



Effect of Metabolic Syndrome on the Outcomes of Hospitalized Heart Failure Patients and Reduced Ejection Fraction

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Abstract:

Background and Objectives: Heart disease and metabolic syndrome are two of the most common health problems in the world. In this study we aimed to assess the relationship between the presence of metabolic syndrome and in-hospital cardiogenic shock, mortality and severity of left ventricular systolic dysfunction in heart failure patients with reduced ejection fraction.

Methods: Utilizing a cross-sectional design, with a duration of 8 months, from March to October 2023, at Hawler Teaching Hospital. We enrolled 104 adult patients aged 18 and above, both genders, 54 men and 50 women patients were categorized based on metabolic syndrome presence. All had clinical and echocardiographic heart failure with reduced ejection fraction, and metabolic syndrome was defined per International Diabetes Federation criteria.

Results: Metabolic syndrome reported in 56 (53.8%) of heart failure patients with reduced ejection fraction. Cardiogenic shock was more common in individuals with metabolic syndrome 13 (23.2%) versus non metabolic syndrome 2 (4.2%), $P < 0.006$. High incidence of severe left ventricular systolic dysfunction reported among patients with metabolic syndrome 47 (88.7%) versus non metabolic syndrome 9 (17.6%), $P < 0.01$.

Conclusions: Metabolic syndrome in heart failure with reduced ejection fraction increases the risk of poor outcomes; severe left ventricle systolic dysfunction and cardiogenic Shock.

Keyword: Heart Failure, In-hospital outcomes, Metabolic syndrome, Reduced Ejection Fraction

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Introduction

Heart failure (HF) is a multifaceted and advancing clinical illness distinguished by inadequate cardiac output to fulfill metabolic requirements. The disease has reached the status of a worldwide epidemic, impacting about 26 million individuals globally.¹ According to the ejection fraction, HF can be classified into three subtypes; Heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF) and heart failure with mildly reduced ejection fraction (HFmrEF). In the current study we will focus on the first type (HFrEF) and exclude the other two types because this type is not well studied particularly in our region.² With regard to the metabolic syndrome MetS, multiple studies and literatures reported that presence of MetS in an individual can increase the risk of developing HF from one side and from the other side in HF patients, MetS can negatively affect the outcomes and prognosis of these patients.³ Metabolic syndrome can be diagnosed using several definitions and criteria. The criteria used in our study included the National Adult Cholesterol Education Program III (NCEP ATP III), the World Health Organization, the American Society of Clinical Endocrinology (AACE), the European Group for the Study of Insulin Resistance (EGIR), and the international diabetes Federation (IDF).⁴ In the United Arab Emirates the prevalence of MetS is 40.5%. In Iraq, according to a recent study, MetS was recorded in 51.9% of the population aged between 18 and 89.^{5, 6} Several studies have shown that Metabolic syndrome is a good predictor of chronic kidney disease. For example, in a study by Ingelsson E et al., it was shown that Metabolic syndrome increases the risk of cardiovascular disease more than three times.⁷ The exact pathophysiological mechanism by which MetS can lead to heart failure is not well known, however, it has

been believed that insulin resistance (IR), hyperglycemia, and diabetes mellitus (DM) may play a role.⁸ Many studies have reported more aggressive form of left ventricular dysfunction and HF in patients with insulin resistance and higher likelihood of mortalities compared to healthy individual. Diabetes mellitus can induce a series of multiple changes that are metabolic, structural and functional which ultimately lead to myocardial damage and progression to heart failure.⁹⁻¹⁰ Studies concerned with clinical characteristics and outcomes of patients with HFrEF and MetS are scarce. We conducted this study to assess the clinical, echocardiographic and other characteristics of these patients and study the possible effect of MetS on the in-hospital outcomes (cardiovascular mortalities, arrhythmias, heart attacks, left ventricular dysfunction) in patients with HFrEF and MetS compared to those who had HFrEF but without MetS.

Patients and methods

The present study was conducted during a period of 8 months; from March to October, 2023 at Howler Teaching Hospital, the Coronary Care Unit (CCU). After ethical approval and consent of patients, we enrolled a total of 104 adult patients aged 18 years and older of both genders who agreed to participate in the study who had HFrEF approved by transthoracic echocardiography. According to the exclusion criteria, patients with rheumatic heart disease, cardiomyopathy, congenital heart disease, cytotoxic cardiomyopathy, alcoholic cardiomyopathy, patients with cardiac assist devices, implantable cardioversion devices, cardiac resynchronization therapy, patients with heart failure with ejection fraction > 41%, chronic kidney disease with advance stages; glomerular filtration rate less than 30 ml/min), with ascites, chronic liver disease and pregnant women were excluded from this study. Data were collected through complete





medical history, complete clinical examination, and initial investigations including electrocardiography, complete blood count, renal function tests, serum electrolytes, lipid profile, serum troponin I, and blood glucose. All patients underwent transthoracic echocardiography in the first 3 days after hospitalization. Using Vivid E9 version 2012 to evaluate left ventricular systolic function using the Teicholz method based on recommendations from the American College of Echocardiography.¹¹ Signs and symptoms of heart failure with reduced ejection fraction are defined as heart failure with LVEF \leq 40% or LVEF \leq 30%. For the purpose of our study, Metabolic syndrome (MetS) was defined according to standard clinical guideline and based on the criteria of the International Diabetes Federation (IDF)⁵.^{1,12} Hypertriglyceridemia was defined when the level of Triglyceride was 150 mg/dL or higher. Low high density lipoprotein (HDL) level was considered in men and women when the HDL level was less than 40 and less than 50 mg/dL, respectively.¹³ Cardiogenic shock is defined as systolic blood pressure less than 90 mm Hg associated with cold limbs, altered mental status, increased serum creatinine and lactate.¹⁴ The research protocol approved by the Kurdistan Higher Council of Medical Specialties KHCMS Ethics Committee on August 15, 2022, based on ethical agreement no. 1409. Statistical analysis was done using the 28th version of the Social Sciences Statistical Package. Chi-square test is used to evaluate the relationship between categorical variables, otherwise Fisher's exact test is used when chi-square is not applicable, Mann-Whitney U test is used to compare scale variables. Furthermore, the odds ratio, which is an estimate of the risk level, was calculated with its 95% confidence interval to determine the degree of association. A higher and significant odds ratio indicates a higher level of risk and probability of the event. A

significance level (p value) \leq 0.05 was considered significant.

Results

Out of the 104 patients who were a part of this study, 56 (53.8%) were found to have MetS based on the criteria set by the International Diabetes Federation (IDF) Figure (1). There was no significant difference in the mean age of the two groups ($P>0.05$), with the MetS group averaging 62.4 ± 10.3 years and the non-MetS group 65.9 ± 12.9 years. There was no discernible difference between the sexes, although men were more prevalent in both. In terms of drinking, history of percutaneous coronary intervention (PCI), and coronary heart disease (CHD), there was no significant difference between the two groups. There was a significant difference in all other variables between the two groups (p value <0.05), as highlighted in Table (1). Figure (2) shows that 51 patients (49% of the total) were found to have moderate heart failure ($EF = 31-40\%$) and 53 patients (51% of the total) were found to have severe heart failure ($EF \leq 30\%$). We observed a strong correlation between the existence of MetS and the degree of heart failure. Patients with MetS had more severe HF, and their mean EF% was much worse than patients without MetS. According to Figure (3), the average EF% was $25.4 \pm 6.5\%$ and $37.2 \pm 4.6\%$, with a p-value less than 0.001. In the MetS group, 47 patients (88.7%) experienced severe left ventricular systolic dysfunction, while only 9 patients (17.6%) in the non-MetS group did so ($p < 0.001$). Cardiogenic shock was more common in individuals with MetS 13 (23.2%) compared to nonMetS 2 (4.2%), with a p-value of less than 0.006. This information is presented in Table (2). Table (3) shows that there was no statistically significant correlation between MetS and any of the following: in-hospital cardiovascular mortality, arrhythmia, or acute coronary syndrome ($P>0.05$).



**Table (1):** Baseline characteristics of patients with MetS versus non- MetS

Characteristics		MetS N= 56	Non-MetS N=48	p value
Age (year) mean (SD)		62.4 (10.3)	65.9 (12.9)	0.150 ns
Gender n (%)	Men	29 (53.7)	25 (46.3)	0.976 ns
	Women	27 (54.0)	23 (46.0)	
BMI (kg/m ²) mean (SD)		36.2 (5.5)	22.9 (3.3)	<0.001 s
WC (cm) mean (SD)	Men	98.8 (5.2)	75.5 (7.6)	<0.001 s
	Women	99.2 (18.4)	70.9 (4.2)	<0.001 s
Alcoholism n (%)		3 (5.4)	0 (0.0)	0.104 ns
Smoking n (%)		23 (41.1)	18 (37.5)	0.006 s
Family History IHD n (%)		3 (5.4)	1 (2.1)	0.622 ns*
Diabetes mellitus n (%)		42 (75.0)	13 (27.1)	<0.001 s
Hypertension n (%)		53 (94.6)	30 (62.5)	<0.001 s
PCI n (%)		37 (66.1)	25 (52.1)	0.165 ns
Previous IHD n (%)		49 (87.5)	30 (62.5)	0.003 s
HDL (mg/dL) mean (SD)	Men	29.7 (5.8)	40.8 (10.0)	<0.001 s
	Women	30.5 (7.1)	45.8 (15.2)	<0.001 s
Triglyceride (mg/dL) mean (SD)		211.1 (74.0)	125.0 (26.4)	<0.001 s
RBS (mg/dL) mean (SD)		210.9 (58.0)	157.6 (57.4)	<0.001 s
B. urea (mg/dL) mean (SD)		58.6 (18.8)	48.6 (18.8)	<0.001 s
S. creatinine (mg/dL) mean (SD)		1.9 (0.9)	1.5 (0.7)	<0.001 s
EF% mean (SD)		25.4 (6.5)	37.2 (4.6)	<0.001 s

None of the patients had family history of HF or cardiomyopathy and none had previous CABG
 SD: standard deviation, WC: waist circumference, HDL: High-density lipoprotein cholesterol,
 PCI: Percutaneous coronary intervention

s: significant, ns not significant,

Chi square test used to compare frequencies in all categorical variables except Family History IHD
 (Fisher's exact test was applied)

Mann-Whitney U test used to compare scale variables



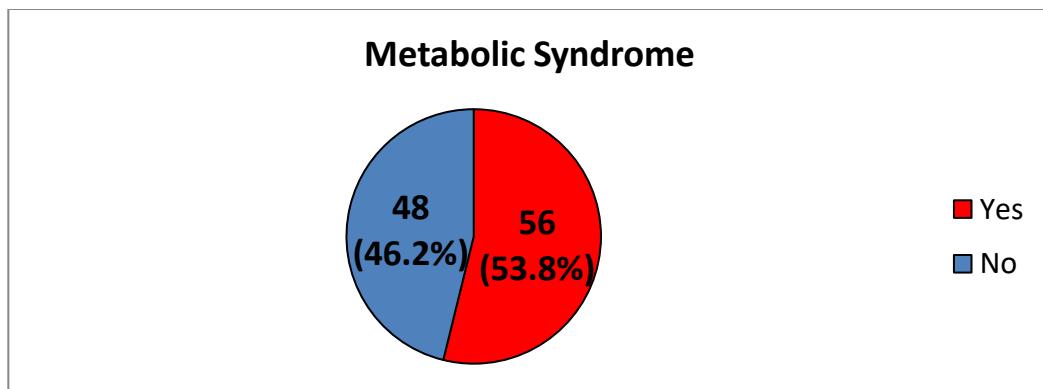


Figure (1): Distribution of the studied group according to the presence of MetS

Table (2): Association between MetS and severity of heart failure

MetS	Severity of LVSD				Total	
	Moderate		Severe			
	No.	%	No.	%	No.	%
Yes	9	17.6	47	88.7	56	53.8
No	42	82.4	6	11.3	48	46.2
Total	51	100.0	53	100.0	104	100.0

LVSD: Left ventricular systolic dysfunction

Odds ratio = 36.6 (95%CI of OR: 12.0 - 111.3) p value < 0.001

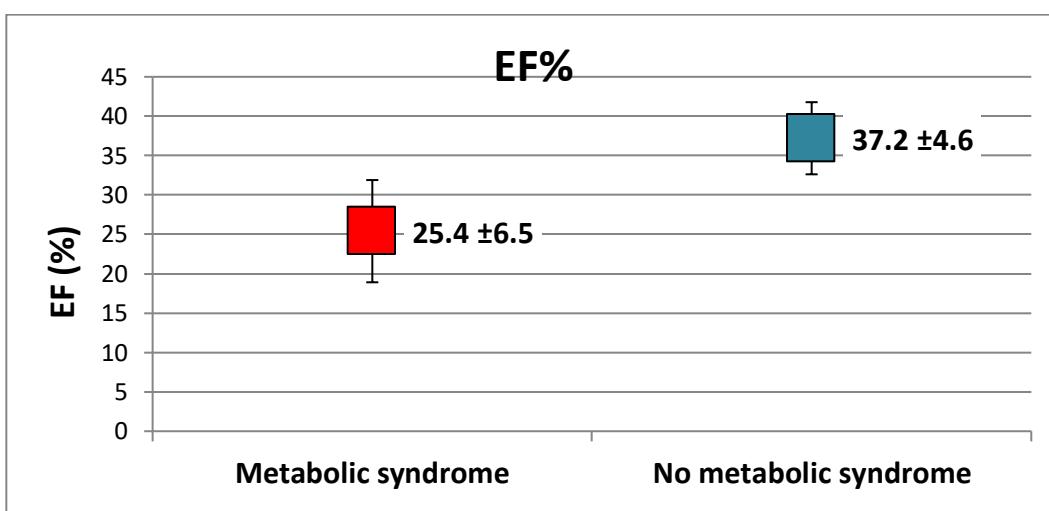


Figure (3): Comparison of mean ejection fraction among patients with and without MetS (p value < 0.001,)



**Table (3):** Association between MetS and in-hospital outcomes of the studied group

		MetS				Total	OR (95% CI)	p value			
Outcome		Yes		No							
		No.	%	No.	%						
Cardiogenic Shock	Yes	13	23.2	2	4.2	15	6.95 (1.48 – 32.62)	0.006 sig			
	No	43	76.8	46	95.8	89					
Acute coronary syndrome	Yes	16	28.6	9	18.8	25	1.73(0.68-4.44)	0.243 ns			
	No	40	71.4	39	81.3	79					
Cardiac Arrhythmia	Yes	3	5.4	0	0	3	RR: 1.91 (1.58 – 2.29)	0.104 ns			
	No	53	94.6	48	100	101					
Atrial Fibrillation/ Flutter	Yes	26	46.4	21	43.8	47	1.11 (0.51 – 2.42)	0.845 ns			
	No	30	53.6	27	56.3	57					
Cardiovascular death	Yes	3	5.4	2	4.2	5	1.3 (0.21 – 8.13)	0.778 ns			
	No	53	94.6	46	95.8	99					

OR: odds ratio, 95%CI: confidence interval of OR,

RR: risk ratio, HF: heart failure, ns: not significant, sig: significant

Discussion

Metabolic Syndrome is one of the most common risk factors that associated with cardiac diseases including heart failure.^{8,15} Our findings revealed a higher risk of left ventricular systolic dysfunction (as evidenced by a lower ejection fraction) in MetS group compared to those who did not have MetS. Furthermore, the risk of severe heart failure was approximately 36.6 times the odds ratio of 36.6 (range 111.3 - 12). This means that cases HFrEF and MetS more likely to have severe HF by almost 36 folds compared to HFrEF cases who did not have MetS. These findings are consistent with data reported in previous studies, with some variation in risk levels reported in these studies, such as the study by Huang et al.³ Furthermore, Zhou et al. reported that after adjustment for other risk factors of HF, MetS has appeared increase the risk by almost 3-fold.¹⁶ The variation in the hazard ratio reported in different studies can be explained by the difference in study design. Furthermore, in the early stages,

hypertension impairs the function of the left ventricle. Chronic high-pressure and mechanical stress can lead to higher levels of some inflammatory markers like such as cytokines, resulting in concentric hypertrophy of the left ventricle and symptomatic HF with normal or abnormal ventricular function. It is worth mentioned that abnormal lipid levels in patients with MetS mainly associated with the development of HF in general and lead to more severe HF compared to patients with normal lipid levels.⁸ Regarding hospital outcomes, we found that patients with MetS and heart failure were approximately 7 times more likely to develop cardiac shock than patients without MetS (odds ratio = 6.95). We also observed an increased risk of myocardial infarction (OR = 1.73), cardiac arrhythmia (OR = 1.91), atrial fibrillation (OR = 1.11) and death (OR = 1.30) in the group with MetS, but no association. reach statistical significance and this non-significance may be attributed to the fact that in our study only few patients developed this finding.





However, previous studies have also confirmed the relationship between poor outcomes of patients with HF and the presence of MetS. demonstrated that the risk of hospitalization and myocardial infarction is greater in patients who had both MetS and HF compared to those with no metabolic syndrome.¹¹ Low HDL levels and high blood sugar levels were significantly associated with higher mortality rates.¹⁷ In a study conducted by Fanta et al. it had been concluded that presence of metabolic syndrome was associated with severe form of HF, higher incidence of cardiac shock, and poor short-term outcomes and prognosis in hospitalized patients, also they found that MetS was associated with higher rates of cardiovascular death.¹⁸ The present study has limitations, firstly it only included cases with HFrEF, so comparisons with HFpEF and the normal population cannot be made. The data collected in this study were mainly based on hospitalized patients, while those who were not hospitalized or left the hospital were not followed up, which may have led to under- or overestimation of the association. However, our study can be used as a basis for large-scale studies to develop a strong hypothesis on the relationship between HFrEF and the presence of metabolic syndrome.

Conclusion

One of the main causes of serious heart failure is metabolic syndrome. Patients with metabolic syndrome are more likely to have left ventricular systolic dysfunction compared to those without metabolic syndrome. Heart failure patients who had metabolic syndrome are more likely to get cardiogenic shock.

Conflict of interest

The authors declare no conflict of interest.

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