

The Burden of Symptoms and Comorbidities in Patients with Heart Failure Admitted to a Teaching Hospital in Iran, 2018-2020

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ABSTRACT

Multiple symptoms and comorbidities complicate management of heart failure. Studies on the identification of comorbidities (cardiac and non-cardiac) and attention to symptom burden in Iran are limited, so the aim of this study was to evaluate the burden of symptoms and comorbidities in hospitalized heart failure patients. In the present descriptive-analytical study, data were collected from 94 patients admitted to the cardiac wards of Lorestan University of Medical Sciences from December 2018 to April 2020. Samples were entered sequentially. Edmonton (ESAS) and Charlsson tools were used for data collection (CCI). The highest frequency of comorbidities was related to coronary artery disease (heart attacks) 73 (77.7%), hypertension 71 (75.5%), peptic ulcer 47 (50%), valvular problems 40 (42.6%) were, diabetes mellitus 30 (31.9%), kidney disease 25 (26.6%) and COPD 23 (24.5%). The lowest frequency of comorbidities was related to liver disease 1 (1.1%) and HIV (0%). The results also showed that the highest incidence of symptoms in patients with heart failure included chest pain of 6.52 ± 1.77 , shortness of breath of 6.41 ± 1.73 , anxiety of 6.22 ± 1.56 and constipation of 6.36 ± 1.72 They were. Depression, loss of appetite, nausea, drowsiness, and lack of well-being or health were the next most common symptoms. Patients with heart failure who have multiple comorbidities (cardiac and non-cardiac), and have multiple symptoms, and in the care of these patients should be considered all aspects, including comorbidities and symptoms. We will need complex management to assist in the care and treatment of these patients.

Keywords: Heart failure; Burden of symptoms; Comorbidities

Introduction:

Heart failure (HF) is a global health challenge and one of the most important causes of readmission. HF patients account for about 26 million people worldwide [3-5], about 6 million in the United States [6], and over 1 million in Iran [6-11]. HF is a syndrome with a wide range of complex symptoms as well as comorbidities [12], cardiac and non-cardiac comorbidities [13-15].

The most common cardiac comorbidities include atrial fibrillation, hypertension,

coronary artery disease and most common non-cardiac diseases include chronic obstructive pulmonary disease, diabetes mellitus and kidney diseases as the most common comorbidities [14-24] and mental disorders, peripheral vascular diseases [23, 25], cognitive changes [26], and a combination of experienced conditions. Comorbidities lead to increased mortality and decreased quality of life in HF patients [1, 17, 27].

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Also, comorbidities have multiple symptoms. These multiple symptoms and clinical events create a negative synergy among HF patients and often challenge self-care among them [28, 29]. Symptomatic HF patients often suffer from exacerbation of symptoms and prefer to control their symptoms for longer survival and improved quality of life [30]. HF patients experience a variety of symptoms during hospitalization, including shortness of breath, fatigue, sleep disturbance, depression, [26], emotional changes [30], nausea, and pain. Foruzkan et al. used Edmonton tools in their study and reported reduced health (95.3%), fatigue (88.2%), dyspnea (84.7%), anxiety (60%), and pain (55.3%) among HF patients [31].

The key symptom of HF is shortness of breath [32] and its mechanism is multifactorial, and physical symptoms, anxiety and depression are the strongest symptoms and determinants of shortness of breath. Also, factors such as old age, chronic obstructive pulmonary disease, body mass index and inflammatory factors such as interleukins 6 and 10 are significantly associated with shortness of breath [33]. Shortness of breath worsens fatigue in patients by limiting daily activities of life [34]. Fatigue is the second symptom of HF [25, 35], which reflects muscle hypoperfusion and an indicator of decreased cardiac output, the severity of which is associated with symptoms of depression, muscle dysfunction and anemia. It is also regarded as an independent predictor of readmission, and mortality in HF patients [34]. Fatigue is characterized by clinical factors such as age, sleep disorders, shortness of breath, decreased exercise capacity and psychological stress [36]. Therefore, fatigue and shortness of breath are several factors that limit daily functioning and self-care and ultimately reduce the quality of life of patients with chronic heart failure [37].

Also, the prevalence of pain among HF inpatients and outpatients is about 60-85% and 52-84% [25.] Pain stimulates the sympathetic nervous system and increases cardiac load and release of norepinephrine and activation of the angiotensin and renin response and as a result, increases anxiety in these patients [38].

Studies on the prevalence of symptoms and comorbidities in other countries have been conducted and significant findings have been reported; however, the burden of comorbidities and symptoms among HF patients is affected by the health system of each country and self-care ability and more appropriate symptom management programs can be designed for these patients by identifying the burden of comorbidities and HF. HF management includes two key elements: comprehensive assessment of symptoms and adequate understanding of the available approaches to reduce the burden of symptoms [39].

If the burden of HF-related symptoms and comorbidities are identified and relevant interventions are implemented, it is possible to help increase the survival and quality of life of these patients and even reduce the use of health services, readmission and costs [28]. In a systematic review study, McGreal et al. stated that self-care interventions were not sufficient to improve health outcomes in HF patients, and referred to the need to perform necessary interventions based on early identification of the burden of symptoms and comorbidities [28]. Successful symptom management considers not only the physical aspects, but also the emotional, social and spiritual dimensions of the patient's suffering [39]. There are many studies on education and self-care among HF patients in Iran, but these studies disregarded the burden of symptoms and comorbidities, so, the aim of the present study was to investigate the burden of symptoms and comorbidities in HF patients admitted to Shahid Madani Medical Educational Center of Khorramabad.

Materials and Methods

This was a descriptive-analytical study. The study population consisted of 94 HF patients aged 30-88 years who were discharged from the Coronary care unit (CCU) and the cardiac ward between 2018-2020, and then entered a clinical trial study. The collected baseline data were used for the present study. The present

study was conducted at Shahid Madani Medical Educational Center of Khorramabad. Sample size was estimated 94 people according to ($\alpha = 5\%$) and $S = 1.5$ (based on pilot or preliminary sample), precision=0.31 and sample size and using Cochran's formula.

Inclusion criteria included willingness to participate in the study, HF with $EF \leq 50$, patients aged 30-88 years, confirmation of heart failure by a physician and based on NYHA classification in class II or more, being aware of time, place and person, stable hemodynamic status and ability to speak Persian. Exclusion criteria included admission to a heart transplant or any cardiovascular intervention and disability in completing the research tools.

Prior to the study, patients were evaluated by a cardiologist and the HF class was determined based on the echocardiographic report and the nurse interview with the patient. On the day of discharge, data collection tools were provided to the patient and questionnaires were completed after obtaining informed consent from patients. The tools were completed by self-report method in literate individuals and by interview method in illiterate individuals, in which case the same questionnaire items were read to them by the researcher without any additional explanation. Data collection tools in the present study consisted of 3 parts: 1. demographic and clinical information of patients, 2. Edmonton Symptom Assessment Scale (ESAS), 3. and Charlson Comorbidity Index (CCI).

Edmonton Symptom Assessment Scale (ESAS) include visual items including chest pain, fatigue and nausea, feelings of depression, anxiety, well-being, appetite, drowsiness and shortness of breath, inability to perform daily activities, difficulty concentrating and constipation. There are a total of 12 items and each item is scored between 0-10 (0=asymptomatic, 10= Highly symptomatic). The possible score range is 0-120.

ESAS was first designed by Bruera et al. (1991) to assess the symptoms of cancer patients [40]. It was used by Feroz Khan et al.

(2015) to assess the symptom load in HF patients [25]. Cronbach's alpha coefficient of the above scale was $\alpha = 0.75$, $\alpha = 0.77$, $\alpha = 0.79$, $\alpha = 0.75$, and $\alpha = 0.75$ in studies carried out by Carvajal et al. in Spain, Yesilbalkan et al. in Turkey, Chang et al. in America, and Chinda et al. in Thailand [41-44]. In Iran, the content and differential validity of the Persian version of ESAS in cancer patients was determined by Khalili et al. The alpha coefficient for the whole tool was $\alpha = 0.88$ [45].

In the present study, the researcher prepared the modified version of ESAS for HF patients by adding three specific criteria (decreased ability to exercise, and difficulty concentrating, and constipation) and modification of pain (chest pain) to the Edmonton visual scale. The validity of this instrument was performed by professors and consultants of the School of Nursing and two cardiologists. Before sampling in the present research project, its reliability was evaluated on HF inpatients firstly on days 1 and 3 of hospitalization by completing the ESAS and Cronbach's alpha was determined at $\alpha = 0.85$.

Charlson comorbidity index (CHI), is used to assess comorbidities in HF patients. It consists of 19 questions, all which are answered based on Yes-No option, except for the first question (age range), which is answered using four options. Comorbidities are scored as follows: Scores 0-4 for age, 0-3 for diabetes, 0-3 for liver disease, 0-6 for malignancy, 0-2 for kidney disease, 0-1 for absence and presence of HF, 0-1 for myocardial infarction, 0-1 for each of chronic obstructive pulmonary disease (COPD), dementia and peripheral arterial disease, and history of stroke or transient brain attack, connective tissue diseases, and peptic ulcer, and 0-2 for unilateral paralysis. The possible score range in this index is 0-41, with A score 0, which is the lowest score, indicating a higher chance of survival, and the higher the score indicating the presence of more comorbidities and lower chance of survival. The Charlson Comorbidity Index (CCI) was first developed by Romano et al. (1992-1993), and a wide range of comorbidities were identified using this index and its specific ICD-9-CM coding index. CCI has been used

internationally in Canada, Australia, France, Japan, New Zealand, Switzerland and the United Kingdom and is available as software on reputable online medical websites. Scores or frequencies of a comorbidity are calculated by entering patient information and patient responses regarding presence or absence of comorbidity [46-49].

The present study was carried out after obtaining the relevant permission from the Vice Chancellor for Research and the Ethics Committee with the code of ethics IR.LUMS.REC.1397.153 of Lorestan University of Medical Sciences. Patients' informed consent to participate in the study was obtained and their names and personal information remained confidential.

Results

In the present study, 94 patients (47 males and 47 females). A total of 86 (91.5%) of patients were married and most of them (n=66, 70.2%) had moderate economic status. A total

of 68 (72.3%) of patients were illiterate. Moreover, 37 (39.7%) of participants were in heart failure (Class III). Etiologically, ischemic diseases were identified as the most common cause of heart failure (n=76 cases, 83%). Also, patients had no previous history of hospital admission in about 25 (53.2%) of cases. Most patients (n=76 cases, 80.9%) had an ejection fraction (EF) of less than 40% (Table 1).

The mean age of patients was 70.1 ±12.17 years and the mean body mass index was within the normal range (BMI ≥26.2). Mean systolic and diastolic blood pressure, as well as the mean of other parameters related to vital signs were in the normal range. However, the mean serum urea and creatinine (48.29 ±20.87, 1.26 ± 0.38) were almost in the normal range. Mean serum electrolytes including sodium and potassium as well as mean hemoglobin and hematocrit were in the normal range (Table 2).

Table 1: Frequency distribution of demographic and clinical variables in HF patients

Variable	Frequency (%)	Variable	Frequency (%)		
Gender	Female	47(50)	Pathology	Ischemic	76(83.3)
	Male	47(50)		Non-ischemic	16(17)
Marital Status	Single	86(91.5)	Admission history	Yes	69(73.4)
	Married	8(8.5)		No	25(26.6)
Income Status	Low	26 (27.7)	NYHA class	II	31(39.7)
	Moderate	66(70.2)		III	37(39.7)
	High	2(2.1)		IV	26(27.7)
Education	Illiterate	68(72.3)		Ejection/Fraction	≥40%
	Elementary	16(17.0)	<40%		76(70.0)
	Diploma and	23(24.4)			
	Upper				

Table 2: Mean vital signs and paraclinical tests of HF patients

Variable	Mean (SD)	Variable	Mean (SD)
Body mass index (kg / m2)	51.4(2.26)	BUN	48.29(20.87)
Systolic blood pressure (mm Hg)	127.25(25/81)	Serum creatinine	1.26(0.38)
Diastolic blood pressure (mm Hg)	79.38(13.31)	Serum Potassium	4.05(0.490)
Heart rate	79.87(15.69)	Sodium serum	140.37(3.70)
Respiratory rate	17.14(1.53)	Hemoglobin	13.36(1.80)
Age	70.10(12.17)	Hematocrit	40.17(5.32)

More than half of the patients (n=45 cases, 47.9%) had used beta-blocker drugs and 71 patients (75.5%) used angiotensin-converting blockers. A total of 54 (57.4%) of the patients used spironolactone and 49 (52.1%) of them used diuretics. Moreover, patients did not use angiotensin-receptor blockers (ARBs) in 82 (87.2%) of cases. Regarding the use of drugs related to comorbidities (diseases other than HF), 13 (13.8%) patients used fewer drugs (0-2) but (86.2%) 81 of them took between 6-9 drugs. (Table 3).

The highest mean burden of symptoms in HF patients were related to chest pain (6.52 ± 1.77), shortness of breath (6.41 ± 1.73), anxiety (6.22 ± 1.56), and constipation (6.36 ± 1.72), respectively. Depression, loss of appetite, nausea, drowsiness, and lack of well-being were the next most common symptoms (Table 1 and Figure 1).

The results also showed that the highest prevalence of comorbidities was related to coronary artery disease (myocardial infarction) (n=73 cases, 77.7%), hypertension (n=71, 75.5%), peptic ulcer (n=47, 50%), warfarin use (valvular problems) (n=40, 42.6%), diabetes mellitus (n= 30, 31.9%), kidney disease (n=25, 26.6%), kidney disease (n=25, 26.6%), and COPD (n=23, 24.5%). The lowest prevalence of comorbidities was related to liver disease (n=1, 1.1%) and HIV (n=0, 0%) (Table 4).

There was a correlation between age and shortness of breath (r = 0.29, p = 0.005) and daily activities (r = 0.29, p = 0.004), which indicates a low but significant positive correlation between these variables, but there was no significant correlation between age with other variables. The mean burden of nausea symptoms (5.87 ± 1.88) and the mean burden of depression symptoms (5.97 ± 1.60) in women were significantly higher than men.

There was a linear correlation between hemoglobin (Hb) with all items of ESAS, except nausea, anxiety, and difficulty concentrating (r = -0.21, -0.29, p = 0.05), which indicates a weak significant inverse correlation between these variables.

There was a significant difference between the mean score of symptom burden of different NYHA classes except nausea, anxiety, well-being and difficulty concentrating. However, there was a significant difference between NYHA class IV and NYHA class II and II in this regard. There were significant differences between NYHA class 4 compared to other classes in terms of mean symptom burden of chest pain, drowsiness and shortness of breath (Table 5).

Table 3. Frequency distribution of drugs related to HF and drugs related to comorbidities in HF patients

Variable	Frequency (%)	Variable	Frequency (%)
Beta-blockers	Yes 45(47.9)	ARBs**	Yes 12(12.8)
	No 49(52.1)		No 82(87.2)
ACI*	Yes 71(75.5)	Digoxin	Yes 32(34.0)
	No 23(24.5)		No 62(66.0)
Spirinolactone	Yes 54(57.4)	Drugs associated with comorbidities	0-2 13(13.8)
	No 40(42.6)		6-9 81(86.2)
Diuretics	Yes 49(52.1)		
	No 45(47.9)		

*Angiotensin converter Inhibitor (ACI); **Angiotensin receptor blockers (ARBs)

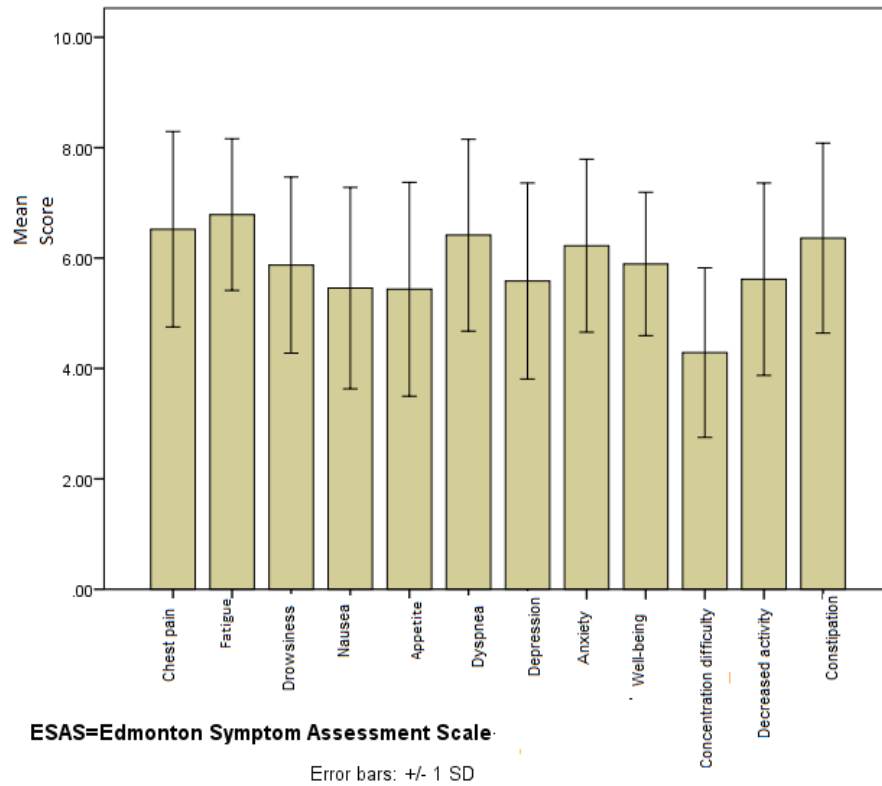


Figure 1. Mean score of symptom burden among studied HF patients

Table 4. Prevalence of comorbidities of studied HF patients

Variable	Frequency (%)	Variable	Frequency (%)
Diabetes mellitus	Yes 30(31.9)	Hypertension	Yes 71(75.5)
	No 64(68.1)		No 23(24.5)
Malignancy history	Yes 11(11.7)	Cerebrovascular diseases	Yes 14(14.9)
	No 83(88.3)		No 80(85.1)
Liver disease	Yes 1(1.1)	Alzheimer	Yes 4(4.3)
	No 93(98.9)		No 90(95.7)
AIDS (HIV)	Yes 0(0.0)	Hemiplegia	Yes 12(12.8)
	No 94(100)		No 82(78.2)
Renal disease	Yes 25(26.6)	Rheumatoid Arthritis	Yes 11(11.7)
	No 69(73.4)		No 83(88.3)
Heart failure diseases	Yes 86(91.5)	Peptic ulcer	Yes 47(50.0)
	No 8(8.5)		No 47(50.0)
Myocardial infarction	Yes 73(77.7)	Peripheral vascular diseases	Yes 8(8.5)
	No 21(22.3)		No 86(91.5)
COPD	Yes 23(24.5)	Depression	Yes 8(8.5)
	No 71(57.5)		No 86(91.5)
Warfarin (valvular disease)	Yes 40(42.6)	Other diseases	Yes 7(7.4)
	No 54(57.4)		No 87(92.6)

Table 5. Comparative table of symptom burden score of HF patients based on NYHA class, ejection fraction (EF), and sex

Variable	NYHA			<i>p</i>	Sex		<i>p</i>	<i>E/p</i>		<i>P</i>
	II	III	IV		Female	Male		<40%	≥40%	
Chest pain	6.25(1.66)	6.22(1.85)	7.26(1.66) *	0.03	6.80(1.56)	6.23(1.92)	0.11	6.61(2.78)	6.11(1.67)	0.27
Fatigue	6.34(1.33)	6.55(1.40)	7.6(0.97) *	<0.001	6.89(1.43)	6.68(1.32)	0.45	6.85(1.40)	6.50(1.24)	0.32
Drowsiness	5.25(1.56)	5.77(1.55)	5.76(1.30) *	0.001	6.12(1.51)	5.72(1.67)	0.36	5.96(1.61)	5.50(1.50)	0.27
Nausea	5.06(1.91)	5.33(1.69)	6.11(1.77) *	0.07	5.87(1.88)	5.04(1.98)	0.02	5.63(1.83)	5.63(1.83)	0.05
Appetite	4.84(1.60)	5.30(2.10)	6.34(1.78)**	0.01	5.74(1.90)	5.12(1.94)	0.12	5.65(1.95)	4.50(1.58)	0.02
Dyspnea	5.40(1.75)*	6.77(1.43)	7.15(1.56)	<0.001	6.48(1.73)	6.34(1.73)	0.68	6.60(1.67)	5.61(1.810)	0.02
Depression	4.90(1.71)	6.00(1.78)**	5.84(1.64)	0.02	5.97(1.60)	5.19(1.86)	0.03	5.56(1.81)	5.66(1.64)	0.83
Anxiety	5.75(1.60)	6.61(1.43)	6.26(1.58)	0.07	6.46(1.42)	5.97(1.67)	0.13	6.27(1.57)	6.00(1.57)	0.50
Well-being	5.59(1.29)	6.11(1.380)	5.96(1.14)	0.25	5.91(1.33)	5.87(1.27)	0.87	5.98(1.27)	5.50(1.38)	0.15
Concentration	4.18(1.49)	4.38(1.64)	4.26(1.48)	0.86	4.38(1.39)	4.19(1.67)	0.54	4.23(1.54)	4.50(1.50)	0.51
Activity	4.81(1.35)	5.58(1.67)	6.65(1.76)*	<0.001	5.72(1.84)	5.51(1.64)	0.55	5.80(1.77)	4.83(1.38)	0.03
Constipation	5.75(1.54)	6.16(1.85)	7.38(1.26)*	0.001	6.70(1.58)	6.02(1.79)	0.05	6.38(1.74)	6.27(1.67)	0.82

The parameters in the table are recorded based on (standard deviation ± mean).

* Significant with other groups - ** Significant compared to NYHA class II.

Discussion

The results showed that the most common symptoms among HF patients included chest pain, shortness of breath, anxiety and constipation. Depression, loss of appetite, nausea, drowsiness and lack of well-being were the next common symptoms. Also, the highest prevalence of comorbidities was related to coronary artery disease (myocardial infarction), hypertension, peptic ulcer, warfarin use (valvular problems and arrhythmias), diabetes mellitus, kidney disease and COPD respectively. The lowest prevalence of comorbidities was related to liver disease and HIV.

Hypertension is the leading cause of HF in many patients, especially women, the elderly, and African Americans. Hypertension is an important risk factor for ischemic heart disease. HF is a disease that can be largely prevented by appropriate adjustment of risk factors such as blood pressure (50).

In the current study, hypertension was the most prevalent comorbidity. Hypertension is

an important cause of diastolic dysfunction and systolic hypertension causes structural changes in the heart such as myocardial hypertrophy and cardiac fibrosis, resulting in decreased functional capacity and increased fatigue. Fatigue is associated with poor self-care, and health care professionals should emphasize the importance of increasing fatigue as a sign of worsening blood pressure [51]. It seems that blood pressure management and its optimal monitoring play an important role in the management of HF patients and symptoms such as fatigue and improving their functional capacity.

Okada et al. (2019) showed in their study that atrial fibrillation (50.5%), valvular diseases (47.7%), hypertension (45%), diabetes mellitus (36.7%) and ischemic diseases (35.8%) are the most common comorbidities among HF patients respectively. Moreover, other cases including kidney disease, anemia and brain diseases were less common in the present study. It was also found that there is a direct relationship between economic, social, clinical and psychological problems of patients with comorbidities and the symptom burden [51].

The current study focused on all cardiac and non-cardiac comorbidities. Savarese et al. (2020) in a clinical trial study reported that the highest percentage of comorbidities in HF patients included atrial fibrillation (56%), kidney disease (24%), diabetes (24%), and all three cases (8%) [52]. This study was had a large sample size and a focused on a limited number of diseases and focused on the association between EF with comorbidities in HF patients. Unlike the current study, gastrointestinal ulcers have been rarely reported as a comorbid in other studies; however, its prevalence *فروانی* was significant in the present study. The reason for this high prevalence seems to be related to the complexity of the drug regimen and drug side effects such as peptic ulcer.

Correale et al. (2019) referred to dyslipidemia, hypertension, diabetes, and chronic kidney disease (CKD), anemia, and coronary artery disease, and cardiac fibrillation, COPD, and depression as the most common comorbidities in HF patients that had a negative prognosis in these patients [24]. These findings were close to the present study. Mastromarino et al. (2014) in their study referred to COPD and obstructive sleep disorders and atrial fibrillation, renal disorders, diabetes mellitus, anemia, cachexia, thromboembolism, systemic infections, and other unpleasant disorders as cardiac and non-cardiac comorbidities in HF patients, [53]. The present study identified a wider range of comorbidities, and the study population is likely to suffer from more comorbidities. Similar to the present study, Nagarajan & Tang (2012) reported a wider range of problems in HF patients such as dementia and depression [14].

According to this hypothesis, the high prevalence of comorbidities such as overweight/obesity, diabetes mellitus, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), and hypertension have led to systemic degenerative diseases that cause inflammation and coronary artery disease. Endothelial inflammation of the coronary arteries leads to cardiomyocyte stiffness and interstitial fibrosis, which in turn

leads to increased left ventricular diastolic stiffness and the progression of heart failure [54].

Respiratory sleep disorders including OSA and central sleep apnea (CSA) have recently been considered as comorbidities among HF patients. OSA is associated with an increased risk of atrial fibrillation among HF patients [14]. Anemia is also a common comorbidity among HF patients, especially in developing countries, associated with a with a negative prognosis [55].

The study by Vader & Rich (2015) was consistent with the present study with regard to non-cardiac comorbidities among HF patients [12]; however, in our study both cardiac and non-cardiac comorbidities were investigated. Some of the differences in the results on the prevalence of comorbidities are related to the tools for screening for comorbidities. Although most studies have used CCI, some have modified it and made changes in the calculation of the prevalence of comorbidities.

In the present study, the highest symptom burden was reported to be chest pain, shortness of breath, fatigue, loss of appetite, anxiety, decreased ability to perform daily tasks and constipation, respectively. These findings were consistent with studies by Salyer et al. (2019) [56] and the study of Feroz Khan et al. (2012). In their prospective cohort study, the burden of symptoms of HF inpatients was measured using ESAS. They referred to shortness of breath, fatigue, decreased well-being, decreased appetite, pain and anxiety as the most common symptoms [25].

Salyer et al. (2019) studied HF patients for behavioral symptoms, including cognitive impairment, anxiety, depression, daytime drowsiness, and fatigue. They found that functional capacity and biochemical parameters are associated with poor cognitive function due to poor cardiac output due to neurological conditions and structural changes in the brain. Regardless of the etiology, cognitive impairment affects the patient's daily functioning and ability to manage chronic diseases. In this study, compared to other

symptoms, the prevalence of anxiety and depression was lower [56], however, depression was more common in the present study. Symptoms of cognitive and emotional depression describe sleep problems as one of the main symptoms of fatigue [57].

Depression is common in heart failure with reduced ejection fraction (HFrEF) and is associated with poor quality of life, limited functional status and increased risk of mortality in this group [55]. Therefore, it can be argued that depression symptoms have a negative effect on the aggravation of other symptoms, management of heart failure and health outcomes; therefore, a special priority should be given to managing depression symptoms and promoting mental health in this group of patients.

Salyer et al. (2019) found that pain was the most common symptom in HF patients [56]. Song et al. (2010) reported symptoms of anorexia, lack of energy and difficulty sleeping. The most influential factors in anorexia are nutritional behaviors and dietary restrictions. Existing symptoms including shortness of breath, feeling nervous, sad, or feeling lonely and lack of energy are also involved in reducing appetite [58,59]. As can be observed, the HF symptoms such as pain, anorexia and shortness of breath are interrelated, and in order to manage them, it is necessary to pay attention to the nutritional therapy style and management of the patient's psychological problems.

The symptom burden can vary in severity depending on the patient's sex. Heo et al. (2019) found in their study that daytime fatigue and shortness of breath was the most common symptom burden in women and men, but severity of distress and anxiety was higher in women than men. Also, the severity of daytime fatigue, edema and shortness of breath during was higher in women than in men. Unfortunately, the symptoms of depression in most HF patients, which is a psychological factor in these patients, are not properly diagnosed and treated [60]. The present study investigates and compares the symptoms between men and women and reminds us to pay more attention to gender differences and

typical and atypical symptoms in the management of symptoms.

Limitations

We were unable to diagnose the cause of comorbidities, the cluster effect of symptoms, and long-term patient care planning due to time constraints. Considering the differences in patients' experiences regarding diagnosing their symptom burden and the variability of perceptions in each patient, it is not possible to consider a special care program for all patients in order to reduce the burden of symptoms individually.

Conclusion

The present study showed that HF patients have multiple comorbidities (cardiac and non-cardiac), and have a high symptom burden. Careful attention to the symptom burden such as depression and cardiac and non-cardiac comorbidities such as hypertension and gastrointestinal disorders is of particular importance. The results of the current study can be used in care planning programs for HF patients. It is suggested to investigate the effect of patient-centered multidisciplinary management programs on the health outcomes of HF patients with comorbidities in different age and sex groups and other settings such as outpatient clinics or primary care in future research.

Conflict of Interests

Authors declare that they do not have any conflict interests.

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