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Gender differences in Clinical Characteristics and Outcomes of Heart Failure with Reduced Ejection Fraction

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Abstract

Background and Objectives: Studies evaluating gender differences and outcomes in heart failure with reduced ejection fraction are limited in Iraq. The aim of this study was to assess the clinical characteristics, risk factors, outcomes and severity of heart failure with reduced ejection fraction in both genders.

Patients and Methods: This is a prospective cohort study of 117 patients aged more than 18 years who had been admitted to the Hawler Cardiac Center or medical ward with heart failure with reduced ejection fraction for the period from December 2021 till 30th of October 2022. The clinical characteristics, severity of left ventricular systolic dysfunction and the outcomes over three months were compared between women and men.

Results: One hundred seventeen patients were included in the study, 61 (52.1%) patients were male and 56 (47.9%) were female with male to female ration (1.09:1), p-value (0.017). Women presented with higher incidence of moderate left ventricular systolic dysfunction 36(64.2%), obesity 43 (76.8%) p-value=0.017*, dyslipidemia 27 (48.2%) p-value=0.038, pulmonary hypertension 4 (7.1%), atrial fibrillation 15(26.8%) and high cardiac hospitalization 12 (21.4%), while men have high incidence severe left ventricular systolic dysfunction 33(54.1%) p-value=0.046, smoking 42 (68.9%); p-value <0.001 and ST-segment elevation myocardial infarction 28 (45.9%) p-value <0.001. the p-values off all above findings are less than <0.05 respectively

Conclusions: There are major differences in risk factors, clinical presentation and outcomes between both genders. The majority of women presented with moderate left ventricular systolic dysfunction and higher rate of cardiac hospitalization while men presented with severe left systolic dysfunction associated with high incidence of ST-elevation myocardial infarction.

Keywords: Heart failure, Left ventricular systolic dysfunction, Gender differences, Clinical outcomes

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Introduction

The prevalence of heart failure (HF) is increasing with 64.34 million cases affected all over the world, however this may continue to raise , particularly as the percentage of people aged 70 or older keeps climbing, Heart failure causes a significant clinical, societal, and economic cost regardless of the underlying etiology.[1] Overall, it seems that 1-3% of the society and 10% of the elderly are affected by HF, heart failure is a wide-ranging clinical condition with a variety of underlying causes.[2] Heart failure was ranked fourth among causes of mortality in Erbil city (Kurdistan region-Iraq).[3] The overall age-standardized prevalence of heart failure with reduced ejection fraction (HFrEF) was higher in women(9%) versus men (7.7%).[4]

Women with HF survive longer than men and have a lower risk of sudden death. Ischemia is the most prominent cause in men, whereas hypertension and diabetes contribute to a greater extent in women.[5] World health organization declared mortality from heart diseases in Iraq reached to 18.5% of total deaths in 2017, ranked 19th at the international level.[6]Ischemic heart disease is responsible for most of the cases of HFrEF in men, while high prevalence of hypertension and diabetes mellitus are recorded in women with HFrEF.[5] However, the etiology of HF varies with different population, in developed countries it is usually due to ischemic heart disease and hypertension . The commonest cause of heart failure in Iraqi woman according to a study done in 1960 was rheumatic heart disease with almost half of patients below age of forty A large number of cases of hypertension and a modest percentage of cases of Cor pulmonale were both linked to bilharziasis,[7]The most common cause of heart failure in Yemen was ischemic heart disease for men and hypertension for women.[2]

Previous studies from western countries as well as in gulf countries about gender differences in HFrEF provided conflicting results, no recent studies done in Iraq on gender differences in HFrEF. On the other hand, it is still need to determine whether there are gender differences among Iraqi HFrEF sufferers. The aim of this study was to assess risk factors, clinical characteristics, outcomes and severity of HFrEF in women compared to men in Erbil, Kurdistan region of Iraq.

Patients and methods

A prospective cohort observational study of 117 consecutive patients aged ≥18 years of both gender who had been admitted to Hawler Cardiac Center or the medical ward of Hawler Teaching Hospital with symptomatic heart failure and ejection fraction (EF%) ≤ 40% for the period from December 2021 till 30th of October 2022 were recruited in this study.

The following conditions were excluded from the study: Peripartum cardiomyopathy, rheumatic valvular heart disease,congenital heart disease, stage four and five chronic kidney disease, patients on cardiac assist device, cardiac resynchronization therapy or pacemaker, moderate or severe COVID-19 infection of less than six months, patients with history of malignancy or on cytotoxic therapy, limited life expectancy and patients with poor acoustic window.

Clinical evaluation had been done for each patient to assess the clinical presentation and risk factors for heart failure. Obesity defined as body mass index more than thirty.[8]Cardiogenic shock defined as patients with blood pressure less than 90mmHg supported by clinical features.[9]Hypertension defined as patients on antihypertensive medication, previously diagnosed or recently diagnosed with two average measurement

systolic blood pressure more than 130 mmHg and or diastolic blood pressure more than 80mmHg.[10]Diabetes mellitus diagnosed as patients on treatment or presented with clinical symptoms and two sample fasting blood sugar more than 126mg/dl or two sample RBS more than 200mg/dl with or without HBA1C more than 6.5%.[11] hyperlipidemia diagnosed as total cholesterol of > 200 mg/dl and low density lipoprotein of >100 mg/dl.[12]Basic investigations were done for all recruited patients on admission.
Transthoracic echocardiography done for all patients with in first 3 days of hospital admission using Vivid E9 Version 2012 to assess the left ventricular systolic function using Teicholz methods according to American College of echocardiography guideline.[13] HFrEF is defined as EF equal or less than 40%. Pulmonary arterial hypertension (PAH) is diagnosed by 2D echocardiography when maximum tricuspid regurgitation velocity is > 2.8 m/s.[14]
The clinical presentations, risk factors, hospital mortality, severity of LV systolic dysfunction and pulmonary hypertension for both genders were compared. All recruited patients were followed for three months by phone contact to assess the gender deference in mortality and the frequency of hospital admission. Ethical consent was obtained from each patient and the study approved by ethics research committee of Kurdistan higher council for medical specialties to the document number (37) dated (9/1/2022).
Statistical Package for the Social Sciences (SPSS) version 25 was used for statistical analysis. The χ^2 test used to compare proportions and Student's *t*-test was used to compare means of two groups. A p-value of ≤0.05 considered statistically significant.

Results

One hundred seventeen patients were presented with clinical and echocardiographic features of HFrEF with higher frequency among men 61 (52.13%) versus women 56(47.86%) p-value (0.017), Male: female ratio (1.09:1) ,The highest incidence of HFrEF was at 60-69 years of age among men (24%) versus women (17 %) without statistically significant value as shown in Figure(1).

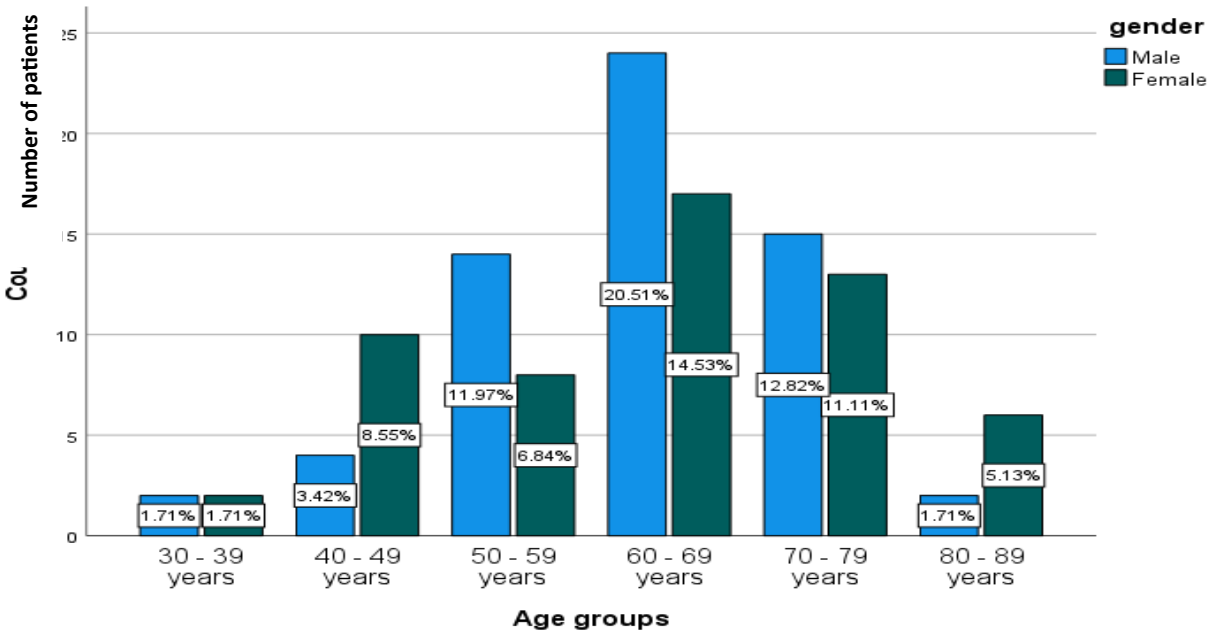

Figure (1): Gender differences of HFrEF according to age groups

The mean age in men was 62.25±10.72 years versus 62.16±13.61 years in women. There was higher incidence of obesity 43(76.8%) and dyslipidemia 27(48.2%) among women versus men 34(55.7%) and 18(29.5%) respectively. Men reported higher incidence of smoking 42(68.9%), ST-segment elevation myocardial infarction (STEMI) 28(45.9%) and Previous percutaneous coronary intervention (PCI)13(21.3%) versus women 2(3.6%),8(14.3%) and 4(7.1%) respectively. Women had a higher mean ejection fraction (%) 33.21±6.38 versus men 31.21 ±6.45, P value 0.047 (Table1).

Table (1): Patient characteristics of HFrEF among men and women

Characteristics	Men (N= 61)	Women (N= 56)	p value
Mean Age (SD)	62.25±10.72	62.16±13.61	0.970
Obesity	34 (55.7%)	43 (76.8%)	0.017*
Diabetes mellitus	24 (39.3%)	27 (48.2%)	0.334
Hypertension	32 (52.5%)	31 (55.4%)	0.753
Dyslipidemia	18 (29.5%)	27 (48.2%)	0.038*
Smoking	42 (68.9%)	2 (3.6%)	<0.001*
STEMI	28 (45.9%)	8 (14.3%)	<0.001*
Previous PCI	13 (21.3%)	4 (7.1%)	0.030*
UA/NSTEMI	6 (9.8%)	6 (10.7%)	0.876
FH (Sudden death)	2 (3.3%)	1 (1.8%)	0.601
Mean (EF%)	31.21±6.45	33.21±	0.047*

*= Statistically significant P value, HFrEF=Heart failure with reducection fraction, , PCI= percutaneous coronary intervention ,UA= unstable angina , NSTEMI= Non-ST segment elevation myocardial infarction, FH=Family history

Higher frequency rate of chest pain on admission to the coronary care unit was reported among men 27(44.3%) versus women 10(17.9%) P= 0.002 while women reported higher frequency of orthopnea 39(69.6%), palpitation 23(41.1%) as compared with men 31(50.8%) and 6(9.8%) respectively. There was a non-significant statistical association among gender in relation to paroxysmal nocturnal dyspnea, edema and cough (Table:2).

Table (2): Gender differences in clinical presentation of HFrEF

Clinical presentation	Men(N=61)	Women(N=56)	p value
Chest pain	27 (44.3%)	10 (17.9%)	0.002*
Orthopnea	31 (50.8%)	39 (69.6%)	0.038

Palpitation	6 (9.8%)	23 (41.1%)	<0.001*
Paroxysmal nocturnal dyspnea	14 (23%)	7 (12.5%)	0.141
Edema	20 (32.8%)	14 (25%)	0.354
Cough	18 (29.5%)	15 (26.8%)	0.744
*= Statistically significant P value, HFrEF=Heart failure with reduced ejection fraction			

Women with HFrEF reported higher incidence of atrial fibrillation 15 (26.8%) and pulmonary hypertension 4 (7.1) versus men 4(6.6%) and 2(3.3%) respectively. Women hospitalized for cardiac causes were reported in 12(21.4%) versus 12(19.7%) in men, most of men 45 (73.8%) stayed at hospital for non-cardiac chest pain while half 28 (50%) of women stayed for non-cardiac cause at hospital, p-value: 0.004. (Table.3).

Table (3): Gender differences in outcomes of HFrEF

Outcomes		Men (N=61)	Women (N=56)	p value
Hospital outcomes	Mortality	6 (9.8%)	6 (10.7%)	0.876
	Cardiogenic shock	14 (23%)	10 (17.9%)	0.495
	Atrial fibrillation	4 (6.6%)	15 (26.8%)	0.003*
	Pulmonary hypertension	2 (3.3%)	4 (7.1%)	0.046*
Number of hospitalizations	Nil	41 (67.2%)	42 (75%)	0.487
	Once	14 (23%)	8 (14.3%)	
	Twice	6 (9.8%)	6 (10.7%)	
Causes for hospitalization	Cardiac	12 (19.7%)	12 (21.4%)	0.004*
	Non cardiac	45 (73.8%)	28 (50%)	
Mortality outside the hospital		8 (13.1%)	6 (10.7%)	0.689

There was a significant statistical association between gender and the severity of left ventricular systolic dysfunction diagnosed by transthoracic echocardiography. High incidence of severe LV systolic dysfunction recorded among men 33(54.1%) while women recorded higher incidence of moderate LV systolic dysfunction 36(64.3%). p value 0.046.(Figure:2).

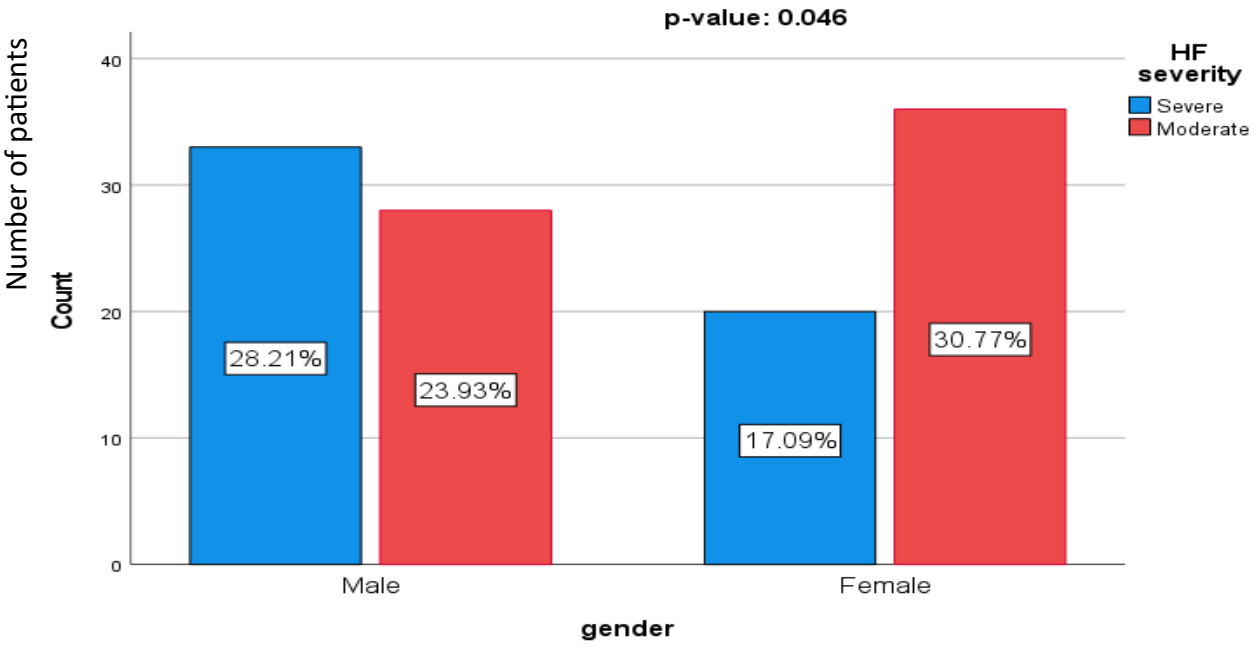

Figure (2): Gender differences in the severity of left ventricular systolic dysfunction

Discussion

Our study showed a major disparity in clinical presentations, risk factors and outcomes among men and women in patients with HFrEF with a lower number of women recruited compared with men. The explanation of the lower rate of women enrollment may be due to the exclusion of women during childbearing age, peripartum cardiomyopathy and elderly women with a lot of comorbidities; our findings going in parallel with Whitelaw S et al and Van Spall HGC et al systematic review studies[15,16]

The average age of HFrEF in our study was 62.25 ±10 in parallel to heart failure registries in other cities of Iraq as this trend also seen in a study conducted in Baghdad city in 2021 where mean age of patients was calculated as 64.75year ,[17]as well as similar to other Arab countries and at least 10 years younger than the average age of heart failure in Western countries.[18]The younger age of HFrEF in men and women our study may be induced by high prevalence of diabetes mellitus, hypertension, ischemic heart disease, smoking and obesity as well as inadequate early primary preventive measures in Arab countries including Iraq as compared with western countries.

Women with HFrEF were more obese than men supported by study done by Badran.[19] Higher frequency rate of dyslipidemia was reported among women versus men with HFrEF in agreement with a study done by Duca F et al.[20] STEMI were higher among men versus women with HFrEF in parallel with a survey done by Dewan and the contrary to a study done by Assiri. [21,22]

There was significant effect of gender on symptomatology in patients with HFrEF as chest pain was more common among males explained by higher prevalence of IHD among men in our region supported by systemic review of IHD risks by Bahaj and Gheisari et al while female presented with high frequency rate of orthopnea and palpitation in concordance with research by Dewan et al. [2,21,23]Atrial fibrillation was more common in women versus men with in

agreement with a study by Assiri.[22] Higher rate of cardiac hospitalization was reported in women versus men going in parallel to Sun L.Y et al and Kocabas U et al.[24,25]
Men presented with severe left ventricular systolic dysfunction while women reported moderate degree of left ventricular systolic dysfunction which may be explained by delay in seeking medical help among men with ischemic heart disease compared with women; our results were comparable to Duca F et al and Eisenberg E et al systematic review studies.[20,26] High frequency rate of pulmonary hypertension associated with HFrEF reported in women as compared with men, our results were compatible with Lakshmanan S et al study. [27]

Limitations of the study:

The limitations of this study included small patients' sample (117 patient). due to the effect of COVID-19 on hospital admission and short follow up period for 3 months.

Conclusion:

male patients presented with severe left ventricular systolic dysfunction associated with high incidence of STEMI while women reported moderate degree of left ventricular systolic dysfunction. There were major differences in risk factors, clinical presentation and outcomes between both genders.

Recommendations:

Larger number of women should be included in heart failure trials in order to adopt a better management strategy and better understanding of the pathophysiology, risk factors, etiologies, clinical features and outcomes of HfrEF in women.

Conflict of interest:

No conflict of interest

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