde, 2021).

Heart rate, stroke volume, preload, afterload, and myocardial contractility are the primary factors that affect how well the heart pumps blood during each cardiac cycle. (Chaudhry et al., 2022).

Ventricular filling, isovolumetric contraction, ventricular ejection, and isovolumetric relaxation are all recurrent phases of the cardiac cycle. The ventricles contract and expel blood into the aorta and pulmonary artery during systole, while they relax and fill with blood during diastole. The typical heart sounds known as S1 and S2 are produced when the atrioventricular and semilunar valves open and close, ensuring one-way blood flow. (Pappano &Wier, 2019).

The heart's natural pacemaker, the sinoatrial node, is where electrical activity starts. The impulse travels via the bundle of His and Purkinje fibers, the atria, the atrioventricular node, and ultimately results in coordinated ventricular contraction. By ensuring that the atria contract before the ventricles, this electrical conduction mechanism facilitates effective ventricular filling and blood ejection. (Bers, 2002).

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about
Online ISSN 3007-2387
Print ISSN 3007-2379

Heart rate multiplied by stroke volume provides cardiac output, which is the volume of blood pumped by the left ventricle in a minute. Preload, afterload, and contractility all affect stroke volume. Increased venous return strains ventricular muscle fibers, resulting in a stronger contraction and a larger stroke volume, according to the Frank-Starling process (Sequeira & van der Velden, 2015).

The heart can modify its output based on the volume of blood returning to it thanks to this mechanism. Heart physiology also depends on autonomic modulation. Particularly during physical activity, stress, or blood loss, sympathetic activation raises heart rate, contractility, and conduction velocity. Atrioventricular conduction is decreased and heart rate is slowed by parasympathetic stimulation, primarily via the vagus nerve. The heart can react rapidly to shifting physiological situations because sympathetic and parasympathetic regulation are in balance. (Floras, 2009).

The transport of calcium within cardiac muscle cells is essential for cardiac contraction at the cellular level. L-type calcium channels allow calcium to enter the cardiac cell during an action potential, which then causes the sarcoplasmic reticulum to release more calcium. Actin and myosin can interact and contract when this calcium binds to troponin. When calcium is taken out of the cytoplasm and either pumped out of the cell or stored again, relaxation takes place (Bers, 2002). The myocardial receives oxygen and nutrients from the coronary circulation. Whenever myocardial oxygen demand increases, coronary blood flow must also rise to meet the heart's high metabolic demand. Coronary arteries widen during physical activity or stress to enhance the flow of oxygen to the heart muscle. Adenosine, nitric oxide, carbon dioxide, and low oxygen tension are examples of local metabolic variables that assist control coronary blood flow (Duncker & Bache, 2008).

1.1.3. Pericardial Disease

The fibrous sac that surrounds the heart is called the pericardium, and it is comparatively avascular. The visceral and parietal pericardium are its two layers. A single layer of mesothelial cells that cling to the cardiac epicardium makes up the visceral pericardium. 2, 3 Collagen and a smaller quantity of elastin make up the fibrous, 2 mm thick parietal pericardium. A potential area that may typically hold 15 to 35 ML of serous fluid, predominantly over the atrial-ventricular and interventricular grooves, separates the two layers of the pericardium. The heart is fixed in the central thorax by the pericardium, which is invested around the major veins and the venae cava and connects to the sternum, diaphragm, and anterior mediastinum. The pericardium may potentially serve as an infection barrier due to its position. Pericardial inflammation can cause excruciating pain and vagally mediated responses because the pericardium is highly

innervated. Additionally, prostaglandins secreted by the pericardium control coronary tone and cardiac reflexes. (Little, W., C., & Freeman, G. L. (2006). Clinical manifestations of pericardial disorders include constrictive pericarditis, cardiac tamponade, acute pericarditis, and pericardial effusion. Patients may then experience recurrent or chronic pericarditis. Congenitally missing pericardium and pericardial cysts are examples of structural defects that are rare and typically asymptomatic.
(Khandaker, Masud H., et al. Elsevier, 2010).

1.1.4. Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder with persistent hyperglycemia resulting from defects in insulin production, insulin action, or both. Normally, insulin allows glucose to enter cells in the body for energy. When this is not working, glucose remains high in the blood and can damage different organs like heart, kidneys, eyes, nerves and blood vessels over time. (American Diabetes Association Professional Practice Committee, 2024). Diabetes mellitus affects the circulation and metabolism. It interferes metabolically with the correct utilization of carbohydrates, lipids and proteins. Over the long term, high blood glucose levels damage the inner lining of blood vessels, cause inflammation, oxidative stress and the process of atherosclerosis. These alterations may lead to an increased risk of cardiovascular problems such as coronary artery disease, hypertension and heart failure (Forbes & Cooper, 2013).

1.1.4.1. Types of Diabetes Mellitus

Type 1 diabetes, type 2 diabetes, gestational diabetes, and other specialized variants are the main categories. Absolute insulin insufficiency is the outcome of type 1 diabetes, which is caused by the autoimmune death of pancreatic beta cells. The most prevalent kind of diabetes, type 2, is brought on by increasing beta-cell failure and insulin resistance. While other forms of diabetes can be brought on by pancreatic illness, genetic flaws, endocrine diseases, or pharmaceutical use, gestational diabetes occurs during pregnancy (American Diabetes Association Professional Practice Committee, 2024).

a) **Causes**: Each type of cause is different. Autoimmune beta-cell damage is the primary cause of type 1 diabetes. Insulin resistance, which is frequently associated with obesity, belly fat, physical inactivity, poor diet, genetic susceptibility, and aging, is the cause of type 2 diabetes. The pancreas eventually runs out of insulin to keep blood glucose levels within normal ranges (DeFronzo et al., 2015).

b) **Risk Factors:** Family history, obesity or overweight, abdominal obesity, physical inactivity, poor diet, aging, hypertension, dyslipidemia, metabolic syndrome, prior

gestational diabetes, and polycystic ovarian syndrome are significant risk factors. These elements boost the risk of long-term vascular problems and insulin resistance.

c) **Symptoms:** Common symptoms include excessive thirst, frequent urination, increased hunger, exhaustion, unexplained weight loss, blurry vision, slow wound healing, recurrent infections, dry skin, and numbness or tingling in the hands and feet. Some people may have type 2 diabetes for years without knowing it. Until complications begin to occur.

d) **Diagnosis:** Diabetes is diagnosed by blood glucose tests. Diagnostic criteria are a fasting plasma glucose level ⩾126 mg/dL, HbA1c ⩾6.5%, two-hour plasma glucose level ⩾200 mg/dL during an oral glucose tolerance test, or random plasma glucose level ⩾200 mg/dL with classic symptoms of hyperglycemia (American Diabetes Association Professional Practice Committee, 2024). Complications over the long-term include coronary artery disease, stroke, chronic kidney disease, neuropathy, retinopathy, foot ulcers, poor wound healing, and heart failure. Prevention and management includes healthy diet, regular physical activity, weight control, blood glucose monitoring, blood pressure control, lipid management, smoking cessation and appropriate medication.

1.1.4.2. Heart Failure

a) **Definition:** The clinical illness known as heart failure occurs when the heart cannot pump enough blood to meet the body's metabolic demands or can only do so at abnormally high filling pressures. The heart has become weak, stiff, or ineffective at filling or pumping blood, but this does not imply that the heart has stopped (Heidenreich et al., 2022). Coordinated chamber contraction, valve movement, coronary blood supply, electrical conduction, and myocardial contraction are how the human heart typically functions. This regular function is disrupted in heart failure. The ventricles may become too stiff to fill appropriately or too weak to adequately expel blood. Fluid may build up in the lungs, legs, abdomen, or other tissues as a result of a decrease in cardiac output.

b) **Types:** Ejection fraction is frequently used to categorize heart failure. When the left ventricle's systolic contraction is feeble and its ejection fraction is 40% or lower, heart failure with reduced ejection fraction occurs. When the ejection fraction is typically 50% or above but the ventricle is rigid and unable to fill correctly, heart failure with intact ejection fraction ensues. These groups include heart failure with a slightly decreased ejection fraction. Other names for it include congestive heart failure, left-sided heart failure, and right-sided heart failure (Heidenreich et al., 2022).

c) **Causes:** Coronary artery disease, prior myocardial infarction, chronic hypertension, diabetes mellitus, valvular heart disease, cardiomyopathy, arrhythmias, congenital heart

disease, chronic kidney disease, obesity, myocarditis, excessive alcohol consumption, and certain cardiotoxic medications are among the main causes.

d) **Risk Factors:** Older age, high blood pressure, diabetes mellitus, smoking, obesity, high cholesterol, physical inactivity, chronic renal disease, coronary artery disease, a family history of heart disease, and an unhealthy diet are significant risk factors. Diabetes is a significant risk factor because it weakens the heart, destroys coronary arteries, stiffens blood vessels, and raises the risk of hypertension and kidney disease (Dunlay et al., 2019).

e) **Symptoms:** Shortness of breath, exhaustion, weakness, decreased ability to exercise, swelling of the feet or ankles, rapid weight gain from fluid retention, a persistent cough, palpitations, discomfort in the chest, and dyspnea when lying flat are common symptoms. While right-sided heart failure frequently results in swelling in the legs, abdomen, and liver region, left-sided heart failure typically produces lung congestion.

f) **Diagnosis:** Clinical history, physical examination, and investigations are used to make the diagnosis. Because it evaluates ejection fraction, chamber size, wall thickness, valve function, and diastolic function, echocardiography is a crucial test. Electrocardiography, chest X-rays, BNP or NT-proBNP testing, kidney and liver function tests, lipid profiles, thyroid function tests, and coronary artery examination are examples of further diagnostics (Heidenreich et al., 2022). Recurrent hospital stays, pulmonary edema, renal failure, arrhythmias, liver congestion, worse quality of life, and higher mortality are all consequences of heart failure. Depending on the kind and severity of heart failure, treatment options may include diuretics, beta-blockers, renin-angiotensin system inhibitors, mineralocorticoid receptor antagonists, SGLT2 inhibitors, salt restriction, fluid control, lifestyle modification, and treatment of the underlying cause (McDonagh et al., 2021).

1.1.4.3. Diabetes mellitus in heart failure patients:

Heart failure is extremely common in people with diabetes, and their prognosis is poorer than that of people without diabetes, according to epidemiologic and clinical evidence collected over the past 20 years. There is growing recognition that patients with diabetes develop heart failure regardless of the presence of coronary artery disease or its associated risk factors, and experimental data indicate that multiple mechanisms contribute to the impairment in systolic and diastolic function in these patients. Furthermore, treatment with the sodium glucose cotransporter 2 inhibitor empagliflozin decreased hospitalization for heart failure in individuals with high cardiovascular risk and

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about
Online ISSN 3007-2387
Print ISSN 3007-2379

type 2 diabetes mellitus, according to recent clinical evidence (Lehrke, M., & Marx, N. (2017).

In populations with heart failure, the prevalence of diabetes mellitus is about 20%, whereas in control populations, it is 4–6%. Epidemiological research has shown that diabetics have a higher risk of heart failure; additionally, poor glycemic management has been linked to a higher risk of heart failure in diabetic populations. Diabetes mellitus may be linked to heart failure through a number of mechanisms: first, related comorbidities like hypertension may be involved; second, diabetes speeds up the development of coronary atherosclerosis; and third, experimental and clinical research supports the existence of a particular diabetic cardiomyopathy linked to microangiopathy, metabolic factors, or myocardial fibrosis. Diabetes is also a significant predictor of heart failure, according to subgroup analysis of randomized studies. Furthermore, it has been proposed that individuals with ischemic cardiomyopathy may be particularly affected negatively by diabetes (Millaire, A., & De Groote, P. (2003).

Type 2 diabetes mellitus (T2DM), is a serious public health issue. It is linked to considerable morbidity and mortality and causes macro- and microvascular damage that promotes long-term consequences including coronary heart disease (CHD), stroke, or diabetic nephropathy. In patients with diabetes mellitus, age, gender, insulin, and glycemic control all affect the risk of CHD and stroke. However, as people age, gender-specific differences in the prevalence of cardiovascular diseases (CVD) may also diminish, particularly in older women with diabetes compared to men of the same age (Kim, H-L., et al. (2019). Patients with diabetes have a cardiovascular risk that is at least double that of people without the disease, and it is significantly higher when diabetic women are taken into account. One major adverse consequence of cardiovascular disease in diabetics is heart failure (HF). However, there is still little data comparing the prevalence of heart failure in diabetic patients by gender (Seghieri, Chiara, et al. (2012).

Diabetes is linked to a number of cardiovascular complications, such as coronary artery disease, impaired systolic and diastolic function, atherosclerosis, renal disease, stroke, and heart failure. Heart failure affects a large population worldwide, and data from the Global Congestive Heart Failure registry shows that clinical characteristics, treatment access, and outcomes differ between men and women across countries with varying income levels. Diabetes and heart failure are two closely related clinical conditions that significantly burden patients, hospitals, and health systems (Walli-Attaei et al., 2024).

1.2. AIM AND OBJECTIVES

1.2.1. AIM OF THE STUDY:

I. To determine to overall prevalence of diabetes in heart failure.
II. To determine the Gender based prevalence of diabetes mellitus with heart failure.

1.2.2. While The Objectives Are:

i. to determine the frequency of other associated risk factors (e.g. hypertension, obesity, dyslipidemia) in diabetic heart failure patients according to gender.
ii. To identify the type of diabetes mellitus, type 1 or type 2, among diabetic heart failure patients.

1.3. Research Significance

This study is significant because it addresses a critical clinical and public health issue in Khyber Pakhtunkhwa: the coexistence of diabetes mellitus and heart failure. Diabetes is an important cardiovascular risk factor and may worsen heart failure outcomes through poor glycemic control, vascular damage, renal dysfunction, hypertension, and other metabolic complications. In Khyber Pakhtunkhwa, diabetes and hypertension are already common non-communicable diseases, especially among older adults, and diabetes is more prevalent in urban settings (Haq et al., 2025). By focusing on heart failure patients at a tertiary care hospital in Peshawar, this study will provide useful local evidence on the distribution of diabetes among male and female patients. The findings can help clinicians identify high-risk patients earlier, improve screening practices, and support better management of patients who have both diabetes and heart failure. The study is also important because Pakistan has limited gender-specific evidence on heart failure risk factors, while previous hospital-based evidence suggests that male and female heart failure patients may have different survival-related predictors (Zahid et al., 2019). Therefore, the results may help improve gender-sensitive clinical assessment, guide patient counseling, support lifestyle recommendations such as smoking cessation and physical activity, and inform future provincial health planning. The evidence may also help tertiary hospitals understand the burden of diabetic heart failure and strengthen routine data collection by including variables such as ejection fraction, HbA1c, random blood sugar, and associated cardiovascular risk factors.

2. LITERATURE REVIEW

Heart Failure and Gender Differences

Savarese et al (2023); Delco et al (2023) investigated that Over 64 million people worldwide suffer from heart failure, which is one of the most common cardiovascular diseases. Its prevalence is increasing due to factors like population aging, higher survival rates from cardiovascular illness, and the growing burden of metabolic risk factors.

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about
Online ISSN 3007-2387
Print ISSN 3007-2379

Groenewegen et al (2020) found that there is a multi-causal condition rather than a single-disease outcome since it frequently arises as the last clinical stage of ischemic heart disease, hypertension, diabetes mellitus, obesity, renal impairment, and atrial fibrillation.

McDonagh et al (2021) examined that Clinically, Heart failure is divided into three categories based on left ventricular ejection fraction: heart failure with reduced ejection fraction, heart failure with minimally reduced ejection fraction, and heart failure with retained ejection fraction. The causes, prognosis, and response to treatment of these phenotypes vary. Heidenreich et al (2022) describe that there is more therapeutic evidence for heart failure with a reduced ejection fraction than for heart failure with a preserved ejection fraction, cardiovascular guidelines recognize this classification as crucial to diagnosis and treatment.

Delco et al (2023) concluded that the lifetime risk of heart failure is roughly equal for men and women, women are more likely to experience heart failure with normal ejection fraction, whereas men are more likely to experience heart failure with reduced ejection fraction because of a higher burden of coronary artery diseases. Dewan et al (2019) study investigated that While men frequently show higher mortality and a stronger correlation with ischemic heart disease, women with heart failure are typically older, have more complications, and report a lower quality of life. Dunlay et al (2017) study examined Heart failure, especially heart failure with normal ejection fraction, is largely caused by diabetes mellitus, hypertension, and obesity.

Kannel & McGee (1979); Ohkuma et al (2019) found that Diabetes increases the risk of heart failure through myocardial fibrosis, endothelial dysfunction, renal impairment, and metabolic remodeling, with several studies reporting a stronger relative effect among women than men. Pandey et al (2017) this study described that Through systemic inflammation, insulin resistance, volume overload, and irregular cardiac morphology, obesity raises the risk of heart failure. It has a particularly high correlation with heart failure with unchanged ejection fraction in women. Kotecha & Piccini (2015) investigated that by decreasing cardiac efficiency, raising the chance of hospitalization, and making long-term disease care more difficult, atrial fibrillation reduces outcomes and raises the risk of heart failure. Delco et al (2023) reveal that in over 70% of heart failure trials, women represent less than one-fourth of the patients. This has led to therapy recommendations that remain largely focused on data collected from men.

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about
Online ISSN 3007-2387
Print ISSN 3007-2379

2.2. Heart Failure in Developed Regions: Aging, Clinical Management, and Treatment Patterns

Conrad et al (2018) study investigates the relationship between Heart failure is strongly linked to aging populations, higher duration of life, better myocardial infarction survival, and higher rates of chronic cardiometabolic disease in highly populated and wealthy areas. Owan et al (2006) found that heart failure with a normal ejection fraction increases significantly with age and is closely associated with hypertension, diabetes, obesity, renal illness, and atrial fibrillation, it has become more significant in these situations. Delco et al (2023) reveal that heart failure with maintained ejection fraction is rare before the age of 55, affects around 5% of the general population after the age of 60, and affects more than 8% of women over the age of 80.

Borlaug, (2020) conducted that preserved ejection fraction is more clinically significant in high-income economies due to their aging population, especially in older women. McDonagh et al (2021) the study investigates the relationship between preserved and lowered ejection fraction has a significant impact on clinical care in developed areas. Angiotensin receptor-neprilysin inhibitors, beta blockers, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors are among the treatments for heart failure with lower ejection fraction that have a greater evidence base. Pieske et al (2019) examined that the Control of congestion, hypertension, diabetes, obesity, atrial fibrillation, and other comorbidities is frequently used to treat heart failure with normal ejection fraction, which is more complex.

Anker et al (2021); Solomon et al (2022) investigated that Although SGLT2 inhibitors have increased therapy choices for a wider range of ejection fractions, recognizing and treating the underlying risk profile is still important for the therapeutic management of preserved ejection fraction. Riedinger et al (2001) revel that in developed-region heart failure care, quality of life continues to be a primary concern. Compared to males, women with heart failure typically experience higher psychological discomfort, reduced physical functionality, more symptoms, and a lower health-related quality of life. Delco et al (2023) note that Although women with heart failure may live longer than males, their extra years are frequently followed by worse quality of life, greater disability, and higher levels of anxiety and depression. Taylor et al (2019) this study described Heart failure patients' exercise capacity, symptoms, and quality of life are all improved by cardiac rehabilitation; however, women are less likely than males to engage because of their advanced age, comorbidities, caregiving responsibilities, and lower reference rates.

Jaarsma et al (2021) examined the study of symptom control, rehabilitation, mental health, functional independence, and patient-centered care are becoming more and more important aspects of long-term management in developed health systems. Zusterzeel et al (2014) note that Although access to and use of advanced heart failure medicines change by sex, they are more readily available in developed regions. Despite indications that certain women may benefit greatly from cardiac resynchronization therapy, women are less likely than males to undergo implanted cardioverter-defibrillators and cardiac resynchronization therapy. Habal et al (2021) investigated that Due in part to body size, referral patterns, disease profiles, device-related problems, and clinical selection procedures, women are also underrepresented among patients undergoing mechanical circulatory support and heart transplantation.

Delco et al (2023) report lower rates of transplantation, mechanical circulatory support, and device use among women, despite potential differences in sex-specific reactions to. Aune et al (2019) found that in high-income environments, lifestyle-related dangers continue to be significant. Smoking is a known risk factor for heart failure, and women who smoke may be at higher relative risk than men (Aune et al., 2019). Obokata et al (2017) study investigated that Through inflammation, insulin resistance, plasma volume expansion, and poor cardiac relaxation, obesity significantly increases the risk of heart failure with normal ejection fraction. Pandey et al (2015) the study described that in patients with chronic heart failure, physical inactivity impairs functional ability and raises cardiovascular risk. Virani et al (2021) conducted that Therefore, long-term management of hypertension, diabetes, obesity, smoking, renal disease, atrial fibrillation, and a lack of physical activity are essential for population-level prevention in developed regions.

2.3. Heart Failure in Developing Regions: Health-System Barriers, and Gendered Risk

Sliwa et al (2014) found the overall prevalence of non-communicable illnesses, infectious or post-infectious cardiac disorders, untreated hypertension, rheumatic heart disease, cardiomyopathies, and limiting access to early diagnosis shapes heart failure in developing and low- and middle-income nations. (Dokainish et al (2017) study investigated that due to delayed diagnosis, poor referral processes, and restricted access to specialized care, many patients in these settings exhibit advanced symptoms and are frequently younger than heart failure patients in high-income nations. Delco et al (2023) report that Compared to high-income patients, low-income heart failure patients are almost twice as likely to experience in-hospital mortality and post-discharge adverse events; women are more likely to fall into this category. Even in high-income nations,

the acute death rate from peripartum cardiomyopathy may be about 4%, but in low- and middle-income nations, it might approach 14%.

Sliwa et al (2010) study analyzed that heart failure in underdeveloped countries is largely influenced by cardiovascular health. Peripartum cardiomyopathy can cause significant left ventricular failure, arrhythmias, thromboembolic events, and maternal mortality. It usually appears around the end of pregnancy or in the months following delivery. Women at risk of pregnancy-related heart failure can experience less avoidable consequences if antenatal risk assessment, postpartum follow-up, and maternal cardiac referral are improved. Bauersachs et al (2019) reveal that Delays in diagnosis, limited echocardiography, inadequate obstetric-cardiology referral systems, and restricted access to emergency cardiac treatment are all linked to increased risk in low-resource settings. Mills et al (2016) found that in emerging health systems, the growing prevalence of diabetes, hypertension, obesity, and renal disease is raising the risk of heart failure in the future. In low- and middle-income nations, hypertension is frequently misdiagnosed or poorly managed, raising the risk of heart failure, stroke, left ventricular hypertrophy, and renal illness.

International Diabetes Federation (2021) describe that Diabetes is becoming more common in many developing countries and is linked to heart failure through vascular damage, renal impairment, autonomic dysfunction, and diabetic cardiomyopathy. Popkin et al (2020) found that in growing city populations are also becoming more obese and physically inactive, which strengthens the cardiometabolic pathway leading to heart failure with unchanged ejection fraction. WHO (2020) described the study of blood pressure monitoring, diabetes diagnosis, renal risk assessment, weight management, and affordable long-term therapy are all essential functions of primary healthcare systems. When specialized resources are located in large cities, community-based care can enhance identification and adherence. Khatib et al (2016) found the study to Compared to episodic hospital-based treatment, comprehensive chronic disease care is necessary for managing heart failure in underdeveloped nations. Early screening for diabetes and hypertension, access to echocardiography, reasonably priced medications, standardized reference systems, patient education, and post-hospitalization follow-up procedures are all critical interventions.

Lam et al (2019) study investigated that female patients may have multiple risks from diabetes, hypertension, obesity, pregnancy-related cardiac problems, and unequal access to care, women-focused prevention is particularly important. Dokainish et al (2017) the study examined that Stronger primary care and referral systems can help

critical heart failure patients receive long-term treatment, reduce unnecessary hospital stays, and faster diagnosis.

2.4 Heart failure and diabetes mellitus

Lehrke, Michael, and Nikolaus Marx (2017) investigated current trial results, SGLT2-inhibiting glucose-lowering medications may be particularly beneficial for those with diabetes and heart failure. Additionally, there is some indication that metformin, which lowers the availability of energy substrates by reducing endogenous glucose synthesis, is beneficial for diabetic heart failure patients. Rosano, Giuseppe MC, Cristiana Vitale, and Petar Seferovic (2017) investigated that Heart failure and diabetes are strongly associated: people with heart failure are more likely to develop diabetes, and people with diabetes are more likely to get heart failure. Additionally, whether a patient already has heart failure or not, taking antibiotics raises the risk of death and hospitalization due to heart failure. The heart failure team must decide on the necessary level of glycemic control, the kind and dosage of glucose-lowering agents, and any modifications to glucose-lowering therapy based on the clinical condition because different medications have different risk-benefit ratios in diabetic patients with heart failure.

Bauters, Christophe, et al (2003) studied that Patients with diabetes have heart failure, which is a serious health issue. Diabetes affects 20–25% of people with heart failure. According to the study of the literature, the diabetic group of HF patients should be given extra attention because, at the moment, the natural history of HF in diabetic patients appears to be distinct, with a greater mortality, particularly in the case of ischemic HF. Tousoulis, Dimitris, et al. (2014) found a strong correlation between DM and HF in both directions. DM (cardiogenic diabetes) can be brought on by HF, and DM is a known risk factor for HF. Numerous pathophysiological processes, such as diabetic cardiomyopathy, HTN, MCD, and CAD, have been linked to the pathophysiology of new-onset HF in DM. These mechanisms often operate against a background of immunological dysregulation in T1DM and obesity in T2DM. SGLT-2i is the most effective antibiotic to stop the development of HF in T2DM patients. It is notable that the same medications, which are currently an effective method for managing HF regardless of LVEF or the presence or absence of DM, are also effective inhibitors of the onset of T2DM in patients with HF.

Seferović, Petar M., et al (2018) described that HF and type 2 diabetes mellitus are prevalent conditions that frequently occur (30–40% of individuals). The causes of HF in T2DM are numerous, but CAD and hypertension are likely the most important contributes to concurrent T2DM and HF, whereas a direct effect of T2DM on the myocardium (e.g. diabetic cardiomyopathy) might also a role.

2.5. Literature Gap

Groenewegen et al., 2020; Lam et al., 2019; Delco et al., 2023) reviewed studies that Strong evidence is available from existing research about the rise in heart failure worldwide, the difference between preserved and lowered ejection fraction, and the significance of gender in therapy response, disease pathways, and quality of life. However, There is still little comparison data on how regional health-system capability, gendered healthcare access, and biological risk factors interact to influence heart failure outcomes in Pakistan, particularly in Khyber Pakhtunkhwa. While women, low-income patients, and patients from low- and middle-income nations are still underrepresented in large datasets and intervention studies, the majority of the greatest therapeutic evidence comes from high-income populations and male-dominated clinical trials (Scott et al., 2018; Santema et al., 2019). Additionally, there is little comprehensive research linking maternal cardiovascular risk, diabetes, hypertension, obesity, kidney illness, treatment access, and quality of life in a single geographically comparable framework. This makes it evident that there is a need for KP research that looks at heart failure as a biological and health-system problem, paying special attention to gendered barriers to care, unique risk, and the uneven burden of cardiovascular illness in developed, developing, and global contexts.

3. METHODOLOGY

3.1 Materials and Methods

3.1.1. Study Design

This study will use a descriptive cross-sectional design to assess the gender-based prevalence of diabetes mellitus among patients diagnosed with heart failure.

3.1.2. Study Setting

The study will be conducted in tertiary care hospitals, where patients with heart failure and diabetes mellitus are commonly diagnosed and managed.

3.1.3. Study Duration

The study will be completed over a period of 6 to 8 months.

3.1.4. Sample Size

The sample size was calculated using the Open Epi sample size calculator. Using a prevalence of 20% (Palazzuoli and Iacoviello, 2023) from a previous study, a 95% confidence interval, and a 5% margin of error, the required sample size was estimated at 246 patients.

Pakistan Journal of Medical & Cardiological Review
https://pakjmcr.com/index.php/1/about
Online ISSN 3007-2387
Print ISSN 3007-2379

Sample Size for Frequency in a Population

Population size(for finite population correction factor or fpc)(*N*):	1000000
Hypothesized % frequency of outcome factor in the population (*p*):	20%+/-5
Confidence limits as % of 100(absolute +/- %)(*d*):	5%
Design effect (for cluster surveys-*DEFF*):	1

Sample Size(*n*) for Various Confidence Levels

ConfidenceLevel(%)	Sample Size
95%	246
80%	106
90%	174
97%	302
99%	425
99.9%	693
99.99%	969

Equation

Sample size $n = [DEFF*Np(1-p)]/ [(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)]$

Results from OpenEpi, Version 3, open source calculator--SSPropor
Print from the browser with ctrl-P
or select text to copy and paste to other programs.

The sample size formula is:

$n = p(1 - p) \times Z^2 / E^2$

Where:

n = required sample size

p = expected prevalence

Z = z-score at 95% confidence level

E = margin of error

Therefore, a total of 246 patients will be selected for this study.

3.1.5. Sampling Technique

A convenience sampling technique will be used to select eligible patients from the study population.

3.2. Sample Selection

3.2.1. Inclusion Criteria

Patients will be included if they have a confirmed diagnosis of heart failure based on echocardiography, a diagnosis of diabetes mellitus based on medical history, laboratory findings, or medication use, and are male or female.

3.2.2. Exclusion Criteria

Patients will be excluded if they have incomplete medical records, no confirmed diagnosis of both heart failure and diabetes mellitus, or only gestational diabetes.

3.2.3. Data Analysis Procedure

The collected data will be entered, cleaned, and analyzed using the latest available version of SPSS software.

3.2.4. Statistical Tests

The chi-square test and Z-test will be applied to analyze the data and compare gender-based differences in the prevalence of diabetes mellitus among heart failure patients.

3.3. Data Collection Procedure

We will collect our data using a pro forma. Our proforma consists of nine parts, including a title and an introduction, which presents the gender-based prevalence of diabetes mellitus among heart failure patients. The second part includes patients' demographics, such as name, age, and gender. The third part includes risk factors such as hypertension and diabetes. The fourth part includes the diagnosis of heart failure. The fifth part includes the classification of HF on EF. The sixth part includes a diagnosis of diabetes. The seventh part includes the type of diabetes diagnosed. The eighth part includes recent lab test results for diabetes. The last part consists of patient consent.

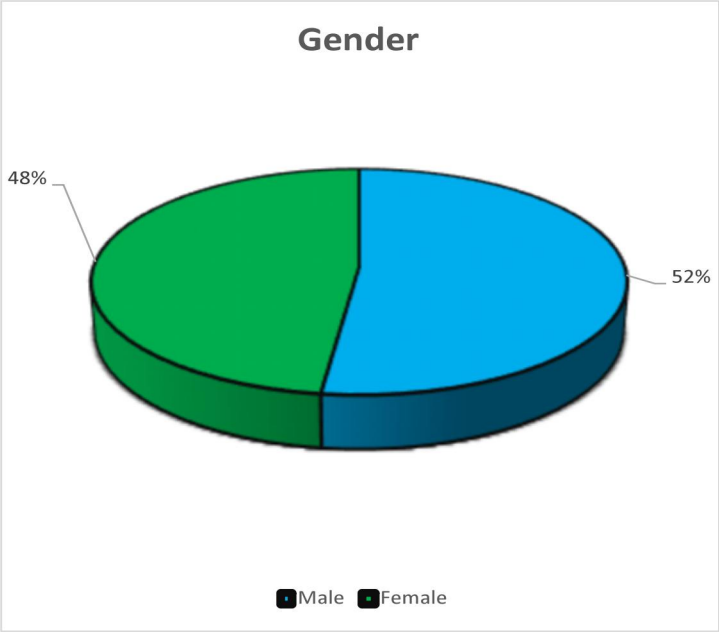
4. RESULTS

4.1. Gender Wise Distribution

Among the 246 study participants, **128 (52.0%) were male** and **117 (47.6%) were female**. The findings indicate a nearly balanced gender distribution, with a slight predominance of male participants in the study population.

4.1 Table Gender Wise Distribution

Gender				
	Frequency	Percent	Valid Percent	Cumulative Percent
Female	117	47.6	47.6	47.6
Male	128	52	52	100
Total	246	100	100	



4.1 Figure Gender Wise Distribution

4.2. Age comparison

Among the 245 study participants, the majority were aged 41–60 years (64.9%, n=159), followed by those aged 61–80 years (22.86%, n=56). Participants aged 20–40 years accounted for 11.02% (n=27), while only 1.22% (n=3) belonged to other age groups. This indicates that the study population was predominantly composed of middle-aged adults

4.1 Table Age Wise Distribution

Age Group	Frequency	Percentage (%)	Cumulative (%)
20–40 years	27	11.02	11.02
41–60 years	159	64.9	75.92
61–80 years	56	22.86	98.78
Other	3	1.22	100
Total	245	100	—

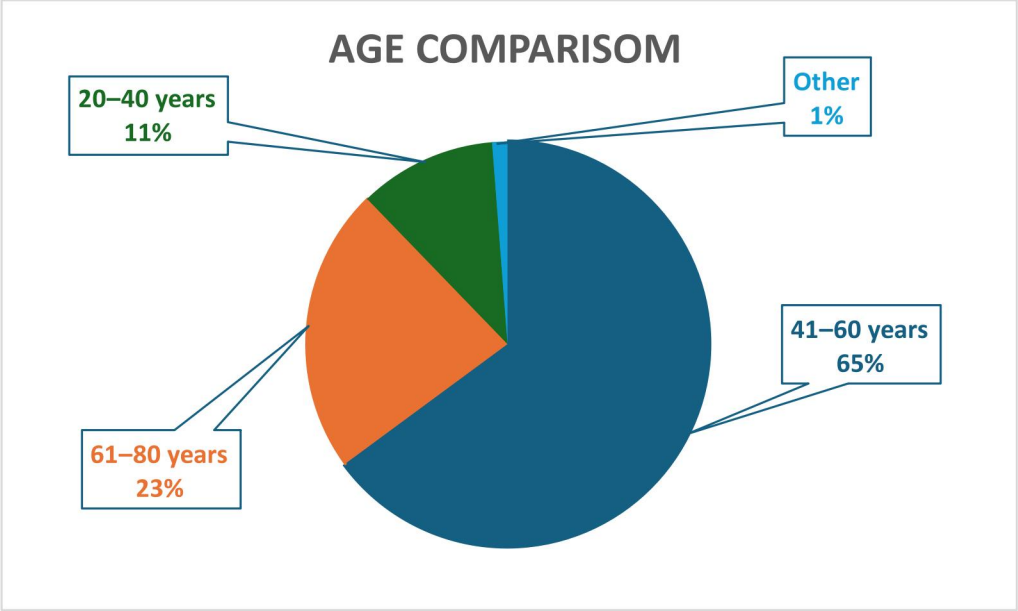
Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379



4.1 Figure Age-Wise Distribution

4.3. HEART FAILURE WISE DISTRIBUTION AND DIAGNOSED WITH HEART FAILURE BASED ON ECHOCARDIOGRAPHIC FINDINGS

4.3.1 Diagnosed with Heart Failure Based on Echocardiographic Findings

Among the 246 study participants, 175 (71.1%) were diagnosed with heart failure based on echocardiographic findings, while 70 (28.5%) had no evidence of heart failure.

Table. 4.3.1: *Diagnosed with heart failure based on echocardiographic findings*

Is the patient diagnosed with heart failure based on echocardiography?				
	Frequency	Percent	Valid Percent	Cumulative Percent
No	70	28.5	28.5	28.9
yes	175	71.1	71.1	100.0
Total	246	100.0	100.0	

4.3.2 Heart Failure-wise Distribution

Regarding the types of heart failure, HFmrEF (EF 40–49%) was the most common subtype, observed in 90 patients (36.6%), followed by HFpEF (EF ⩾50%) in 82 patients (33.3%) and HFrEF (EF <40%) in 73 patients (29.7%). Only one patient (0.4%) was categorized as having another type of heart failure. These findings indicate a high prevalence of heart failure in the study population, with HFmrEF being the most frequently identified subtype.

Types				
	Frequency	Percent	Valid Percent	Cumulative Percent
HFmEF: 40-49%	90	36.6	36.6	36.6
HFpEF: >50%	82	33.3	33.3	69.9
HFrEF: <40%	73	29.7	29.7	99.6
Other	1	0.4	0.4	100.0
Total	246	100.0	100.0	

Table. 4.3.2 Heart Failure wise Distribution

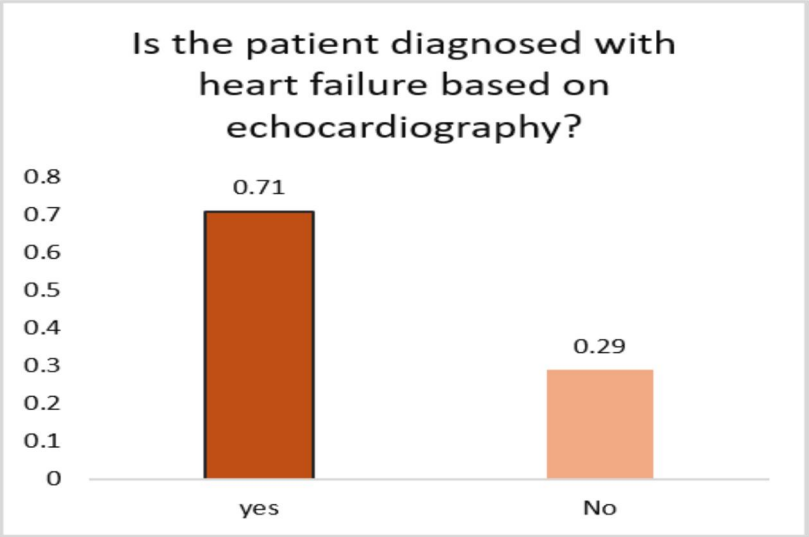


Figure 4.2: Echocardiography-based diagnosis of heart failure among study participants

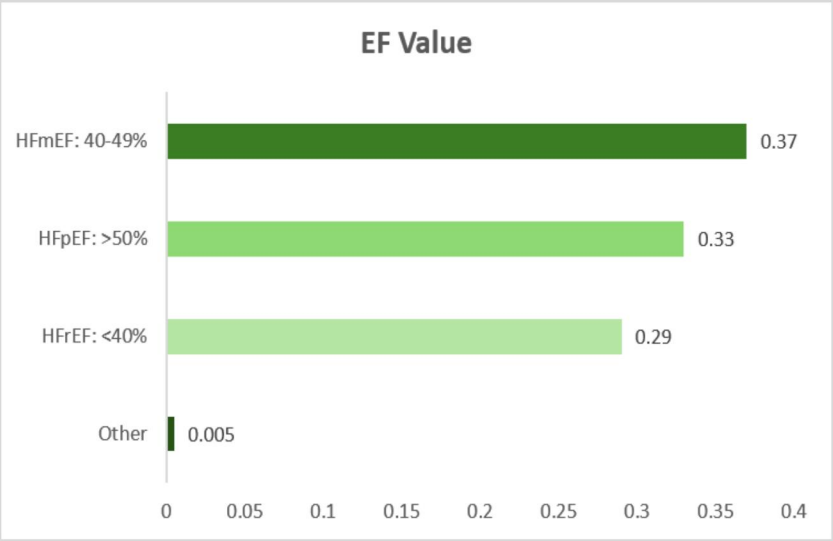


Figure 4.3.2 Heart Failure wise Distribution

4.4. DM and Type of DM Wise Distribution

Among the 246 study participants, 100 (41%) had no diabetes mellitus, while 80 (33%) were diagnosed with Type 1 diabetes mellitus and 65 (26%) had Type 2 diabetes mellitus. The findings indicate that a substantial proportion of participants were affected by diabetes, with Type 1 diabetes mellitus being the most common form among those diagnosed.

Does the patient have diabetes mellitus?				
	Frequency	Percent	Valid Percent	Cumulative
No	102	41	41	43
yes	141	57	57	100
Total	246	100	100	

What is the type of diabetes mellitus?				
	Frequency	Percent	Valid Percent	Cumulative Percent
none	100	41	41	41
Type 1 diabetes mellitus	80	33	33	73
Type 2 diabetes mellitus	65	26	26	100
Total	246	100	100	

Table 4.4. DM and Type of DM Wise Distribution

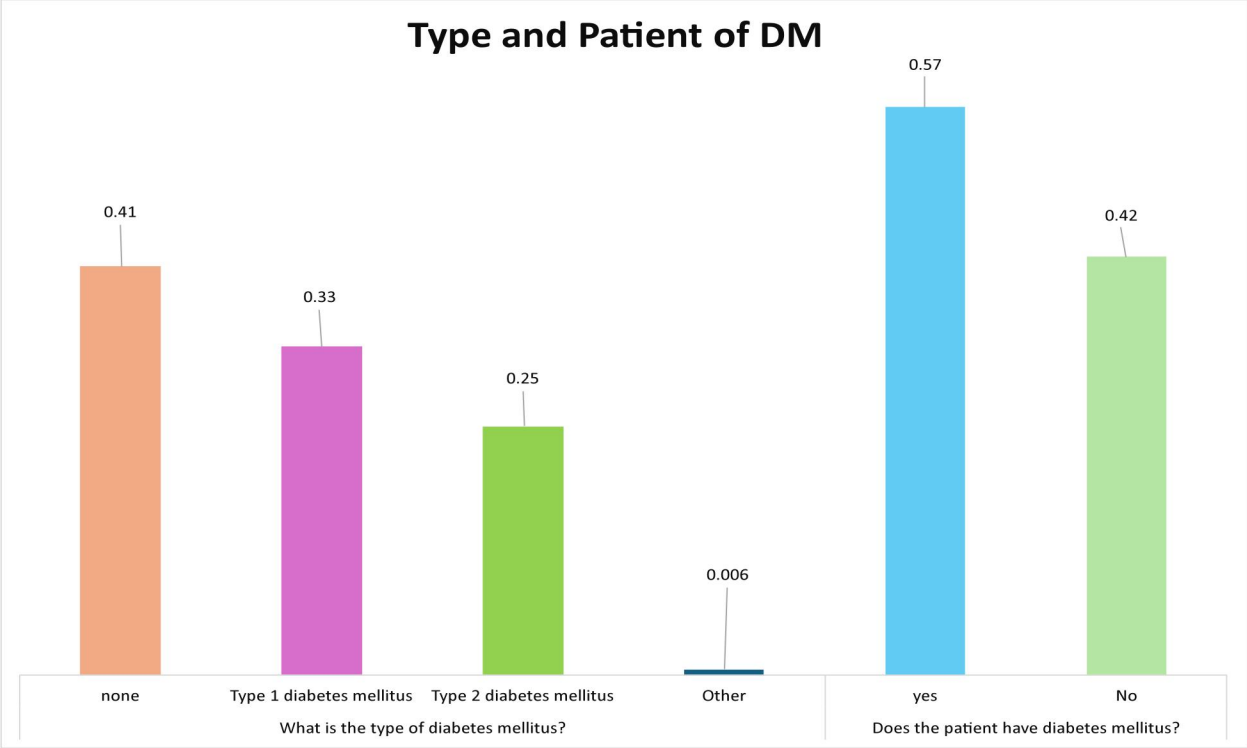


Figure 4.4. DM and Type of DM Wise Distribution

4.5. Risk factors Wise Distribution

Among the 246 study participants, **128 (52%)** had **hypertension**, while **117 (48%)** did not have hypertension. This indicates that slightly more than half of the participants were hypertensive, suggesting a high prevalence of hypertension within the study population.

Table 4.5: Distribution of hypertension in study participants

Does the patient have hypertension?				
	Frequency	Percent	Valid Percent	Cumulative Perce
No	117	48	48	48
Yes	128	52	52	100
Total	246	100	100	

Among the 246 study participants, 126 (51%) reported having a family history of diabetes or cardiovascular disease, while 117 (48%) reported no such family history. This indicates that slightly more than half of the participants had a positive family history of these chronic conditions.

Vol. 5 No. 1 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Table 4.5: *Distribution of family history in study participants*

Does the patient have a family history of diabetes or cardiovascular disease?

	Frequency	Percent	Valid Percent	Cumulative Percent
No	117	48	48	49
Yes	126	51	51	100
Total	246	100	100	

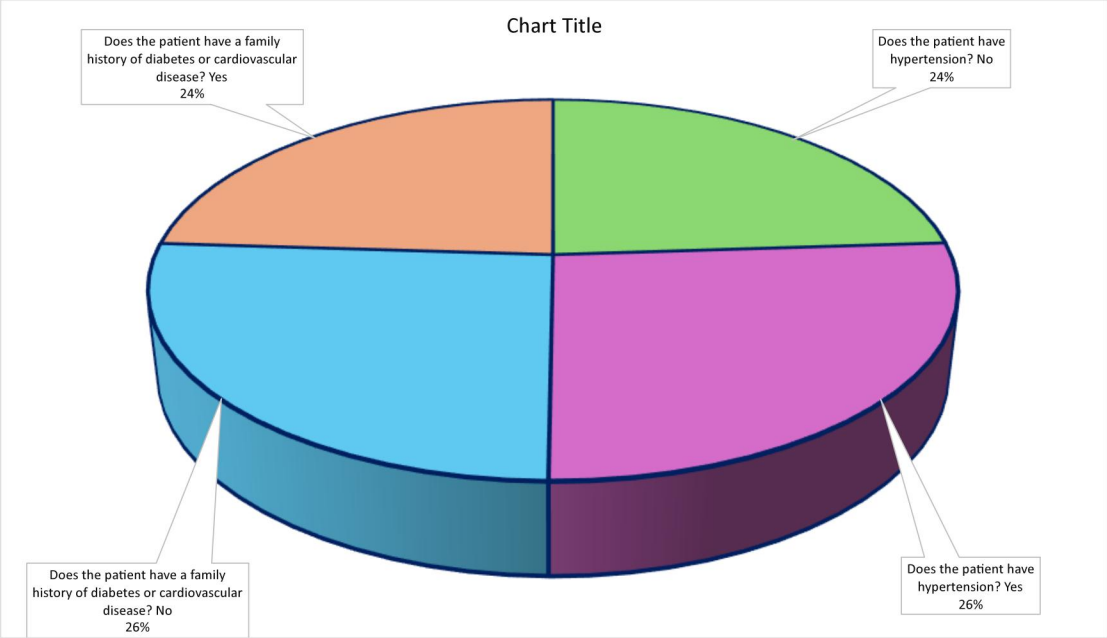


Figure 4.5: Distribution of family history and hypertension among study participants

Discussion

This chapter concludes that diabetes mellitus is highly prevalent among heart failure patients admitted to tertiary care hospitals of Peshawar. The findings show that the study population was almost equally distributed by gender, with males representing 52% and females 48% of the participants. This near-balanced gender distribution strengthens the relevance of the findings for both male and female heart failure patients, although male patients were slightly more represented in the sample. The age profile indicates that most participants were middle-aged and older adults. The largest group was aged 41–60 years, comprising 68% of the sample, followed by the 61–80-year age group at 20%. The overall mean age was 51 years, with participants ranging from 22 to 80 years. This suggests that heart failure and diabetes-related clinical conditions were more common among middle-aged and elderly patients. The relatively smaller

proportion of younger adults indicates that age remains an important clinical factor in the assessment and management of cardiovascular and metabolic diseases.

Clinical findings further show that a majority of the participants had echocardiography-based evidence of heart failure. About 63% of patients were diagnosed with heart failure, while 36% were not confirmed through echocardiography. Regarding ejection fraction, the largest proportion of patients fell into the HFmEF category, followed by HFpEF and HFrEF. This indicates that mildly reduced and preserved ejection fraction were more common than severely reduced ejection fraction among the study participants. The findings also reveal a considerable burden of diabetes mellitus among heart failure patients. More than half of the participants, 54%, were diabetic, while 44% were non-diabetic. Among diabetes types, type 1 diabetes mellitus was the most frequently reported category, followed by type 2 diabetes mellitus. This highlights the importance of routine diabetes screening among heart failure patients, as diabetes may worsen cardiovascular outcomes and complicate clinical management.

The presence of associated risk factors further strengthens the clinical importance of the study. Hypertension was reported among 51.9% of patients, while 48.1% had a family history of diabetes or cardiovascular disease. These findings indicate that heart failure patients in this sample commonly had overlapping metabolic and cardiovascular risk factors. aFinally, the study concludes that diabetes mellitus, hypertension, family history, age, and cardiac dysfunction are important clinical features among heart failure patients in tertiary care hospitals of Peshawar. The findings emphasize the need for early diagnosis, regular blood pressure and glucose monitoring, echocardiographic assessment, and integrated management strategies. A combined approach addressing both cardiovascular and metabolic risk factors may help improve patient outcomes, reduce disease complications, and support better clinical decision-making in heart failure care.

Limitations

The following are the limitations of our study.

First, the diagnosis of heart failure and related cardiac changes was based primarily on echocardiography, without incorporating additional diagnostic modalities such as ECG, MRI, or CT scan, which may have provided more detailed assessment. Second, the study did not fully adjust for the influence of comorbid conditions such as diabetes mellitus, dyslipidaemia, and chronic kidney disease, which may affect the severity and progression of heart failure. Third, the study was conducted in selected tertiary care

hospitals of Peshawar, which may limit the generalizability of the findings to the broader population.

Recommendations

Gender-Specific Screening Strategies:

Based on the study topic, Gender Based Prevalence of Diabetes Mellitus in Heart Failure Patients, it is recommended that hospitals implement gender-focused screening programs. Early identification of diabetes in both male and female heart failure patients can improve risk stratification and clinical outcomes.

Routine Screening for Diabetes in Heart Failure Patients:

All patients diagnosed with heart failure should undergo regular screening for diabetes mellitus, as co-existence of these conditions is common and significantly affects prognosis. Early detection can help in timely management and prevention of complications.

Lifestyle Modification Programs:

Community-based health education programs should be strengthened to promote healthy lifestyle practices including regular physical activity, balanced diet, weight control, and avoidance of sedentary behaviour. These interventions should target both diabetic and heart failure patients.

Regular Monitoring and Follow-Up:

Patients with coexisting heart failure and diabetes mellitus should be placed under strict follow-up schedules to monitor disease progression, treatment response, and complication development.

Further Multi-Centre and Longitudinal Studies:

Future research should be conducted on a larger scale across multiple hospitals with a longitudinal design to better understand gender-based differences and long-term outcomes in diabetic heart failure patients.

Conclusion

This study assessed the prevalence of diabetes mellitus among heart failure patients in tertiary care hospitals of Peshawar along with key clinical and demographic factors. The results showed a nearly equal gender distribution, with most patients in the 41–60 years age group. Diabetes mellitus was highly prevalent among heart failure patients, indicating a strong coexistence of metabolic and cardiovascular disease. HFmrEF was the most common heart failure subtype, followed by HFpEF and HFrEF. Hypertension and a positive family history of diabetes or cardiovascular disease were also frequently observed. Overall, the findings highlight a high burden of diabetes and cardiovascular

risk factors in heart failure patients, emphasizing the need for early screening, integrated management, and risk factor control to improve clinical outcomes.

References

1. American Diabetes Association Professional Practice Committee. (2024). Classification and diagnosis
2. Anderson, R. H., Razavi, R., & Taylor, A. M. (2004). Cardiac anatomy revisited. Journal of Anatomy, 205(3), 159–177.
3. Anker, S. D., Butler, J., Filippatos, G., Ferreira, J. P., Bocchi, E., Böhm, M., Brunner-La Rocca, H. P., Choi, D. J., Chopra, V., Chuquiure-Valenzuela, E., Giannetti, N., Gomez-Mesa, J. E., Janssens, S., Januzzi, J. L., Gonzalez-Juanatey, J. R., Merkely, B., Nicholls, S. J., Perrone, S. V., Piña, I. L., … Packer, M. (2021). Empagliflozin in heart failure with a preserved ejection fraction. New England Journal of Medicine, 385(16), 1451–1461.
4. Aune, D., Schlesinger, S., Norat, T., & Riboli, E. (2019). Smoking, smoking cessation, and the risk of heart failure: A systematic review and meta-analysis. European Journal of Preventive Cardiology, 26(3), 279–288.
5. Bauersachs, J., König, T., van der Meer, P., Petrie, M. C., Hilfiker-Kleiner, D., Mbakwem, A., Hamdan, R., Jackson, A. M., Forsyth, P., de Boer, R. A., Mueller, C., Lyon, A. R., Lund, L. H., Piepoli, M. F., Heymans, S., Chioncel, O., Anker, S. D., Ponikowski, P., Seferovic, P. M., … Sliwa, K. (2019). Pathophysiology, diagnosis and management of peripartum cardiomyopathy: A position statement from the Heart Failure Association of the European Society of Cardiology. European Journal of Heart Failure, 21(7), 827–843.
6. Bauters, C., Lamblin, N., Mc Fadden, E. P., Van Belle, E., Millaire, A., & De Groote, P. (2003). Influence of diabetes mellitus on heart failure risk and outcome. Cardiovascular diabetology, 2(1), 1.
7. Bauters, C., Lamblin, N., Mc Fadden, E. P., Van Belle, E., Millaire, A., & de Groote, P. (2003). Influence of diabetes mellitus on heart failure risk and outcome. Cardiovascular Diabetology, 2, Article 1.
8. Bers, D. M. (2002). Cardiac excitation–contraction coupling. Nature, 415(6868), 198–205.
9. Borlaug, B. A. (2020). Evaluation and management of heart failure with preserved ejection fraction. Nature Reviews Cardiology, 17, 559–573.
10. Chaudhry, R., Miao, J. H., & Rehman, A. (2022). Physiology, cardiovascular. In StatPearls. StatPearls Publishing.
11. Conrad, N., Judge, A., Tran, J., Mohseni, H., Hedgecott, D., Crespillo, A. P., Allison, M., Hemingway, H., Cleland, J. G., McMurray, J. J. V., & Rahimi, K. (2018). Temporal

trends and patterns in heart failure incidence: A population-based study of 4 million individuals. The Lancet, 391(10120), 572–580.

12. DeFronzo, R. A., Ferrannini, E., Groop, L., Henry, R. R., Herman, W. H., Holst, J. J., Hu, F. B., Kahn, C. R., Raz, I., Shulman, G. I., Simonson, D. C., Testa, M. A., & Weiss, R. (2015). Type 2 diabetes mellitus. Nature Reviews Disease Primers, 1, Article 15019.
13. Delco, C., et al. (2023). Full source details not available in the provided text. Please verify the article title, journal name, volume, issue, pages, and DOI before final submission.
14. Dewan, P., et al. (2019). Full source details not available in the provided text. Please verify the article title, journal name, volume, issue, pages, and DOI before final submission.
15. Dokainish, H., Teo, K., Zhu, J., Roy, A., AlHabib, K. F., ElSayed, A., Palileo-Villanueva, L., Lopez-Jaramillo, P., Karaye, K., Yusoff, K., Orlandini, A., Sliwa, K., Mondo, C., Lanas, F., Khatib, R., Temizhan, A., Kruger, A., Badr, A., Elmaghawry, M., … Yusuf, S. (2017). Global mortality variations in patients with heart failure: Results from the International Congestive Heart Failure prospective cohort study. The Lancet Global Health, 5(7), e665–e672.
16. Drake, R. L., Vogl, A. W., & Mitchell, A. W. M. (2020). Gray's anatomy for students (4th ed.). Elsevier.
17. Duncker, D. J., & Bache, R. J. (2008). Regulation of coronary blood flow during exercise. Physiological Reviews, 88(3), 1009–1086.
18. Dunlay, S. M., Givertz, M. M., Aguilar, D., Allen, L. A., Chan, M., Desai, A. S., Deswal, A., Dickson, V. V., Kosiborod, M. N., Lekavich, C. L., McCoy, R. G., Mentz, R. J., Piña, I. L., & American Heart Association Heart Failure and Transplantation Committee. (2019). Type 2 diabetes mellitus and heart failure: A scientific statement from the American Heart Association and the Heart Failure Society of America. Circulation, 140(7), e294–e324.
19. Dunlay, S. M., Roger, V. L., & Redfield, M. M. (2017). Epidemiology of heart failure with preserved ejection fraction. Nature Reviews Cardiology, 14, 591–602.
20. Floras, J. S. (2009). Sympathetic nervous system activation in human heart failure: Clinical implications of an updated model. Journal of the American College of Cardiology, 54(5), 375–385.
21. Forbes, J. M., & Cooper, M. E. (2013). Mechanisms of diabetic complications. Physiological Reviews, 93(1), 137–188.
22. Groenewegen, A., Rutten, F. H., Mosterd, A., & Hoes, A. W. (2020). Epidemiology of heart failure. European Journal of Heart Failure, 22(8), 1342–1356.

23. Habal, M. V., et al. (2021). Full source details not available in the provided text. Please verify the article title, journal name, volume, issue, pages, and DOI before final submission.
24. Hall, J. E. (2021). Guyton and Hall textbook of medical physiology (14th ed.). Elsevier.
25. Heidenreich, P. A., Bozkurt, B., Aguilar, D., Allen, L. A., Byun, J. J., Colvin, M. M., Deswal, A., Drazner, M. H., Dunlay, S. M., Evers, L. R., Fang, J. C., Fedson, S. E., Fonarow, G. C., Hayek, S. S., Hernandez, A. F., Khazanie, P., Kittleson, M. M., Lee, C. S., Link, M. S., … Yancy, C. W. (2022). 2022 AHA/ACC/HFSA guideline for the management of heart failure. Circulation, 145(18), e895–e1032.
26. Heidenreich, P. A., Bozkurt, B., Aguilar, D., Allen, L. A., Byun, J. J., Colvin, M. M., Deswal, A., Drazner, M. H., Dunlay, S. M., Evers, L. R., Fang, J. C., Fedson, S. E., Fonarow, G. C., Hayek, S. S., Hernandez, A. F., Khazanie, P., Kittleson, M. M., Lee, C. S., Link, M. S., … Yancy, C. W. (2022). 2022 AHA/ACC/HFSA guideline for the management of heart failure. Circulation, 145(18), e895–e1032.
27. International Diabetes Federation. (2021). IDF diabetes atlas (10th ed.). International Diabetes Federation.
28. Jaarsma, T., Hill, L., Bayes-Genis, A., La Rocca, H. P. B., Castiello, T., Čelutkienė, J., Marques-Sule, E., Plymen, C. M., Piper, S. E., Riegel, B., Rutten, F. H., Ben Gal, T., Bauersachs, J., Coats, A. J. S., Chioncel, O., Lopatin, Y., Lund, L. H., Lainscak, M., Moura, B., … Strömberg, A. (2021). Self-care of heart failure patients: Practical management recommendations from the Heart Failure Association of the European Society of Cardiology. European Journal of Heart Failure, 23(1), 157–174.
29. Jia, G., Hill, M. A., & Sowers, J. R. (2018). Diabetic cardiomyopathy: An update of mechanisms contributing to this clinical entity. Circulation Research, 122(4), 624–638.
30. Jia, G., Hill, M. A., & Sowers, J. R. (2018). Diabetic cardiomyopathy: An update of mechanisms contributing to this clinical entity. Circulation Research, 122(4), 624–638.
31. Kannel, W. B., & McGee, D. L. (1979). Diabetes and cardiovascular disease: The Framingham study. JAMA, 241(19), 2035–2038.
32. Kawashima, T. (2005). The autonomic nervous system of the human heart with special reference to its origin, course, and peripheral distribution. Anatomy and Embryology, 209, 425–438.
33. Khandaker, Masud H., et al. "Pericardial disease: diagnosis and management." Mayo Clinic Proceedings. Vol. 85. No. 6. Elsevier, 2010.
34. Khatib, R., McKee, M., Shannon, H., Chow, C., Rangarajan, S., Teo, K., Wei, L., Mony, P., Mohan, V., Gupta, R., Kumar, R., Vijayakumar, K., Lear, S. A., Diaz, R., Avezum, A., Lopez-Jaramillo, P., Lanas, F., Yusoff, K., Ismail, N., … Yusuf, S. (2016). Availability and

affordability of cardiovascular disease medicines and their effect on use in high-income, middle-income, and low-income countries: An analysis of the PURE study data. The Lancet, 387(10013), 61–69.

35. Kim, H-L., et al. "Gender difference in the impact of coexisting diabetes mellitus on long-term clinical outcome in people with heart failure: a report from the Korean Heart Failure Registry." Diabetic Medicine 36.10 (2019):
36. Klabunde, R. E. (2021). Cardiovascular physiology concepts (3rd ed.).
37. Kotecha, D., & Piccini, J. P. (2015). Atrial fibrillation in heart failure: What should we do? European Heart Journal, 36(46), 3250–3257.
38. Lam, C. S. P., Arnott, C., Beale, A. L., Chandramouli, C., Hilfiker-Kleiner, D., Kaye, D. M., Ky, B., Santema, B. T., Sliwa, K., & Voors, A. A. (2019). Sex differences in heart failure. European Heart Journal, 40(47), 3859–3868.
39. Lehrke, M., & Marx, N. (2017). Diabetes mellitus and heart failure. The American journal of cardiology, 120(1), S37-S47.
40. Lehrke, M., & Marx, N. (2017). Diabetes mellitus and heart failure. American Journal of Cardiology, 120(1 Suppl), S37–S47. Please verify DOI before final submission.
41. Little, W. C., & Freeman, G. L. (2006). Pericardial disease. Circulation, 113(12), 1622-1632.
42. Loukas, M., Bilinsky, S., Bilinsky, E., El-Sedfy, A., Anderson, R. H., & Cardoso, H. F. V. (2009). The clinical anatomy of the coronary arteries. Journal of Cardiothoracic Surgery, 4, Article 61.
43. McDonagh, T. A., Metra, M., Adamo, M., Gardner, R. S., Baumbach, A., Böhm, M., Burri, H., Butler, J., Čelutkienė, J., Chioncel, O., Cleland, J. G. F., Coats, A. J. S., Crespo-Leiro, M. G., Farmakis, D., Gilard, M., Heymans, S., Hoes, A. W., Jaarsma, T., Jankowska, E. A., ... Skibelund, A. K. (2021). 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal, 42(36), 3599–3726.
44. McDonagh, T. A., Metra, M., Adamo, M., Gardner, R. S., Baumbach, A., Böhm, M., Burri, H., Butler, J., Čelutkienė, J., Chioncel, O., Cleland, J. G. F., Coats, A. J. S., Crespo-Leiro, M. G., Farmakis, D., Gilard, M., Heymans, S., Hoes, A. W., Jaarsma, T., Jankowska, E. A., ... Skibelund, A. K. (2021). 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal, 42(36), 3599–3726.
45. Mills, K. T., Bundy, J. D., Kelly, T. N., Reed, J. E., Kearney, P. M., Reynolds, K., Chen, J., & He, J. (2016). Global disparities of hypertension prevalence and control: A systematic analysis of population-based studies from 90 countries. Circulation, 134(6), 441–450.

46. Moore, K. L., Dalley, A. F., & Agur, A. M. R. (2023). Clinically oriented anatomy (9th ed.). Wolters Kluwer.
47. Obokata, M., Reddy, Y. N. V., Pislaru, S. V., Melenovsky, V., & Borlaug, B. A. (2017). Evidence supporting the existence of a distinct obese phenotype of heart failure with preserved ejection fraction. Circulation, 136(1), 6–19
48. Ohkuma, T., Komorita, Y., Peters, S. A. E., & Woodward, M. (2019). Diabetes as a risk factor for heart failure in women and men: A systematic review and meta-analysis of 47 cohorts including 12 million individuals. Diabetologia, 62, 1550–1560
49. Owan, T. E., Hodge, D. O., Herges, R. M., Jacobsen, S. J., Roger, V. L., & Redfield, M. M. (2006). Trends in prevalence and outcome of heart failure with preserved ejection fraction. New England Journal of Medicine, 355(3), 251–259
50. Pandey, A., et al. (2017). Full source details not available in the provided text. Please verify the article title, journal name, volume, issue, pages, and DOI before final submission.
51. Pandey, A., Garg, S., Khunger, M., Darden, D., Ayers, C., Kumbhani, D. J., Mayo, H. G., de Lemos, J. A., & Berry, J. D. (2015). Dose-response relationship between physical activity and risk of heart failure: A meta-analysis. Circulation, 132(19), 1786–1794.
52. Pieske, B., Tschöpe, C., de Boer, R. A., Fraser, A. G., Anker, S. D., Donal, E., Edelmann, F., Fu, M., Guazzi, M., Lam, C. S. P., Lancellotti, P., Melenovsky, V., Morris, D. A., Nagel, E., Pieske-Kraigher, E., Ponikowski, P., Solomon, S. D., Vasan, R. S., Rutten, F. H., & Voors, A. A. (2019). How to diagnose heart failure with preserved ejection fraction: The HFA–PEFF diagnostic algorithm. European Heart Journal, 40(40), 3297–3317.
53. Popkin, B. M., Corvalan, C., & Grummer-Strawn, L. M. (2020). Dynamics of the double burden of malnutrition and the changing nutrition reality. The Lancet, 395(10217), 65–74.
54. Riedinger, M. S., Dracup, K. A., Brecht, M. L., Padilla, G., Sarna, L., & Ganz, P. A. (2001). Quality of life in patients with heart failure: Do gender differences exist? Heart & Lung, 30(2), 105–116. Please verify DOI before final submission.
55. Rosano, G. M. C., Vitale, C., & Seferovic, P. (2017). Heart failure in patients with diabetes mellitus. Cardiac Failure Review, 3(1), 52–55.
56. Santema, B. T., Ouwerkerk, W., Tromp, J., Sama, I. E., Ravera, A., Regitz-Zagrosek, V., Hillege, H., Samani, N. J., Zannad, F., Dickstein, K., Lang, C. C., Ng, L. L., Anker, S. D., Metra, M., ter Maaten, J. M., Cleland, J. G., Givertz, M. M., van Veldhuisen, D. J., Metra, M., … Voors, A. A. (2019). Identifying optimal doses of heart failure medications in men compared with women: A prospective, observational, cohort study. The Lancet, 394(10205), 1254–1263.

57. Savarese, G., Becher, P. M., Lund, L. H., Seferovic, P., Rosano, G. M. C., & Coats, A. J. S. (2023). Global burden of heart failure: A comprehensive and updated review of epidemiology. Cardiovascular Research, 118(17), 3272–3287.
58. Scott, P. E., Unger, E. F., Jenkins, M. R., Southworth, M. R., McDowell, T. Y., Geller, R. J., Elahi, M., Temple, R. J., & Woodcock, J. (2018). Participation of women in clinical trials supporting FDA approval of cardiovascular drugs. Journal of the American College of Cardiology, 71(18), 1960–1969. Please verify DOI before final submission.
59. Seferović, P. M., Petrie, M. C., Filippatos, G. S., Anker, S. D., Rosano, G. M. C., Bauersachs, J., Paulus, W. J., Komajda, M., Cosentino, F., de Boer, R. A., Farmakis, D., Doehner, W., Lambrinou, E., Lopatin, Y., Piepoli, M. F., Theodorakis, M. J., Wiggers, H., Lekakis, J., Mebazaa, A., … McMurray, J. J. V. (2018). Type 2 diabetes mellitus and heart failure: A position statement from the Heart Failure Association of the European Society of Cardiology. European Journal of Heart Failure, 20(5), 853–872.
60. Seghieri, Chiara, et al. "Gender effect on the relation between diabetes and hospitalization for heart failure." Experimental and clinical endocrinology & diabetes 120.01 (2012): 51-55.
61. Sequeira, V., & van der Velden, J. (2015). Historical perspective on heart function: The Fran
62. Sliwa, K., et al. (2014). Full source details not available in the provided text. Please verify the article title, journal name, volume, issue, pages, and DOI before final submission.
63. Sliwa, K., Hilfiker-Kleiner, D., Petrie, M. C., Mebazaa, A., Pieske, B., Buchmann, E., Regitz-Zagrosek, V., Schaufelberger, M., Tavazzi, L., van Veldhuisen, D. J., Watkins, H., Shah, A. J., Seferovic, P. M., Elkayam, U., & Pankuweit, S. (2010). Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy. European Journal of Heart Failure, 12(8), 767–778
64. Solomon, S. D., McMurray, J. J. V., Claggett, B., de Boer, R. A., DeMets, D., Hernandez, A. F., Inzucchi, S. E., Kosiborod, M. N., Lam, C. S. P., Martinez, F., Shah, S. J., Desai, A. S., Jhund, P. S., Belohlavek, J., Chiang, C. E., Borleffs, C. J. W., Comin-Colet, J., Dobreanu, D., Drozdz, J., … Vaduganathan, M. (2022). Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. New England Journal of Medicine, 387(12), 1089–1098.
65. Standring, S. (Ed.). (2020). Gray's anatomy: The anatomical basis of clinical practice (42nd ed.). Elsevier.
66. Starling law. Biophysical Reviews, 7(4), 421–447..

67. Taylor, R. S., Long, L., Mordi, I. R., Madsen, M. T., Davies, E. J., Dalal, H., Rees, K., Singh, S. J., & Gluud, C. (2019). Exercise-based rehabilitation for heart failure. Cochrane Database of Systematic Reviews, 2019(4), Article CD003331.
68. Tousoulis, D., Oikonomou, E., Siasos, G., & Stefanadis, C. (2014). Diabetes mellitus and heart failure. European Cardiology Review. Full volume, issue, page range, and DOI need verification before final submission.
69. Virani, S. S., Alonso, A., Aparicio, H. J., Benjamin, E. J., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Cheng, S., Delling, F. N., Elkind, M. S. V., Evenson, K. R., Ferguson, J. F., Gupta, D. K., Khan, S. S., Kissela, B. M., Knutson, K. L., Lee, C. D., Lewis, T. T., … Tsao, C. W. (2021). Heart disease and stroke statistics—2021 update: A report from the American Heart Association. Circulation, 143(8), e254–e743.
70. Walli-Attaei, Marjan, et al. "Health-related quality of life and healthcare costs of symptoms and cardiovascular disease events in patients with atrial fibrillation: a longitudinal analysis of 27 countries from the EURObservational Research Programme on Atrial Fibrillation general long-term registry." Europace 26.6 (2024).
71. Wolters Kluwer. Pappano, A. J., & Wier, W. G. (2019). Cardiovascular physiology (11th ed.). Elsevier.
72. World Health Organization. (2020). WHO package of essential noncommunicable disease interventions for primary health care. World Health Organization. Please verify edition/report title before final submission.
73. Zusterzeel, R., Spatz, E. S., Curtis, J. P., Sanders, W. E., Selzman, K. A., Piña, I. L., Bao, H., Ponirakis, A., Varosy, P. D., Masoudi, F. A., & Canos, D. A. (2014). Cardiac resynchronization therapy in women: US Food and Drug Administration meta-analysis of patient-level data. JAMA Internal Medicine, 174(8), 1340–1348.
74. Palazzuoli, A. and Iacoviello, M. (2023) “Diabetes leading to heart failure and heart failure leading to diabetes : epidemiological and clinical evidence,” Heart Failure Reviews, 28(3), pp. 585–596. Available at: https://doi.org/10.1007/s10741-022-10238-6.