Association of Metabolic Syndrome with Types of Heart Failure in Patients Referred to Hawler Teaching Hospital

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Abstract: Metabolic syndrome consists of some risk factors that are associated with heart failure. It has been found that it is significantly associated with mortality in patients having heart failure. This study aimed to assess the prevalence of metabolic syndrome among patients with symptomatic stages C or D of heart failure and find out any possible association of metabolic syndrome with different types of heart failure. Between December 2017 and June 2018; 50 patients were included in a cross-sectional study. Careful history was taken and clinical examination was done to conclude that they fulfill the Framingham's criteria of heart failure and then trans-thoracic echocardiography was performed to confirm the diagnosis and categorize the patients to have failure with preserved, mid-range and reduced ejection fraction. Waist circumference, plasma glucose, blood pressure and lipid profile checked to find out whether they have metabolic syndrome or not. Statistical analysis was conducted using (version 22) and a p-value <5 % was regarded as statistically significant. Metabolic syndrome was observed in 38 (76%) of the patients, but its prevalence was not statistically different between the types of heart failure; as its prevalence was 83.3 % in heart failure with preserved ejection fraction, 75 % in mid-range ejection fraction, and 71.4 % in reduced ejection fraction. Metabolic syndrome is highly existent among patients with heart failure, but there is no considerable difference in its existence among the different types of heart failure.

Keywords: Metabolic Syndrome, Heart Failure, Ejection Fraction, Central Obesity, Dyslipidaemia, Hyperglycaemia, Hypertension, Echocardiography

1. Introduction

Heart failure and metabolic syndrome are among global health concerns and their worldwide prevalence fixedly increases. It is predicted that 1–2% and 34% of the world's general population complains from heart failure and metabolic syndrome respectively (Filardi *et al*, 2015).

The existence of metabolic syndrome in our region varies; reaching up to 44% in Turkey, 42% in Iran, 41% in Saudi Arabia and 36% in Kuwait (Ansarimoghaddam *et al*, 2018). But unfortunately there are not any reliable data about the existence of heart failure and metabolic syndrome in Iraq; however it is well known that the cardiovascular diseases are the commonest causes of death among Iraqi people. From 1989 to 1999; there have been a 65% increase in hospital admissions for cardiovascular diseases (Alwan, 2004) , and from 2005 to 2016; the mortality rate has been increased for the following health problems by the following percentages: ischemic heart disease; 16.3%, diabetes; 39.9% and other cardiovascular diseases; 19.2% (Institute for Health Metrics and Evaluation, 2018).

A few studies have been conducted on the association between heart failure and metabolic syndrome. Ingelsson, Ärnlöv, Lind and Sundström, (2006) have found that metabolic syndrome is a powerful factor that predicts heart failure, and Tamariz *et al*. (2009) have found that metabolic syndrome raises mortality in patients with heart failure. But still there is not any study on the relation of metabolic syndrome with the different types of heart failure. The aim of this study was to clarify the existence of metabolic syndrome among patients with heart failure and the association of the former with the different types of the latter.

2. Method

This was a cross-sectional study conducted in Hawler teaching hospital, a governmental hospital in Erbil city, between December 2017 and June 2018. During this period, 110 patients of both gender aged ≥18 years with clinical features suspected to be related to heart failure who had been admitted in the Coronary Care Unit of the hospital studied. After applying Framingham's criteria for clinical diagnosis of Heart Failure, abbreviated as HF, supported with trans-thoracic echocardiography; a total of 50 patients had symptomatic New York Heart Association classes II, III and IV-stages C & D heart failure. All of them were included in the study. Trans-thoracic echocardiography study was performed by using Vivid E9 (General Electric) machine.

Diastolic function of the heart was evaluated with traditional PW Doppler of transmittal flow applied in a four-chamber apical view with the sample volume being placed between the tips of mitral leaflets. Early diastolic wave (E), late diastolic wave (A), early to late peak velocity ratio (E/A) and E velocity deceleration time (DT) were calculated.

Pulsed wave Tissue Doppler imaging was performed in the four-chamber view. A sample volume was placed within mitral annulus septal myocardial wall; early diastolic waves (E') were used for studying the left ventricular diastolic function. The diastolic function was classified into:

1. Normal diastolic function: characterized by E/A ratio <2 and E/E' <10.
2. Mild diastolic dysfunction: characterized by E/A ratio ≤0.75 and E/E' <10.
3. Moderate diastolic dysfunction: characterized by E/A ratio <2 and E/E' ≥10.
4. Severe diastolic dysfunction: characterized by E/A ratio >2 and E/E' ≥10.

Two-dimensional M-mode echocardiography was used to evaluate the left ventricular systolic function in the long parasternal axis view and the cursor positioned perpendicular to the interventricular septum was just below mitral leaflets' tips (Feigenbaum, 2004).

The types of HF were classified regarding the left ventricular ejection fraction and diastolic function of the heart into:

1. Heart failure with reduced ejection fraction (HFrEF): presence of symptoms ± signs with LVEF < 40%.
2. Heart failure with mid-range ejection fraction (HFmrEF): presence of symptoms ± signs with LVEF 40 – 49%and diastolic dysfunction diagnosed by trans-thoracic echocardiography.
3. Heart failure with preserved ejection fraction (HFpEF): availability of symptoms ± signs as well as LVEF ≥ 50% and diastolic dysfunction diagnosed by trans-thoracic echocardiography (Ponikowski *et al*, 2016).

All the patients were checked for metabolic syndrome, abbreviated as MetS, according to International diabetes federation, which defines it by truncal obesity (determined by waist circumference ≥94 cm for men and ≥80 cm for women) with any two of the followings: Fasting

triglycerides >150 mg/dL, HDL <40 mg/dL (for men) and <50 mg/dL (for women), systolic BP >130 mm Hg or diastolic BP >85 mm Hg or being on antihypertensive medications, fasting plasma glucose ≥100 mg/dL or previously diagnosed Type 2 DM or being on antidiabetic medications (IDF, 2006).

Waist circumference is used to describe truncal obesity, its measurement is done at the central point between the costal margin and the iliac crests. Body mass index (BMI) is expressed as the body weight (in kilograms) is divided by the height (in metres) to the power of two (Hübers, Pourhassan, Braun, Geisler & Müller, 2017). Hypertension was defined as history of having hypertension with or without being on its treatment or newly discovered hypertension with two separate readings of SBP ≥130 mmHg and/or DBP ≥80 mmHg (Whelton, 2018). Diabetes Mellitus was defined as: two separate measurements of fasting plasma glucose ≥126 mg/dL or random plasma glucose ≥200 mg/dL (ADA, 2018).

Patients having; pacemakers, congenital heart diseases, rheumatic heart disease, hypertrophic or postpartum cardiomyopathies, chronic obstructive pulmonary disease, those taking cytotoxic medications or radiotherapy, malignancies, established renal failure with eGFR ≤30 ml/min, liver diseases, ascites, pregnancy, pericardial diseases and diseases causing iron overload; were excluded from the study. A written consent was taken from every participant, which was then approved by the ethical committee of Kurdistan Board for Medical Specialties.

2.1 Statistical Analysis

Data were analyzed by (SPSS, version 22). Means and standard deviations were calculated to summarize the numerical variables, whereas proportions had been used to summarize the categorical variables. In order to compare the proportions of the study groups; Fisher's exact test was used rather than the Chi square test when the expected count of more than fifth of the cells of the table was less than 5. A p value of ≤ 0.05 was regarded as statistically significant.

3. Results

Fifty patients with HF were studied. Their mean age ($\pm$SD) was 63.94 $\pm$ 11.78 years, ranging from 35 to 88 years. Two thirds of the patients aged sixty years and older, and the male: female ratio was 1: 1. More than one third of the patients (34%) were obese (BMI $\geq$ 30 kg/m^2), and more than one third (38%) were smokers (see Table 1).

Table 1: Basic characteristics of the studied sample

	No.	%	Mean	(± SD)
Age (years)			63.94	(11.78)
30-39	1	2.0		
40-49	5	10.0		
50-59	11	22.0		
60-69	13	26.0		
70-79	16	32.0		
80-89	4	8.0		
Gender				
Men	25	50.0		
Women	25	50.0		
BMI (kg/m^2)			30.11	(6.74)
< 25	10	20.0		
25-29	23	46.0		
30-34	8	16.0		
≥ 35	9	18.0		
Smoking				
Never smoked	22	44.0		
Ex-smoker	9	18.0		
Smoker	19	38.0		
Total	50	100.0		

The existence of MetS in the studied sample was 76%. The most abundant element of MetS was hypertension (96%), followed by diabetes/impaired glucose tolerance (94%), low HDL (90%) and high triglyceride (68%) (see Table 2).

Table 2: Existence of MetS and its elements

Existence	No.	% (n = 50)
Metabolic syndrome	38	(76.0)
Hypertension	48	(96.0)
Diabetes mellitus/impaired GT	47	(94.0)
Low HDL	45	(90.0)
Central obesity	38	(76.0)
High triglyceride	34	(68.0)

High frequency rate of MetS was reported among patients with HFpEF (83.3%), followed by

HFmrEF (75%) and HFrEF(71.4%) (Figure 1); but without statistical significant difference between the types (p=0.774).

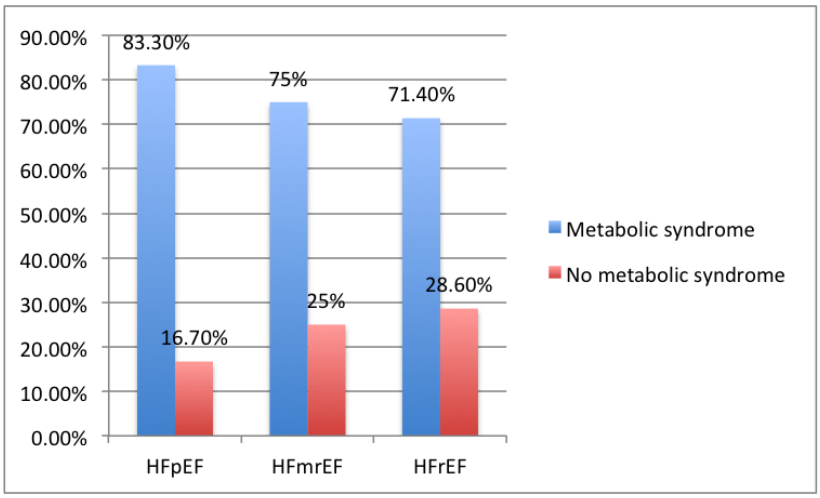

Figure 1: Existence of MetS by types of HF

There was not any considerable difference between the types of HF in relation to age and gender (see Table 3).

Table 3: Age and gender distribution of the HF types

	Types of heart failure						
	HFrEF		HFmrEF		HFpEF		
	No.	(%)	No.	(%)	No.	(%)	P
Age							
30-39	1	(3.6)	0	(0.0)	0	(0.0)	
40-49	2	(7.1)	1	(25.0)	2	(11.1)	
50-59	6	(21.4)	2	(50.0)	3	(16.7)	0.885*
60-69	8	(28.6)	0	(0.0)	5	(27.8)	
70-79	9	(32.1)	1	(25.0)	6	(33.3)	
80-89	2	(7.1)	0	(0.0)	2	(11.1)	
Gender							
Males	17	(60.7)	2	(50.0)	6	(33.3)	0.231*
Females	11	(39.3)	2	(50.0)	12	(66.7)	
Total	28	(100.0	4	(100.0)	18	(100.0)	

*By Fisher's exact test

Furthermore there was not any considerable association between the types of HF with the various elements of MetS, as shown in (see Table 4).

Table 4: Existence of MetS and its elements by types of HF

	HFrEF (n = 28)		HFmrEF (n = 4)		HFpEF (n = 18)		
	No.	(%)	No.	(%)	No.	(%)	P
Met. Syndrome	20	(71.4)	3	(75.0)	15	(83.3)	0.774*
Central obesity	20	(71.4)	3	(75.0)	15	(83.3)	0.774*
High TG	20	(71.4)	1	(25.0)	13	(72.2)	0.232*
Low HDL	24	(85.7)	4	(100.0)	17	(94.4)	0.763*
High SBP	16	(57.1)	1	(25.0)	13	(72.2)	0.184*
High DBP	14	(50.0)	1	(25.0)	8	(44.4)	0.689*
Hypertension	28	(100.0)	3	(75.0)	17	(94.4)	0.064*
Diabetes/High FBS	26	(92.9)	4	(100.0)	17	(94.4)	> 0.999*

*By Fisher's exact test.

4. Discussion

MetS by itself and its elements significantly raise the risk of atherosclerosis, ischemic heart diseases and therefore HF (Biagi, Nardi, Mathieu, Vescovo & Scanelli, 2014). But unfortunately we found out that there is not any study conducted on the relation of MetS with different types of symptomatic HF on the basis of left ventricular ejection fraction; namely HFrEF, HFmrEF and HFmrEF, while LVEF is a powerful predictor of morbidity and mortality in HF (Breathett, Allen, Udelson, Davis & Bristow, 2016).

Male to female ratio in the randomized sample of the study was 1, and although they were of different ages ranging from 35-88 years, most of them were elderly people (63.94 + 11.78), which reflects the already well-known information that HF is a disease that its existence increases with age. This is compatible with Rotterdam study which has discovered that existence of HF is nearly the same between the two genders and significantly increases with age; being 1% and more than 10% in age groups 55–64 and more than 85 years respectively (Mosterd *et al*, 2009).

In this study; MetS is highly existent in patients with symptomatic HF (76%), with the element of highest abundance being hypertension (96%), followed by diabetes (94%) and dyslipidaemia (90%) with no considerable association being detected between the types of HF and the existence of each elements of MetS; Comparable results reported by (Miura *et al*, 2010) which have found that the elements of MetS were comparably related to both HFpEF and HFrEF with high existence of each elements.

In our study we found that metabolic syndrome is highly existent in all the types of symptomatic HF based on left ventricular ejection fraction; 83%, 75% and 71.4% for HFpEF, HFmrEF and HFrEF respectively. But when they were compared to each other; there was no statistical difference between them. In a study in United States' Hispanics/Latinos; Peña *et al*. (2018) found that MetS was related to bad left ventricular systolic and diastolic function. It means that although MetS is a potent risk factor for HF, it is not a factor that affects on determining the type of HF. We couldn't find any study done on the relation of MetS with different types of HF.

The limitations of the study are small sample size and the unavailability of B-natriuretic Peptide (BNP) blood test; which has an important role in the diagnosis of HFmrEF & HFpEF.

5. Conclusion

Metabolic syndrome is highly existent in heart failure with preserved, mid-range and reduced ejection fraction, but without considerable difference in its existence among the mentioned types.

Conflicts of interest

The authors declare no conflicts of interest.

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