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Corresponding Author:

Dr. Sameer Abdul Rauf, Liaquat National Medical College, Karachi, Pakistan.

Email: sameerrauf80@gmail.com

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Original Article

Clinical and Angiographic Differences among Male and Female Patients Presenting with Heart Failure with Reduced Ejection Fraction

Samina Yaqoob¹, Ghulam Abbas Shaikh¹, Hussain Haider Shah², Muhammad Abdul Wasay Zuberi², Hasan Tariq², Radeyah Waseem², Sameer Abdul Rauf³

¹Dr Ruth KM Pfau Civil Hospital, Karachi, Pakistan, ²Dow University of Health Sciences, Karachi, Pakistan, ³Liaquat National Medical College, Karachi, Pakistan

Abstract

Objectives: This study investigates the clinical characteristics and angiographic differences between male and female patients diagnosed with Heart Failure with Reduced Ejection Fraction (HFrEF) at Civil Hospital Karachi, with a focus on gender-related disparities in risk factors and treatment outcomes.

Methodology: Conducted from October 2023 to March 2024, this observational study included 150 hospitalized patients (61 females and 89 males) aged 20 to 70 years, who presented with HFrEF and had no prior history of coronary artery disease. Data were collected on demographic information, comorbidities, risk factors, and angiographic findings. Statistical analyses were performed to assess gender differences in clinical presentations and treatment strategies.

Results: Of the 150 patients, 61 (40.7%) were female, and 89 (59.3%) were male, with a median age of 56.0 years (range: 22 to 78 years, SD = 11.36). A total of 81 patients had diabetes, of which 62 had uncontrolled diabetes; 139 patients were hypertensive, with 86 experiencing uncontrolled hypertension. The study revealed significant gender differences in angiographic findings ($p < 0.001$), severity of coronary artery disease (CAD) ($p < 0.001$), and treatment modalities following left heart catheterization ($p = 0.003$). Males exhibited a higher prevalence of multi-vessel disease and obstructive CAD compared to females.

Conclusion: The findings of this study highlight notable gender-specific differences in the clinical presentation and angiographic outcomes of patients with HFrEF. These results emphasize the importance of considering gender when evaluating risk factors and tailoring treatment strategies in heart failure management, ultimately aiming for improved patient care and outcomes.

Keywords: Heart Failure, Reduced Ejection Fraction, HFrEF, Gender Differences, Angiographic Findings

INTRODUCTION

Heart failure (HF) is a highly morbid condition with a growing global prevalence, currently affecting over 23 million people worldwide [1]. In Pakistan, the burden of cardiovascular diseases, including heart failure, is substantial. The Global Burden of Disease study in 2019 estimated an age-standardized incidence rate of 918.18 per 100,000 population for cardiovascular diseases in the country, underscoring the critical public health challenge [2]. A recent cross-sectional observational survey conducted across 100 healthcare facilities in Pakistan found that 25.9% of patients with heart failure had moderate left ventricular dysfunction (ejection fraction between 30% and 39%), while 29.1% had severe dysfunction (ejection fraction below 30%) [3]. The same study revealed that nearly half (46.9%) of these patients were classified in New York Heart Association (NYHA) Class II, followed by 33.0% in Class III, and 20.1% in the most severe Class IV category [3].

Heart failure is commonly categorized based on left ventricular ejection fraction (LVEF), which helps differentiate between various forms of the condition [4]: Heart Failure with Reduced Ejection Fraction (HFrEF) – LVEF <40%, Heart Failure with Mid-Range Ejection Fraction (HFmrEF) – LVEF between 40–50%, Heart Failure with Preserved Ejection Fraction (HFpEF) – LVEF >50%.

A meta-analysis has shown that while patients with HFpEF tend to have a lower risk of death compared to those with HFrEF, their absolute mortality remains high [5]. In Pakistan, heart failure primarily arises from ischemic heart disease, hypertension, valvular heart disease, and cardiomyopathies [6]. Despite ongoing efforts to strengthen cardiac care, the infrastructure remains insufficient. Currently, there are only around 130 cardiac catheterization laboratories nationwide, and just 36 of these provide 24/7 primary percutaneous coronary intervention (PCI) services, highlighting the gaps in access to timely care [2].

Gender disparities in heart failure have also been recognized globally. Studies have shown that women with heart failure tend to experience delays in seeking medical care, receive less intensive medical intervention, and face longer times to diagnosis compared to men [7,8]. These gender-based differences may contribute to variations in disease

progression, management, and outcomes between male and female patients.

While there is substantial evidence on sex differences in general cardiovascular disease, whether these disparities exist in patients with heart failure and reduced ejection fraction (HFrEF) remains insufficiently explored. To address this gap, our study aims to investigate sex-based differences in patients with HFrEF presenting at Civil Hospital Karachi, focusing on clinical presentation, risk factors, and treatment strategies.

METHODOLOGY

Study Design: This was a hospital-based, cross-sectional study conducted to assess specific clinical parameters related to heart failure with reduced ejection fraction (HFrEF). The study was carried out at the Civil Hospital Karachi (CHK), a major public sector hospital, from October 2023 to March 2024. An enumerative non-probability sampling technique was employed for participant selection. The design allowed for the prospective collection of clinical data, ensuring that all participants met pre-defined inclusion and exclusion criteria.

Ethics: The study followed the ethical guidelines outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB) of Dow University of Health Sciences, under the reference number IRB-3198/DUHS/2023/396. All participants provided informed consent, which was documented through a signed written agreement. Confidentiality was maintained throughout the study, with restricted access to participant data and careful data handling to protect privacy.

Setting: The research was conducted at Civil Hospital Karachi, specifically within the Cardiology Department. This hospital serves a diverse patient population and is a recognized center for cardiovascular care. The setting allowed for access to a wide range of patients diagnosed with heart failure, enabling a comprehensive data collection process. All patients included in the study underwent echocardiography and angiography at the hospital's facilities.

Participants: The study population consisted of adult patients aged between 20 and 70 years who were

diagnosed with heart failure with reduced ejection fraction (HFrEF). Inclusion criteria were strict to ensure homogeneity of the study sample: only patients with an ejection fraction (EF) \leq 40% were included. Additionally, all participants were required to have no history of coronary artery disease (CAD) or prior revascularization surgery. Exclusion criteria were equally specific, excluding patients with significant valvular diseases such as more than moderate primary mitral regurgitation, mitral stenosis, aortic stenosis, aortic regurgitation, prosthetic valves, or those with end-stage renal disease (eGFR $<$ 30 ml/min/1.73m²). Furthermore, patients with hepatitis (Child-Pugh C), congenital heart disease, and peripartum cardiomyopathy were not included in the study.

Variables: The primary outcome variable was the ejection fraction (EF), which was measured using biplanar Simpson's method via echocardiography. Secondary variables included age, gender, presence or absence of valvular disease, and kidney function assessed through estimated glomerular filtration rate (eGFR). A comprehensive medical history and physical examination were also recorded, which helped ensure the accuracy of the clinical diagnoses and ascertain the eligibility of the participants.

Data Sources/Measurements: Data were collected prospectively from patients admitted to the Cardiology Ward at Civil Hospital Karachi. All patients underwent echocardiography, and their ejection fraction was calculated using biplanar Simpson's method. Additionally, coronary angiography was performed to rule out coronary artery disease (CAD). Patient demographic data, clinical history, and physical examination findings were documented in a standardized data collection form. All diagnostic and procedural data were collected by trained cardiologists and health professionals to ensure accuracy and reliability.

Bias: To minimize selection bias, an enumerative non-probability sampling technique was used, ensuring that all eligible patients were included regardless of clinical presentation. Information bias was minimized by using standardized procedures for both the collection of clinical data and the performance of diagnostic tests, such as echocardiography and angiography. Furthermore, data collection forms were consistently used by the research team to ensure uniformity in recording patient information.

Study Size: The study was designed to include a sample size of approximately 200 patients over the six-month period. This sample size was determined based on an expected prevalence of heart failure in the general population and the number of eligible patients admitted to the hospital during the study timeframe. The aim was to achieve a statistically significant sample that would allow for meaningful conclusions about heart failure with reduced ejection fraction (HFrEF) in this population.

Quantitative Variables: Key quantitative variables included age, ejection fraction (EF), and estimated glomerular filtration rate (eGFR). These were recorded numerically and analyzed for trends and significance. Ejection fraction was assessed continuously, with a cutoff of \leq 40% being used to define heart failure with reduced ejection fraction (HFrEF). Other variables, such as gender, presence of valvular disease, and exclusion criteria like hepatitis status, were categorical.

Statistical Methods: Data were entered and analyzed using SPSS Version 24.0. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Categorical variables, such as gender and the presence of valvular disease, were reported as frequencies and percentages. For continuous variables like age and ejection fraction, the normality of data was assessed using the Shapiro-Wilk test. Based on the distribution of the data, either parametric (e.g., t-test) or non-parametric tests (e.g., Mann-Whitney U test) were used for comparisons between groups. Chi-square tests were employed for analyzing categorical variables. A p-value of less than 0.05 was considered statistically significant for all analyses.

RESULTS

Participants: A total of 150 patients diagnosed with heart failure with reduced ejection fraction (HFrEF) and no prior history of coronary artery disease (CAD) were enrolled in the study during the six-month period. The cohort comprised 61 females (40.7%) and 89 males (59.3%), reflecting a gender distribution that leaned slightly toward male patients. The median age of the participants was 56 years, with a wide age range spanning from 22 to 78 years. The non-normal age distribution was characterized by a standard deviation of 11.36 years. The patient population was

further categorized into distinct age groups for better interpretation: 2 patients were classified as young (20–30 years), 43 as middle-aged (31–50 years), 101 as elderly (51–70 years), and 4 as old-aged (>70 years). This distribution highlighted the demographic diversity among patients affected by HFrEF, underscoring its prevalence across different age categories.

Descriptive Data: Comorbidities and lifestyle factors were significant in this patient population. Diabetes mellitus was a prevalent comorbidity, affecting 81 patients (54%). Among these, 62 patients (76.5%) had uncontrolled diabetes, whereas 19 patients (23.5%) had well-controlled diabetes. Hypertension was another common condition, present in 139 patients (92.7%), with 86 individuals (61.9%) having uncontrolled hypertension, a critical factor in heart failure progression and exacerbation. Obesity was documented in 52 patients (34.7%), marking it as another major risk factor in this population.

Table 1: Data related to HFrEF and associated risk factors

	Female	Male	Total	p-value
Family history of Coronary Artery Disease (CAD)	20/61	21/89	41/150	0.215
Presence of Dyslipidemia	29/61	26/89	55/150	0.022
Baseline Troponin Levels Elevated but ECG Normal	17/61	25/89	42/150	0.976
Treatment after Left Heart Catheterization (LHC)				
Medical Management	36/61	26/89	62/150	0.003
Stent to Culprit artery	10/61	29/89	39/150	
Coronary Artery Bypass Graft (CABG)	15/61	32/89	47/150	
Percutaneous Old Balloon Angioplasty (POBA)	0/61	2/89	2/150	

Smoking habits were also assessed. A total of 49 patients (32.7%) were current smokers, 11 (7.3%) were ex-smokers, and 90 patients (60%) were non-smokers. Family history of CAD was reported in 41 patients (27.3%), with a slightly higher proportion in male patients (21 males, 20 females), although this difference was not statistically significant (p=0.215).

Table 1 below outlines the data on these risk factors, stratified by gender. Of note, dyslipidemia was

significantly more prevalent in females than males, with 29 females (47.5%) and 26 males (29.2%) affected (p=0.022). Elevated baseline troponin levels, despite a normal ECG, were noted in 42 patients (28%) with no significant gender difference (p=0.976).

Outcome Data: Following diagnostic evaluation and treatment decisions post-angiography, significant findings emerged in terms of the types and severity of CAD identified. Out of 150 patients, 55 (36.7%) presented with classical heart failure symptoms, and 47 (31.3%) were diagnosed with unstable angina. Other diagnostic findings included STEMI in 12 patients (8%), NSTEMI in 32 patients (21.3%), and stable angina in 4 patients (2.7%). The type of CAD diagnosed varied significantly between males and females, with unstable angina and NSTEMI more commonly seen in male patients, although this difference did not reach statistical significance (p=0.053).

Angiographic findings revealed that 44 patients (29.3%) had normal coronary arteries, while 106 patients (70.7%) had some form of coronary artery disease. Specifically, 27 patients (18%) were diagnosed with single vessel disease (SVD), 17 (11.3%) with two vessel disease (TVD), and 53 (35.3%) with three vessel disease (TVD), indicating a high prevalence of multivessel involvement. Notably, gender differences were significant in angiographic findings (p=0.00). Male patients were more likely to present with more severe forms of CAD, such as three vessel disease, while female patients had a higher proportion of non-obstructive or normal findings (31 out of 61 females, 44.3%).

Main Results: Gender-specific differences were significant in the study, particularly concerning angiographic findings, CAD severity, and post-LHC treatment strategies. As shown in Table 2, males exhibited more severe coronary artery involvement compared to females, with 38 males (42.7%) diagnosed with three vessel disease versus 15 females (24.6%). Males also had higher rates of obstructive CAD (67 males vs. 27 females, p=0.00), while females had a greater likelihood of non-obstructive CAD (26 females vs. 6 males, p=0.00).

Post-LHC treatment approaches differed significantly between genders (p=0.003). Medical management was more frequently employed for females (36

females vs. 26 males), whereas more aggressive interventions, such as coronary artery bypass grafting (CABG) and stent placement, were more commonly performed in males (32 males vs. 15 females for CABG; 29 males vs. 10 females for stent placement). These differences highlight the potential role of gender in guiding treatment decisions following diagnostic angiography.

Table 2: Diagnostic Criteria, Angiographic Findings, and CAD Severity by Gender

	Female	Male	Total	p-value
Diagnostic Criteria/ Type of CAD diagnosed				
Heart Failure Symptoms	21/61	34/89	55/150	
STEMI	2/61	10/89	12/150	0.053
Unstable Angina	19/61	28/89	47/150	
NSTEMI	15/61	17/89	32/150	
Stable Angina	4/61	0/89	4/150	
Angiographic Findings				
Single vessel disease	7/61	20/89	27/150	
Two vessel disease	4/61	13/89	17/150	
Three vessel disease	15/61	38/89	53/150	<0.001
Left main plus two vessel disease	4/61	5/89	9/150	
Normal	31/61	13/89	44/150	
Severity of Coronary Artery Disease (CAD)				
Non Obstructive CAD	26/61	6/89	32/150	
Obstructive CAD	27/61	67/89	94/150	<0.001
Heavily Calcified	0/61	5/89	5/150	
No Apparent CAD	8/61	11/89	19/150	

DISCUSSION

This study aimed to explore gender differences in the diagnosis, severity, and treatment of heart failure with reduced ejection fraction (HFrEF) in patients without prior coronary artery disease (CAD). The results reveal notable gender-based variations in the clinical presentation, distribution of risk factors, and treatment strategies, consistent with existing literature, while also presenting some unique findings specific to our cohort. Our cohort comprised 150 HFrEF patients, including 61 women (40.7%) and 89 men (59.3%), with a median age of 56 years and a wide age range (22 to 78 years). The inclusion of young, middle-aged, elderly, and old-aged patients highlights the broad age spectrum over which CAD and heart failure manifest, reaffirming that these conditions impact individuals across various life stages.

We found significant differences in the distribution of risk factors between men and women. Notably, women had higher rates of dyslipidemia, with 47.5%

of women affected compared to 29.21% of men ($p=0.022$). This is in line with findings from the Framingham Heart Study [9], which reported that women with CAD are more likely to have isolated hypertriglyceridemia, a specific form of dyslipidemia that elevates cardiovascular risk [10]. In contrast, men demonstrated a higher prevalence of multi-vessel disease and obstructive CAD, reflecting a more severe disease burden in terms of coronary artery involvement.

Interestingly, while 81 patients had diabetes, uncontrolled diabetes was more common in both genders (76.5% of diabetics), though no significant gender-specific trend was noted in the control of diabetes. Hypertension, on the other hand, was prevalent in 139 patients (92.7%), with 61.9% having uncontrolled blood pressure. While hypertension is a known risk factor for CAD, its higher prevalence in men, specifically uncontrolled hypertension, aligns with general knowledge that hypertension disproportionately affects males in the progression of cardiovascular disease [11,12].

Smoking, obesity, and family history of CAD were other significant risk factors in our cohort. A total of 49 patients were current smokers, and 52 patients were classified as obese, factors that compound cardiovascular risk. Although family history of CAD was noted in 41 patients, it did not reach statistical significance in terms of gender correlation ($p=0.215$). This is consistent with previous research indicating that while family history is a powerful predictor of CAD, gender does not significantly alter its influence [13].

In terms of diagnostic criteria, men were more likely to present with severe forms of CAD, such as STEMI or NSTEMI, while unstable angina was more evenly distributed between genders. However, the type of CAD diagnosed did not significantly vary by gender ($p=0.053$), supporting previous studies that have found similar trends in the clinical presentation of CAD between men and women. Despite this, the angiographic findings showed a significant gender disparity, with men being more likely to present with multi-vessel disease (62.92% of males vs. 37.7% of females; $p=0.00$), while women had a higher likelihood of normal or non-obstructive CAD. This finding aligns with a Saudi Arabian study that reported more vessel involvement in men [14].

The differences in the severity of CAD between men and women could be attributed to biological and hormonal factors. The protective effects of estrogen in premenopausal women, for instance, may delay the development of significant atherosclerosis, contributing to the higher rates of non-obstructive CAD in women. As estrogen levels decline with age, postmenopausal women may experience accelerated coronary artery disease progression, as suggested by the Australian Heart Eye Study, which reported a decline in normal coronary arteries in women aged 45–59 years compared to those aged 30–44 years [15].

Treatment decisions following left heart catheterization (LHC) also demonstrated significant gender-based differences ($p=0.003$). Women were more likely to receive medical management, while men were more often treated with invasive interventions, such as stent placement or coronary artery bypass grafting (CABG). These findings could reflect differences in disease severity, as men were more frequently diagnosed with multi-vessel disease and obstructive CAD. This is consistent with the global trend of more aggressive treatment for men with CAD, who tend to present with more advanced disease [16].

Moreover, while medical management was more common in women, studies suggest that women may derive similar, if not greater, benefits from guideline-directed medical therapy compared to men, particularly in cases of non-obstructive or stable CAD [17]. However, these differences in treatment raise concerns about potential gender biases in the management of CAD, as women have been historically under-treated compared to men, particularly in the setting of acute coronary syndromes. Further research is needed to determine whether these differences reflect appropriate clinical decision-making based on disease presentation or whether gender disparities in care persist despite efforts to improve equity.

Our findings are consistent with several large-scale studies that have identified gender differences in cardiovascular risk factors, disease severity, and outcomes. For example, the Iranian study from 2020 similarly found that hypertension was a more significant risk factor for ischemic heart disease (IHD) in men, while dyslipidemia and increased blood pressure were stronger predictors in women.

Moreover, the Australian Heart Eye Study reported a lower mean extent of coronary artery involvement in women compared to men, mirroring our findings of less severe angiographic findings in females [18].

However, our study contrasts with some prior research in terms of the lack of a statistically significant association between age and gender. While younger men in our cohort were more likely to present with CAD, we found no significant difference in the age distribution between men and women ($p=0.619$). This differs from a Canadian study that identified a higher prevalence of CAD in younger men compared to women [10].

Limitations: This study has several limitations that should be considered when interpreting the results. First, the sample size is relatively small, which may limit the generalizability of the findings. Additionally, the cross-sectional design limits our ability to infer causality, particularly in the relationship between gender and CAD outcomes. Further longitudinal studies are required to better understand how these gender differences evolve over time.

CONCLUSION

Our study demonstrates significant gender differences in the presentation, severity, and treatment of CAD in HFREF patients. While women were more likely to have non-obstructive CAD and receive medical management, men presented with more severe forms of CAD, requiring more invasive interventions. These findings underscore the importance of considering gender-specific factors in the diagnosis and treatment of heart failure and CAD. Tailoring treatment strategies to account for these differences could improve outcomes for both men and women.

AUTHORS' CONTRIBUTION

SY, GAS, HHS, MAWZ, HT, RW, and SAR: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. SY, GAS, HHS, MAWZ, HT, RW, and SAR: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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REFERENCES

1. Roger VL. Epidemiology of heart failure. *Circ Res*. 2013;113(6):646-59.
2. Samad Z, Hanif B. Cardiovascular Diseases in Pakistan: Imagining a Postpandemic, Postconflict Future. *Circulation*. 2023;147(17):1261-1263.
3. Memon AG, Khan MN, Naeem H, Mian FA, Khan MI, Ahmad F, et al. Prevalence of Severity-based Evaluation of Heart Failure (PROBE) and its Impact on Health-related Quality of Life: An Observational Study. *Pak Heart J*. 2023;56(3):219-23.
4. Harper AR, Patel HC, Lyon AR. Heart failure with preserved ejection fraction. *Clin Med*. 2018;18(2):s24-9.
5. Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. *Eur Heart J*. 2012;33(14):1750-7.
6. Khan Z, Khan B, Hiader I, Khan I, Din J, Khan H. Etiology of congestive heart failure at a tertiary care hospital. *RMJ*. 2010;35(2):141-4.
7. Lichtman JH, Leifheit-Limson EC, Watanabe E, Allen NB, Garavalia B, Garavalia LS, Spertus JA, Krumholz HM, Curry LA. Symptom recognition and healthcare experiences of young women with acute myocardial infarction. *Circ Cardiovasc Qual Outcomes*. 2015;8(2 Suppl 1):S31-8.
8. Zhai C, Fan H, Zhu Y, Chen Y, Shen L. Coronary functional assessment in non-obstructive coronary artery disease: Present situation and future direction. *Front Cardiovasc Med*. 2022;9:934279.
9. Gheisari F, Emami M, Raeisi Shahraki H, Samipour S, Nematollahi P. The role of gender in the importance of risk factors for coronary artery disease. *Cardiol Res Pract*. 2020;2020.
10. Chiha J, Mitchell P, Gopinath B, Plant AJ, Kovoor P, Thiagalingam A. Gender differences in the severity and extent of coronary artery disease. *IJC Heart Vasc*. 2015;8:161-6.
11. Hajar R. Risk factors for coronary artery disease: historical perspectives. *Heart views*. 2017;18(3):109-14.
12. Lloyd-Jones DM, Nam BH, D'Agostino Sr RB, Levy D, Murabito JM, Wang TJ, et al. Parental cardiovascular disease as a risk factor for cardiovascular disease in middle-aged adults: a prospective study of parents and offspring. *JAMA*. 2004;291(18):2204-11.
13. Hindieh W, Pilote L, Cheema A, Al-Lawati H, Labos C, Dufresne L, et al. Association between family history, a genetic risk score, and severity of coronary artery disease in patients with premature acute coronary syndromes. *Arterioscler Thromb Vasc Biol*. 2016;36(6):1286-92.
14. Lloyd-Jones DM, O'Donnell CJ, D'Agostino RB, Massaro J, Silbershatz H, Wilson PW. Applicability of cholesterol-lowering primary prevention trials to a general population: the Framingham Heart Study. *Arch Intern Med*. 2001;161(7):949-54.
15. Banks E, Welsh J, Joshy G, Martin M, Paige E, Korda RJ. Comparison of cardiovascular disease risk factors, assessment and management in men and women, including consideration of absolute risk: a nationally representative cross-sectional study. *BMJ open*. 2020;10(12):e038761.
16. Ko SH, Kim HS. Menopause-associated lipid metabolic disorders and foods beneficial for postmenopausal women. *Nutrients*. 2020;12(1):202.
17. Yousif N, Shahin M, Lüscher TF, Obeid S. Gender differences in types, frequency, clinical manifestations and atherosclerotic burden of coronary artery anomalies. *Rev Recent Clin Trials*. 2019;14(1):41-6.
18. Sayed AI. Gender Differences in Coronary Artery Disease, Clinical Characteristics, and Angiographic Features in the Jazan Region, Saudi Arabia. *Cureus*. 2022;14(10).