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Clinical characteristics and outcomes of Yemeni patients with acute heart failure aged 50 years or younger: Data from Gulf Acute Heart Failure Registry (Gulf CARE)

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ABSTRACT

Aims: There is a shortage of data about acute heart failure (AHF) in the young, including its underlying causes, clinical presentation and outcomes. We aim to describe clinical characteristics, causes and outcomes of AHF in Yemeni patients aged 50 years or younger.

Methods and results: we evaluated Yemeni patients with AHF enrolled in Gulf CARE registry. Patients were divided into two groups: young patients (≤50 years) and older patients (>50 years). A total of 1536 patients with AHF were enrolled, of whom 635 (41.3%) were 50 years old or younger. The mean age for this group was 38.8 (±9.5) years; and 399 (62.8%) were males. Younger patients had a higher prevalence of non-ischemic cardiomyopathy (41% vs 11.1%, $p < 0.001$), primary valvular disease (27.9% vs 3.2%, $p < 0.001$), viral myocarditis (0.8% vs 0, $p < 0.001$). Ischemic heart disease (61.6% vs 25.5%, $p < 0.001$) and hypertensive heart disease (18.3% vs 6.3%, $p < 0.001$) were more frequent in the elderly group. Cardiogenic shock was more frequent among younger patients (13.7% vs 7.0, $p < 0.001$). In-hospital mortality was higher in patient aged ≤50 years (12% vs 7.6%, $p = 0.002$) while no difference in all-cause mortality was present at 3 months (17.8 vs 14.5, $p = 0.089$) and after 1 year (21.9% vs 20.6%, $p = 0.56$).

Conclusion: This analysis of Gulf CARE registry represents the largest report of patients admitted with AHF in Yemen. There were differences among cause of HF and precipitating factors of AHF among younger and elderly patients. Younger patients had higher in-hospital mortality and more severe clinical condition at admission.

1. Introduction

Heart failure (HF) is a complex clinical syndrome characterized by high mortality, frequent hospitalizations and by having a major economic impact on health care systems [1,2]. There are few data about HF in low-income countries, such as Yemen, including its underlying causes, clinical presentation and outcomes [3]. The prevalence of HF in developed countries is about 1–2% of the adult population, which raises to 10% among persons 70 years of age or older [4]. Nearly one million hospitalizations in Europe are attributed to acute episodes of HF each year [5,6]. However, data of HF patients aged <50 years are still limited [7,8]. The age distribution among Yemen population indicates that young age group is the largest age group, with 74% of the total population younger than 50 years of age [9]. Moreover, Yemen is one of the low income countries where rheumatic heart disease is still highly prevalent [10,11], while in more developed countries the most common cause of HF is no longer hypertension or valvular heart disease, but rather coronary artery disease (CAD) [12]. Thus, a clear understanding of the clinical and social challenges set by HF in low income countries is of considerable interest for the community and health services. This

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study aimed to describe the clinical characteristics, underlying causes, treatment and outcome of HF in Yemeni patients aged 50 years or younger using data from Gulf CARE Registry.

2. Materials and methods

Gulf CARE is a prospective, multicenter, multinational registry of patients admitted with the final diagnosis of acute HF (AHF) to 47 hospitals in 7 Middle East Arab countries. Registry design, methodology, and hospital characteristics have been previously described in detail [13]. Briefly, patient above 18 year of age, admitted to the participating hospitals with the admission diagnosis of AHF between 14 February 2012 and 14 November 2012 were recruited. Baseline and admission-based variables captured data on demographics, co-morbidities, risk factors, clinical presentation, laboratory data including troponin and BNP, medication regimens, in-hospital outcome, etiology, and precipitating factors for AHF. Whenever performed, echocardiography and coronary angiogram data along with cardiac procedures such as PCI, coronary artery bypass surgery (CABG), device therapy, or any cardiac surgery data were collected during admission and on follow-up. Follow-up of patients at 3 months and 1 year was performed. Follow-up was done by telephone at 3 months and either by telephone or by a clinic visit at 1 year. Data entry was done online using a custom-designed electronic case record form (CRF) at the Gulf CARE website (www.gulfcare.org). Institutional or national ethical committee or review board approval was obtained in each of the seven participating countries. The study is registered at clinicaltrials.gov (NCT01467973). Inclusion criteria were: age > 18 years, admission diagnosis of AHF. AHF was defined according to the European Cardiac Society (ESC) as rapid onset of symptoms and signs secondary to abnormal cardiac function and included: (i) symptoms (dyspnea at rest or on exercise, fatigue, tiredness, ankle swelling), (ii) signs (tachycardia, tachypnea, elevated jugular venous pressure, pulmonary rales, pleural effusion, hepatomegaly, peripheral edema), and, (iii) objective evidence of structural or functional abnormality of heart at rest (third heart sound, murmurs, cardiomegaly, abnormal echocardiogram, raised natriuretic peptide concentration). AHF was further classified as either acute decompensated chronic HF (ADCHF) or new-onset AHF (de novo AHF) based on ESC guidelines [6]. ADCHF was defined as worsening of HF in patients with a previous diagnosis or hospitalization for HF. New-onset AHF (de novo AHF) was defined as AHF in patients with no prior history of HF. Exclusion criteria: Patients whose final diagnosis was not HF were excluded from the final analyses. Yemen data were collected in eight major hospitals all over the country. An institutional ethical approval was obtained in each of the eight participating hospitals, and all patients provided informed consent. A total of 1536 Yemeni patients were enrolled in this registry from February 14, 2012 to November 13, 2012. Data of Yemeni patients were extracted from the whole registry data and were categorized into two age groups: patients aged 50 years and younger (Group A) and patient aged above 50 years (Group B). Demographic factors, clinical characteristics, and underlying causes, precipitating factors, management and outcomes with the mortality at 3-months and one year follow up were analyzed using SPSS version 21 (IBM, Armonk, New York, U.S.).

2.1. Statistical analysis

Data are presented as mean ± standard deviation for continuous data or as n and (%) for discrete variables unless otherwise specified. Continuous variables were shown as median and interquartile range (IQR) when they had a skewed distribution. Distributions of continuous data variables were compared using either the *t*-test or the Mann-Whitney test, depending on whether the data followed a normal distribution. We compared distributions of categorical variables, expressed as frequency (and percentage) using the chi-square test. Univariable and multivariable logistic-regression analyses were performed to evaluate the relation between in-hospital and 1-year mortality and the following baseline variables: age, sex, hypertension, smoke habit, khat habit, diabetes mellitus, coronary artery disease, valvular heart disease, previous stroke, LVEF, heart rate, systolic blood pressure, cardiogenic shock, elevation in troponin T, eGFR, hemoglobin, elevated jugular venous pressure (JVP), ascites, hepatomegaly, presence of gallop, pleural effusion, use of inotropes, need of mechanical ventilation, de novo vs acute decompensated chronic HF. Variables with a probability value < 0.05 by univariable analysis were entered as covariates in the multivariable model. Multivariable models were constructed from variables having significant associations, with the outcome with p 0.05 using forward selection with a 0.10 significance level for keeping. Model calibration was assessed by Hosmer-Lemeshow goodness-of-fit test.

A p value of < 0.05 was considered to be statistically significant. All data analyses were carried out using the Statistical Package for Social Sciences version 21 (SPSS, Inc., Chicago, Illinois, USA).

3. Results

A total of 1536 Yemeni patients with AHF were enrolled during the study period. The mean age of the population was 53.6 (±15.3) years and the majority were male (64.5%). Patients aged ≤50 years (group A) were 635 (41.3%). Baseline demographic and clinical characteristics of the population divided into two age groups (group A: aged ≤50 years; group B aged >50 years) are summarized in Table 1. The patients in the younger group had a mean aged of 38.8 (±9.5) years and 62.8% were males. Younger patients had a longer hospital stay (10.5 ± 8.5 vs 9.5 ± 7.6 days, p < 0.02). Elderly patients were more likely to have hypertension (47.9% vs 18.7%, p < 0.001), dyslipidemia (14.7% vs 3.8%, p < 0.001) and diabetes mellitus (28.9% vs 10.6%; p < 0.001). More than one half of patients were Khat users with no difference between group A and B (53.4% vs 57.3%, p = ns).

Left ventricular ejection fraction did not differ between the two age groups (40.1 ± 12% vs 39.1 ± 13%, p = ns), whereas elderly patients had lower eGFR (70 ± 35 vs 87 ± 44 mL/min, p < 0.001). Younger patients presented with more pronounced signs and symptom of congestion: patients in group A were more likely to be have dyspnea in NYHA class III to IV (78.9% vs 73.9%; p < 0.05), paroxysmal nocturnal dyspnea (79.7% vs 73%, p < 0.001), raised JVP (73% vs 54%, p < 0.001), lower limb edema (67.1% vs 55.8%, p < 0.001), hepatomegaly (70% vs 51%, p < 0.001), weight gain before admission (48% vs 32.8%, p > 0.001).

There were differences in two groups regarding the cause of HF (Table 2). Younger patients had a higher prevalence of non-ischemic cardiomyopathy (41% vs 11.1%, <0.001), primary (rheumatic) valvular disease (27.9% vs 3.2%, p < 0.001), viral myocarditis (0.8% vs 0, p < 0.001). Ischemic heart disease (61.6% vs 25.5%, p < 0.001) and hypertensive heart disease (18.3% vs 6.3%, p < 0.001) were more frequent in the elderly group.

Presumed precipitating cause of HF and in hospital course are shown in Table 3. The leading precipitating cause of HF was infection (22.8%) in group A and acute coronary syndromes (27.1%) in group B. Cardiogenic shock at admission or during hospitalization was more frequent among younger patient (13.7% vs 7.0, p < 0.001). Accordingly, younger patients were more likely to be treated with inotropes (26.6% vs 19.1, p < 0.001) and with invasive ventilation (11.5% vs 6.4%, p < 0.001).

Table 1
Baseline and clinical characteristics of the patients.

Characteristic	≤50 years (n = 635)	>50 years (n = 901)	p value
Mean age	38.8 (±9.4)	64.1 (±8.6)	
Female	236 (37.2)	309 (34.3)	0.256
Hospital stay (days)	10.5 (±8.5)	9.5 (±6.24)	0.02
Risk factors			
Smoking (all forms)	207 (32.6)	312 (34.6)	0.452
Khat use	339 (53.4)	516 (57.3)	0.731
Diabetes mellitus	67 (10.6)	269 (28.9)	<0.001
Hypertension	119 (18.7)	432 (47.9)	<0.001
Hyperlipidemia	24 (3.8)	132 (14.7)	<0.001
Family history cardiomyopathy	52 (8.2)	59 (6.5)	0.231
Clinical presentation			
LVEF (%)	40.1 (±12.1)	39.1 (±13.5)	0.15
Cardiac Arrest on Arrival	31 (4.9)	34 (3.8)	0.30
Dyspnea (NYHA III-IV)	501(78.9)	666 (73.9)	0.05
Paroxysmal nocturnal dyspnea	506 (79.7)	658 (73)	<0.001
Lower Limb Edema	426 (67.1)	503 (55.8)	<0.001
Weight Gain	305 (48)	296 (32.8)	<0.001
Chest pain	288 (45.4)	540 (59.9)	<0.001
Heart rate (beats/min)	105 (±20)	96 (±21)	<0.001
Systolic BP (mm Hg)	122 (±28)	136 (±31)	<0.001
Diastolic BP (mm Hg)	77 (±19)	84 (±17)	<0.001
Respiratory rate (/min)	26 (±5)	25 (±5)	<0.001
BMI (kg/m2)	25 (±4)	26 (±4)	<0.001
Raised JVP	466 (73%)	490 (54%)	<0.001
Enlarged Tender Liver	445 (70%)	466 (51%)	<0.001
Gallop	408 (64.3%)	453 (50.3%)	<0.001
eGFR(mL/min)	87 (±44)	70 (±35)	<0.001
Atrial fibrillation	90 (14.2)	40 (4.4)	<0.001
Third degree AV block	4 (0.7)	43 (4.8)	<0.001

LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; BP: blood pressure; BMI: body mass index, JVP: jugular venous pressure; eGFR: estimated glomerural filtration rate; AV: atrio-ventricular.

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