ORIGINAL ARTICLE

SYMPTOMATIC INFECTIONS IN PATIENTS WITH ACUTE HEART FAILURE IN A LARGE TERTIARY CARE CARDIOLOGY HOSPITAL

Abrar Ahmad Chughtai,[1] Hina Najmi,[2] Syed Zahid Jamal,[3] Maha Pervaz Iqbal,[1] Lubna Ansari Baig,[2] Farhana Shahid[2]

[1]University of New South Wales, Sydney, Australia, [2]Jinnah Sindh Medical University, Karachi, Pakistan, [3]National Institute of Cardiovascular Diseases, Karachi, Pakistan

Objectives: To estimate the rates of symptomatic respiratory, gastrointestinal and urinary infections in patients hospitalized with acute heart failure and to describe the clinical characteristics of these patients.

Methodology: A cross sectional study was conducted in a large tertiary care cardiology hospital and patients hospitalized due to non-infective causes of heart failure were invited to participate. Trained research assistants collected data using a semi-structured questionnaire. Patients' medical records were also reviewed.

Results: A total of 335 patients were recruited in the study and of them around two thirds (65.7%, 220/335) had the first-time heart failure and one third (34.5%, 115/335) had recurrent heart failure. Acute myocardial infarction rate was significantly higher in first-time heart failure patients, compared to recurrent heart failure patients (p value <0.001). Among all heart failure cases, 140 (41.8%) had symptoms of respiratory infections, 36 (10.7%) had symptoms of diarrhoea, 32 (9.5%) had symptoms of urinary infection, 77 (23.0%) had influenza like illness and 81 (24.2%) had fever during last 2 weeks. Rates of symptomatic respiratory infection, influenza like illness and fever were consistently higher in first-time heart failure patients, however, only respiratory infection during last week was significantly associated with first-time acute heart failure (OR 1.68, 95% CI, 1.02-2.77).

Conclusion: This study showed high rates of respiratory and other symptomatic infections in acute heart failure patients. Like other precipitating factors, infections may trigger acute heart failure directly in elderly people. Elderly people should use influenza vaccines to protect from influenza and influenza like illness.

Keywords: Acute heart failure, acute myocardial infarction, respiratory infections, influenza, urinary infections, gastrointestinal infections, infections

Citation: Chughtai AA, Najmi H, Jamal SZ, Iqbal MP, Baig LA, Shahid F. Symptomatic Infections in Patients with Acute Heart Failure in a Large Tertiary Care Cardiology Hospital. Pak Heart J. 2022;55(03):253-259. DOI: https://doi.org/10.47144/phj.v55i3.2325

INTRODUCTION

Acute heart failure (AHF) is a clinical syndrome and one of the major causes of emergencies and hospitalization in elderly patients.[1] According to a global burden of disease study, an estimated 40 million cases of heart failure were reported in 2015, leading to 4.2 million years lived with disability (YLDs).[2] Around two third case (68.7%) of heart failure were due to ischaemic heart disease, chronic obstructive pulmonary diseases (COPD), hypertensive heart disease, and rheumatic heart disease. Initial diagnosis of AHF is generally based on signs and symptoms of abnormal cardiac function, with or without previous heart disease. Based on left ventricular ejection fraction (LVEF) on echocardiography, AHF is generally classified into either heart failure associated with a reduced LVEF below 50% (HFrEF) or heart failure associated with a preserved LVEF of 50% or higher (HFpEF).[3]

Many precipitating factors cause pathophysiological changes and increase in fluid retention, which increase the risk of AHF.[1] Common factors include uncontrolled hypertension, acute cardiac ischemia/myocardial infarction, arrhythmias, systemic infections (respiratory, urinary, etc.) and development of comorbidities (e.g. anaemia, hypothyroidism, renal failure, etc.).[4] These precipitating factors should be identified early since they may have an impact on prognosis after an AHF decompensation. Though infections are reported one of precipitating factors of ACH, the data is limited on type and nature of infections leading to AHF.[5] The frequency of infections reported among AHF cases range from 6% in patients admitted in a cardiology department[5] to 58% in patients admitted in internal medicine wards.[6] According to a Spanish study, respiratory infections were one of the leading factors associated with decompensation of heart failure in patients over 70 years of age (21.2%), both in internal

medicine and emergency services.[7] Community-acquired pneumonia (CAP) is one of the leading causes of morbidity and mortality globally and may trigger acute cardiac events, including AHF.[8] Recent data suggest that COVID-19 infection can cause or exacerbate heart failure through different mechanisms.[9]

Morbidity and mortality due to AHF is also reported to be higher during the winter seasons, particularly in the elderly. According to a study approximately one-fifth of the winter excess in admissions due to AHF is attributable to respiratory diseases.[10] More cases of AHF are admitted during the influenza season than in the non-influenza season.[11]

Ischemic heart diseases are among the major contributors of global mortality and morbidity. Many studies have shown a relationship between acute respiratory infection (ARI) and ischemic heart diseases, such as acute myocardial infarction (AMI).[12] Influenza is associated with AMI in many studies and cardiovascular incidents are reported to be increased during the influenza seasons. Similarly, lower respiratory tract infections (e.g. pneumonia) and urinary tract infections (UTIs) were associated with AMI in some studies.[13,14]

The main aim of this study was to estimate symptomatic infection rates among patients with AHF. Secondary objective was to describe the clinical characteristics of patients hospitalized with AHF in a large tertiary care cardiology hospital.

METHODOLOGY

A cross sectional study was conducted in a large tertiary care cardiology hospital in Karachi Pakistan from November 2018 to February 2019.The selected hospital provides services to a large and diverse population, including around 400,000 outpatients, 200,000 emergency cases and 37,000 inpatients every year. All patients aged ≥18 years, hospitalized due to AHF, were invited to participate in the study. AHF was diagnosed according to the following criteria;[3] 1) Heart failure with reduced ejection fraction (HFrEF): Symptoms with or without signs of heart failure and LVEF <50%, 2) Heart failure with preserved ejection fraction (HFpEF): Symptoms with or without signs of heart failure and LVEF ≥50% and objective evidence of relevant structural heart disease (LV hypertrophy, left atrial enlargement) or diastolic dysfunction, with high filling pressure demonstrated by echocardiography.

We included patients presenting for the first time with typical symptoms and signs of heart failure (de novo AHF) and patients with worsening of their pre-existing cardiac condition (acute decompensated heart failure). We only included cases presented with following non-infective causes of heart failure in this study1) acute myocardial infarctions (AMI), 2) old myocardial infarctions who present with heart failure, 3) valvular heart diseases, 4) congenital heart diseases, and, 5) cardiac arrhythmias. Patients with endocarditis, myocarditis and other infectious causes of acute heart failure were not included in the study.

Diagnosis of AMI was based on combination of the following clinical inclusion criteria; a) ischemic symptoms: chest or arm pain, nausea/vomiting, sweating, shortness of breath AND electrocardiogram findings (ST segment elevation or depression, Pathological Q waves) OR change in blood level of cardiac biomarkers (Typical rise and gradual fall in Troponin orMore rapid rise and fall in Creatine Kinase MB (CK-MB)).

We excluded patients admitted with chronic cardiac illnesses, chronic liver or renal impairment, malignancy or autoimmune disorders and patients with infective cause of heart failure such as cardiomyopathy and myocarditis.

Trained research assistants collected data from emergency and inpatient wards, using a semi-structured questionnaire. Every morning, they reviewed admission records of the emergency department to locate potential participants who meet the study criteria. Research assistants also visited the wards where cardiology patients were admitted. Once a potential participant was identified, they reviewed the hospital records and consultí with the attending physicians to confirm the diagnosis. Once confirmed, the research assistants further assessed the patients to ensure that the patients did not have any exclusion criteria.

After enrolment and informed consent, patients were interviewed face to face to record epidemiological and clinical data, including socio-demography, physical health, smoking, alcohol, dietary patterns, history past illnesses and vaccine/ drug intake, and symptoms of respiratory, gastrointestinal and urinary infections during last few weeks. Questionnaire was translated into local language (Urdu).

Some data were also collected from patients' medical records, such as details about current heart disease, physical exam, laboratory tests and treatment provided. We only recorded results of laboratory tests routinely done in the hospitals, and did not collect specimens/samples for laboratory analysis.

The main outcome measures were; 1) symptoms of respiratory illness, defined as two or more respiratory symptoms (cough, nasal congestion, runny nose, sore throat or sneezes) or one respiratory symptom and a systemic symptom (chill, lethargy, loss of appetite, abdominal pain, muscle or joint aches); 2) Symptoms of diarrhoea, defined as passage of three or more loose or liquid stools per day (or more frequent passage than is normal for the individual), with or without fever and passage of blood in stool, and 3) Symptoms of urinary tract infections, defined as pain during urination or blood in urine. Secondary outcomes were 4) influenza like illness (ILI), defined as fever ≥38°C plus one respiratory symptom, and 5) fever only. Data were collected on symptoms of these infections during the last 2 weeks and during the last one week (including current symptoms).

Categorical variables were presented as counts and percentages, while continuous variables were expressed as means and standard deviation. Characteristics of "first" and "recurrent" heart failure cases were compared. Then characteristics of "AMI patients" were compared with all "other patients" admitted with heart failure during the study period due to valvular heart diseases, congenital heart diseases, arrhythmias and old myocardial infarctions. Rates of symptomatic infections were calculated in various patients' groups. Rates were calculated during the last 2 weeks, during the last one week (including current symptoms) and current symptoms only. Finally, Odds Ratios (ORs) were calculated to estimate the difference in the rates of symptomatic infections among patients with "first" and "recurrent" AHF cases and patients with AMI and other causes of acute heart failure. Data were entered and analyzed in SPSS version 26.

Assuming 30% infection rate among AHF patients,[6] the required sample size was 225 participants, with 0.05 alpha and 6% margin of error.

Ethics approval was obtained from University of New South Wale Human Research Ethics Committee (Approval number HC180565) and Ethics Committee of National Institute of Cardiovascular Diseases Karachi Pakistan (Ref number ERC-20/2018).

RESULTS

We recruited 335 patients in this study and of them 200 (60%) were male, 32 (10%) were smokers, 219 (65.4%) lived in urban areas, 141 (42.2%) had diabetes, 196 (58.5%) had hypertension, 65 (20.2%) had high cholesterol and 100 (30%) had any other illness. Mean age of participants was 56.7 years (SD13.9). Only 9 participants (2.7%) had been doing exercise regularly and one (0.3%) had received influenza vaccine during the study season. Of the total 335 cases, around two thirds (65.7%, 220/335) had first-time heart failure and one third (34.5%, 115/335) had recurrent heart failure.

Table 1 shows sociodemographic characteristics, precipitating factors and clinical presentation of first-time heart failure patients and recurrent heart failure patients. Compared to recurrent heart failure patients, the first-time heart failure patients were older (p=0.015), more likely to live in urban areas (p<0.001), more likely to be hypertensive (p<001) and less likely to have other medical illnesses (p=0.042). AMI was the main precipitating factor for acute heart failure; however the rate of AMI was significantly higher in first-time heart failure patients, compared to recurrent heart failure patients (p<0.001). ST-Elevation Myocardial Infarction (STEMI) was also higher in first-time heart failure patients, compared to recurrent heart failure patients (p=0.004). Mean systolic BP was slightly higher in first-time heart failure patients compared to recurrent heart failure patients, however the difference was not statically significant (p=0.272). Other sociodemographic and clinical characteristics were similar between first-time heart failure patients and recurrent heart failure patients.

Table 1: Characteristics of first and recurrent cases admitted with acute heart failure (AHF)

	First-time heart failure	Recurrent heart failure	P value
Total (N)	**220**	**115**	-
Gender			
Female	90 (40.9%)	45 (39.1%)	0.815
Male	130 (59.1%)	70 (60.9%)	
Age (years)			
Mean and SD	58 ±12.9	54.1 ± 15.5	0.015
Education			
No education/ primary	95 (43.2%)	52 (45.2%)	0.729
Secondary and higher	125 (56.8%)	63 (54.8%)	
Occupation			
Employed	159 (72.3%)	91 (79.1%)	0.171
Unemployed	61 (27.7%)	24 (20.9%)	
Location			
Rural	44 (21.1%)	71 (56.8%)	<0.001
Urban	169 (78.9%)	54 (43.2%)	
Exercise daily			
Yes	4 (1.8%)	5 (4.3%)	0.284
No	216 (98.2%)	110 (95.7%)	
Smoking			
No/ former	20 (9.1%)	12 (10.4%)	0.699
Current	200 (90.9%)	103 (89.6%)	
Co-morbidities			
Diabetes	94 (42.7%)	47 (41.2%)	0.816
Hypertension	146 (66.4%)	50 (43.5%)	<0.001
High cholesterol	41 (19.4%)	24 (21.8%)	0.661

Any other illness**	58 (26.4%)	42 (37.2%)	0.044
Flu vaccine in 2018			
Yes	0 (0%)	1 (0.9%)	0.349
No***	213 (100%)	113 (99.1%)	
Causes of AHF			
AMI	160 (72.7%)	50 (43.5%)	<0.001
Old MI	24 (10.9%)	32 (27.8%)	
Valvular heart disease	23 (10.5%)	29 (25.2%)	
Congenital heart disease	3 (1.4%)	1 (0.9%)	
Cardiac arrhythmias	10 (4.5%)	3 (2.6%)	
Type of MI			
STEMI****	48 (30%)	5 (10%)	0.005
Non STEMI	112 (70%)	45 (90%)	
LF function			
<40%	129 (58.6%)	74 (64.3%)	0.405
40-49%	34 (15.5%)	12 (10.4%)	
≥ 50%	57 (25.9%)	29 (25.2%)	
Mean systolic BP (SD)	125 ± 27.9	121 ± 31.2	0.272

** Non AMI include old myocardial infarction, valvular heart disease, congenital heart disease and cardiac arrhythmias, ** kidney diseases, liver diseases, asthma, COPD, TB, allergy or cancer, *** Missing data, **** ST-Elevation Myocardial Infarction (STEMI)*

Table 2 shows sociodemographic characteristics, precipitating factors and clinical presentation in heart failure patients with and without AMI. Compared to heart failure patients without AMI, patients with AMI were older (p<0.001), more likely to live in urban areas (p<0.001), more likely to have diabetes (p=0.010), hypertension (p<001) and high cholesterol (p=0.020) and less likely to have other medical illnesses (p<0.001). In most cases, AMI patients presented with first time heart failure (p<0.001) and had low LF function <50% (p<0.012). Other sociodemographic and clinical characteristics were similar between AHF cases with and without AMI.

Table 2: Characteristics of acute myocardial infarction (AMI) and other patient admitted with acute heart failure

	Heart failure with AMI	**Heart failure with Non-AMI***	**P value**
Total (N)	**210**	**125**	**-**
Gender			
Female	82 (39%)	53 (42.4%)	0.546
Male	128 (61%)	72 (57.6%)	
Age (years)			
Mean and SD	59.5 ± 10.9	51.9 ± 17.1	<0.001
Education			
No education/ primary	95 (45.2%)	52 (41.6%)	0.570
Secondary and higher	115 (54.8%)	73 (58.4%)	
Occupation			
Employed	157 (74.8%)	93 (74.4%)	>0.999
Unemployed	53 (25.2%)	32 (26.5%)	
Location			
Rural	44 (21.1%)	71 (56.8%)	<0.001
Urban	165 (78.9%)	54 (43.2%)	
Exercise daily			
Yes	6 (2.9%)	3 (2.4%)	>0.999
No	204 (97.1%)	122 (97.6%)	
Smoking			
Current	23 (11%)	9 (7.2%)	0.370
No/ former	187 (89%)	116 (92.8%)	
Co-morbidities			
Diabetes	77 (36.7%)	28 (23%)	0.010
Hypertension	147 (70%)	49 (32.9%)	<0.001
High cholesterol	49 (24.3%)	16 (13.4%)	0.022
Any other illness**	50 (23.8%)	50 (40.7%)	0.002
Flu vaccine in 2018			
Yes	0 (0%)	1 (0.8%)	0.370
No***	206 (100%)	120 (99.2%)	
Heart failure			
Recurrent	50 (23.8%)	65 (52%)	<0.001
First	160 (76.2%)	60 (48%)	
LF function			
<40%	127 (60.5%)	76 (60.8%)	0.010
40-49%	37 (17.6%)	9 (7.2%)	
≥50%	46 (21.9%)	40 (32%)	
Type of MI			
STEMI	53 (25.2%)	-	-
Non-STEMI	157 (74.8%)	-	
Mean systolic BP (SD)	127 ± 28.5	118 ± 29.1	<0.05

Non AMI include old myocardial infarction, valvular heart disease, congenital heart disease and cardiac arrhythmias, ** kidney diseases, liver diseases, asthma, COPD, TB, allergy or cancer, * Missing data, **** ST-Elevation Myocardial Infarction (STEMI)*

Among all AHF cases, 140 (41.8%) had symptoms of respiratory infections, 36 (10.7%) had symptoms of diarrhoea, 32 (9.5%) had urinary symptoms and 168 (50.1%) had symptoms of any infection two week prior to the admission. ILI and fever were reported in 77 (23.0%) and 81 (24.2%) acute heart failure cases respectively during the last 2 weeks. Similarly, among AHF cases, 112 (33.4%) had symptoms of respiratory infections, 19 (5.7%) had symptoms of diarrhoea, 26 (7.8%) had urinary symptoms and 137 (40.9%) had symptoms of any infection one week prior to the admission. ILI and fever were reported in 58 (17.3%) and 37 (11%) AHF cases respectively during the last 1 week. Generally, rates of symptomatic respiratory infection, ILI and fever were reported to be higher after first-time heart failure, compared to recurrent heart failure.

Rate of respiratory infection during last week was significantly higher among first-time acute heart failure patients, compared to recurrent heart failure patients (OR 1.68, 95% CI, 1.02-2.77). ILI and fever rates were also consistently higher among first time acute heart failure patients in all three periods (current, within 1 week and within 2 weeks), however differences were not statistically significant (Table 3).

Table 3: Various types of infections and acute heart failure

	First-time	Recurrent	OR (95%CI)
Total (N)	**220**	**115**	**-**
Infection symptoms (currently)			
Respiratory	18.6% (41)	17.4% (20)	1.09 (0.60-1.96)
Gentro-intestinal	3.2% (7)	3.5% (4)	0.91 (0.26-3.18)
Urinary	5.5% (12)	5.2% (6)	1.05 (0.38-2.87)
Any infection	24.1% (53)	22.6% (26)	1.09 (0.64-1.85)
ILI	9.5% (21)	7.8% (9)	1.24 (0.55-2.81)
Fever	10% (22)	9.6% (11)	1.05 (0.49-2.25)
Infection symptoms (during last 1 week)			
Respiratory	37.3% (82)	26.1% (30)	1.68 (1.02-2.77)
Gentro-intestinal	5.5% (12)	6.1% (7)	0.89 (0.34-2.33)
Urinary	7.3% (16)	8.7% (10)	0.82 (0.36-1.88)
Any infection	43.6% (96)	35.7% (41)	1.40 (0.88-2.22)
ILI	19.1% (42)	13.9% (16)	1.46 (0.78-2.73)
Fever	10.9% (24)	11.3% (13)	1.01 (0.79-1.30)
Infection symptoms (during last 2 week)			
Respiratory	45% (99)	35.7% (41)	1.48 (0.93-2.35)
Gentro-intestinal	11.4% (25)	9.6% (11)	1.21 (0.57-2.56)
Urinary	9.5% (21)	9.6% (11)	1.00 (0.47-2.15)
Any infection	53.2% (117)	44.3% (51)	1.42 (0.91-2.24)
ILI	25% (55)	19.1% (22)	1.41 (0.81-2.46)
Fever	25.5% (56)	21.7% (25)	1.23 (0.72-2.10)

Rates of respiratory infections were reported to be higher among AMI patients compared to all other patients during all three periods, however the differences were not statistically significant (Table 4). No other infections were significantly associated with AMI in our dataset.

Table 4: Various types of infections and acute myocardial infarction

	Acute myocardial infarction		OR (95%CI)
	Yes	No	
Total (N)	**210**	**125**	**-**
Infection symptoms (currently)			
Respiratory	19.5% (41)	16% (20)	1.27 (0.71-2.29)
Gentro-intestinal	3.3% (7)	3.2% (4)	1.04 (0.30-3.64)
Urinary	3.8% (8)	8% (10)	0.45 (0.17-1.19)
Any infection	23.3% (49)	24% (30)	0.96 (0.57-1.62)
ILI	8.6% (18)	9.6% (12)	1.88 (0.41-1.90)
Fever	9% (19)	11.2% (14)	0.79 (0.38-1.63)
Infection symptoms (during last 1 week)			
Respiratory	36.2% (76)	28.8% (36)	1.40 (0.87-2.26)
Gentro-intestinal	5.2% (11)	6.4% (8)	0.81 (0.32-2.07)
Urinary	6.7% (14)	9.6% (12)	0.67 (0.30-1.50)
Any infection	41.9% (88)	39.2% (49)	1.12 (0.71-1.76)
ILI	17.6% (37)	16.8% (21)	1.06 (0.59-1.91)
Fever	10% (21)	12.8% (16)	0.76 (0.38-1.51)
Infection symptoms (during last 2 week)			
Respiratory	45.2% (95)	36% (45)	1.47 (0.93-2.31)
Gentro-intestinal	9.5% (20)	12.8% (16)	0.72 (0.36-1.44)
Urinary	9% (19)	10.4% (13)	0.86 (0.41-1.80)
Any infection	52.4% (110)	46.4% (58)	1.27 (0.81-1.98)
ILI	23.3% (49)	22.4% (28)	1.05 (0.62-1.79)
Fever	24.3% (51)	24% (30)	1.02 (0.60-1.70)

DISCUSSION

In this study we found high rates of symptomatic infections in patients admitted to hospital due to heart failure. Among the total heart failure cases, more than half had infection symptoms within the past two weeks and around a quarter had symptoms of current infections. However, a causal link between infections and heart failure cannot be established due to descriptive study design and small sample size. High infection symptoms in heart failure cases (particularly those with AMI) should be investigated further with large scale case control studies using laboratory confirmed diagnosis methods.

Most of the previous studies examined association between infections and acute heart failure exacerbations. Daering et al examined data of 1880 patients to examine the relationship of influenza infection and acute heart failure exacerbations.[15] There was no statistically significant difference amongst the rate of heart failure exacerbations between influenza positive and influenza negative cases. A study in Brazil showed an association of infection with decompensated heart failure in 45.8% of the patients. The study also reported high mortality in that group.[16] We did not study acute heart failure exacerbations; however rate of respiratory infections during last week was significantly higher among first-time acute heart

failure patients, compared to recurrent heart failure patients.

Around two thirds of total AHF cases in this study were admitted due to AMI. 45% of AMI cases had respiratory infections during the past 2 weeks, while 36% had respiratory infections during the last one week. Previous studies also reported high rates of respiratory and other infections in patients with AMI. Smeeth et al conducted a study in the UK to estimate the risks of AMI and stroke after common vaccinations and naturally occurring infections.[13] The results showed that acute lower respiratory tract infections and urinary tract infections were associated with a transient increase in the risk of AMI. A case control study in similar setting showed that the risk of respiratory infection increased three times during the 10 days before the myocardial infarction but no significant association with urinary tract infection was reported.[14]

As reported in other studies, respiratory infections were among the leading causes of infections in cardiac patients. Although the risk of myocardial infarction with serologically identified influenza is less evident, the risk of influenza like illness is reported to be higher in AMI cases. This could be due to various factors, but an increase in the respiratory infections in winter months could be a possible causal link. Although the risk of AMI with serologically defined influenza is less evident, the risk of influenza like illness is reported to be higher in MI cases. A meta-analysis suggested that influenza-like illness is associated with a twofold increase in MI.[17] Therefore, influenza vaccine can protect serious illness in these cases and can reduces the risk of hospitalizations due to AHF.[18] WHO also strongly recommend immunizing elderly people against pneumococcus and influenza. In this study only one participant was vaccinated against influenza. Influenza vaccination rates in this cohort should be improved. Some risk factors for AMI in this study were age, diabetes, hypertension, high cholesterol and presence of pre-existing illness, such as kidney diseases, liver diseases, asthma, COPD, TB, allergy or cancer. Previous studies in Pakistan identified hypertension, high cholesterol, lack of physical activity, smoking and diabetes are risk factors for developing AMI.[19] However, no study in Pakistan examined the rates of infections in AMI and other patients admitted with AHF. In Pakistan influenza season is during November to March every year, with a peak in December while in summer, sporadic influenza cases are detected. Death from cardiovascular diseases, particularly AMI, is more during winter than summer.[20]

Researchers suggest that the effect of infections on cardiovascular risk may be generic and is not linked to specific types of infection.[13] Large scale studies also show an increased risk of ischemic stroke (relative risk 1.30; P=0.007), myocardial infarction (relative risk 1.56, P<0.001), and vascular death (relative risk 1.51; P<0.001), among patients with high leukocyte count (>8.2x10(9)/L), compared to patients with low counts at baseline (<5.9x10(9)/L).[21] Inflammation contributes to both initiation and progression of atherosclerosis, and to acute rupture of atherosclerotic plaques with superimposed thrombus formation. Studies show that inflammatory markers, such as fibrinogen, C-reactive protein (CRP), and albumin and leukocyte count, predict first-time ischemic events.[22]

Infections may increase the risk of AHF in patients with pre-existing heart diseases through the several pathophysiological mechanisms, including delayed diastolic filling due to fever associated tachycardia, increases right ventricular afterload due to hypoxemia associated with severe respiratory infections and the inflammation of cardiac muscles due to infections.[1] A large cohort study showed that AHF triggered by infections may result in higher death rates, but the risk was not significant after adjustment for confounding factors. Authors concluded that the patient characteristics and severity of the AHF episode are likely to be more important determinants of mortality than the infection itself.[23] In this study long term mortality data was not available.

This study has limitations. We collected self-reported data on infection symptoms, which is subject to recall bias. All infectious cases should ideally be laboratory confirmed. Moreover, causality cannot be established due to cross-sectional study. Large scale studies should be conducted to examine the association between laboratory confirmed infections and heart failure.

CONCLUSION

To our knowledge this was the first study in Pakistan to estimate rates of infections among AHF cases. We reported very high rates of symptomatic infection among AHF cases, however, we could not establish a causal link. Large scale cohort or record linkage studies should be conducted to examine association of infections and risk of acute heart failure. Influenza vaccine uptake was very low in our cohort, so vaccines should be offered to elderly people, particularly those with pre-existing heart conditions.

AUTHORS' CONTRIBUTION

AAC designed the study, secured funding, performed data analysis and prepared the first draft of the manuscript. HN, SZJ and LB assisted in data collection.

MP assisted in data analysis and manuscript writing. FS supervised study in the field and assisted in data collection. All authors reviewed the final version and gave feedback.

Conflict of interest: Authors declared no conflict of interest.

REFERENCES

1. Tejedo AA, Miró Ò, Deza G, Martín-Ezquerra G, Gómez J, Pujol RM, et al. Precipitating factors in acute heart failure: a review. Emergencias. 2017;29(3):185-93.
2. Vos T, Allen C, Arora M, Barber RM, Bhutta ZA, Brown A, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1545-602.
3. Atherton JJ, Audehm R, Connell C. Heart failure guidelines A concise summary for the GP. Med Today. 2019;20(6):14-24.
4. Arrigo M, Jessup M, Mullens W, Reza N, Shah AM, Sliwa K, et al. Acute heart failure. Nature Reviews Disease Primers. 2020;6(1):1-15.
5. Pinho-Gomes AC, Cardoso JS, Azevedo LF, Almeida R, Pinho T, Maciel MJ. Characterization of acute heart failure hospitalizations in a Portuguese cardiology department. Rev Port Cardiol. 2013;32(7-8):567-75.
6. Sarmento PM, Fonseca C, Marques F, Ceia F, Aleixo A. Acutely decompensated heart failure: characteristics of hospitalized patients and opportunities to improve their care. Rev Port Cardiol. 2006;25(1):13-27.
7. Domínguez J, Harriague C, García-Rojas I, González G, Aparicio T, González-Reyes A. Insuficiencia cardiaca aguda en pacientes de 70 años o más: factores precipitantes de descompensación. Rev Clin Esp. 2010;210(10):497-504.
8. Corrales-Medina VF, Suh KN, Rose G, Chirinos JA, Doucette S, Cameron DW, et al. Cardiac complications in patients with community-acquired pneumonia: a systematic review and meta-analysis of observational studies. PLoS Med. 2011;8(6):e1001048.
9. DeFilippis EM, Reza N, Donald E, Givertz MM, Lindenfeld J, Jessup M. Considerations for heart failure care during the COVID-19 pandemic. Heart Fail. 2020;8(8):681-91.
10. Stewart S, McIntyre K, Capewell S, McMurray JJ. Heart failure in a cold climate: seasonal variation in heart failure-related morbidity and mortality. J Am Coll Cardiol. 2002;39(5):760-6.
11. Sandoval C, Walter S, Krueger P, Smieja M, Smith A, Yusuf S, et al. Risk of hospitalization during influenza season among a cohort of patients with congestive heart failure. Epidemiol Infect. 2007;135(4):574-82.
12. Musher DM, Abers MS, Corrales-Medina VF. Acute infection and myocardial infarction. N Engl J Med. 2019;380(2):171-6.
13. Smeeth L, Thomas SL, Hall AJ, Hubbard R, Farrington P, Vallance P. Risk of myocardial infarction and stroke after acute infection or vaccination. N Engl J Med. 2004;351(25):2611-8.
14. Meier CR, Jick SS, Derby LE, Vasilakis C, Jick H, Meier C, et al. Acute respiratory-tract infections and risk of first-time acute myocardial infarction. Lancet. 1998;351(9114):1467-71.
15. Daering NJ, Aurora L, Maahs LG, Bauer Z, Dakka A, Raychouni L. Acute Heart Failure Exacerbation and Influenza Infection. J Gen Intern Med 2019;34(2):S121.
16. Cardoso JN, Del Carlo CH, Oliveira Junior MTd, Ochiai ME, Kalil Filho R, Barretto ACP. Infection in patients with decompensated heart failure: in-hospital mortality and outcome. Arq Bras Cardiol. 2018;110:364-70.
17. Kwok CS, Aslam S, Kontopantelis E, Myint PK, Zaman MJS, Buchan I, et al. Influenza, influenza- like symptoms and their association with cardiovascular risks: a systematic review and meta- analysis of observational studies. Int J Clin Pract. 2015;69(9):928-37.
18. Bin Seo Y, Suk Choi W, Hyeon Baek J, Lee J, Young Song J, Soo Lee J, et al. Effectiveness of the influenza vaccine at preventing hospitalization due to acute exacerbation of cardiopulmonary disease in Korea from 2011 to 2012. Hum Vaccin Immunother. 2014;10(2):423-7.
19. Rasheed K, Hussain S, Alam M. Awareness of coronary artery disease risk factors among patients at a tertiary care hospital in rawalpindi pakistan. Pakistan J Public Health. 2019;9(1):12-4.
20. Moholdt T, Afoakwah C, Scuffham P, McDonald CF, Burrell LM, Stewart S. Excess mortality at Christmas due to cardiovascular disease in the HUNT study prospective population-based cohort in Norway. BMC Public Health. 2021;21(1):1-11.
21. Semerano A, Strambo D, Martino G, Comi G, Filippi M, Roveri L, et al. Leukocyte counts and ratios are predictive of stroke outcome and hemorrhagic complications independently of infections. Front Neurol. 2020;11:201.
22. Nguyen NPT, Cong TL, Tran TTH, Do BN, Nguyen ST, Vu BT, et al. Lower Plasma Albumin, Higher White Blood Cell Count and High-Sensitivity C-Reactive Protein are Associated with Femoral Artery Intima-Media Thickness Among Newly Diagnosed Patients with Type 2 Diabetes Mellitus. Int J Gen Med. 2022;15:2715.
23. Miró Ò, Takagi K, Gayat É, Gil V, Llorens P, Martín-Sánchez FJ, et al. Time-pattern of adverse outcomes after an infection-triggered acute heart failure decompensation and the influence of early antibiotic administration and hospitalisation: results of the PAPRICA-3 study. Clin Res Cardiol. 2020;109(1):34-45.

Address for Correspondence:

Abrar Ahmad Chughtai MBBS, MPH, PhD, Senior Lecturer (Epidemiologist), School of Population Health, Samuels Building, Kensington Campus, UNSW Sydney NSW 2052 Australia.
Email: abrar.chughtai@unsw.edu.au