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Original Article

Comparison of Indian subcontinent and Middle East acute heart failure patients: Results from the Gulf Acute Heart Failure Registry

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ABSTRACT

Objective: To compare Middle East Arabs and Indian subcontinent acute heart failure (AHF) patients.
Methods: AHF patients admitted from February 14, 2012 to November 14, 2012 in 47 hospitals among 7 Middle East countries.
Results: The Middle Eastern Arab group (4157) was older (60 *vs.* 54 years), with high prevalence of coronary artery disease (48% *vs.* 37%), valvular heart disease (14% *vs.* 7%), atrial fibrillation (12% *vs.* 7%), and khat chewing (21% *vs.* 1%). Indian subcontinent patients (382) were more likely to be smokers (36% *vs.* 21%), alcohol consumers (11% *vs.* 2%), diabetic (56% *vs.* 49%) with high prevalence of AHF with reduced ejection fraction (76% *vs.* 65%), and with acute coronary syndrome (46% *vs.* 26%). In-hospital mortality was 6.5% with no difference, but 3-month and 12-month mortalities were significantly high among Middle East Arabs, (13.7% *vs.* 7.6%) and (22.8% *vs.* 17.1%), respectively.
Conclusions: AHF patients from this region are a decade younger than Western patients with high prevalence of ischemic heart disease, diabetes mellitus, and AHF with reduced ejection fraction.

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There is an urgent need to control risk factors among both groups, as well as the need for setting up heart failure clinics for better postdischarge management.

1. Introduction

Many studies have observed worse prognosis among most migrant groups or minorities compared to local population following acute heart failure (AHF) admission.[1–3] In addition, it is noted that people of South Asian (Indian subcontinent) descent have a high prevalence of comorbidities, which lead to increased occurrence of heart failure (HF) among these population.[4–7] Furthermore, the etiology and management of ethnic minority HF patients may vary. Hence, in 2010, the Canadian Cardiovascular Society published guidelines on HF in ethnic minority populations in Canada.[8] Presently, there is a significant percentage of South Asian population residing in the Middle East, but little is known about the etiology, presentation, management, and prognosis for this population compared to the Middle East population. In a previous retrospective single-center study from Qatar, it was observed that HF patients in the Middle East present at relatively younger age regardless of ethnicity and they tend to have more comorbidites.[9] Gulf CARE (aCute heArt failuRe rEgistry) is a prospective, multinational, multicenter registry of patients admitted with the diagnosis of AHF to 47 hospitals in 7 Middle Eastern countries.[10] The aim of this paper is to compare clinical characteristics, management, and outcomes between Middle East Arabs and Indian subcontinent AHF patients enrolled in the Gulf CARE study.

2. Methods

Gulf CARE registry design, methodology, and hospital characteristics have been previously described in detail.[10] Briefly, patients admitted to the participating hospitals between February 14, 2012 and November 14th, 2012 were recruited. Included patients were males and females above 18 year of age with admission diagnosis of AHF. Middle Eastern Arabs included those from Oman, Yemen, Saudi Arabia, Kuwait, United Arab Emirates, Qatar, and Bahrain, while those from the Indian subcontinent included nationals from India, Pakistan, Afghanistan, Bangladesh, Sri Lanka, and Nepal. Indian subcontinent ethnicity was determined by self-report, the gold standard, as well as identifying country of birth from passport and other national identity documents. Online data were captured, which included demographic data, comorbidities, risk factors, precipitating factors, clinical presentation, investigations, medication history and their dosages, in-hospital management, and outcome. Follow-up of patients at 3 months and 1 year was performed. Telephonic follow-up was done at 3 months and either telephonic or clinic visit at 1 year. Institutional or national ethical committee or review board approvals were obtained in each of the seven participating countries. The study is registered at clinicaltrials.gov (NCT01467973).

AHF was defined based on ESC criteria.[11] AHF was further classified as either acute decompensated chronic heart failure (ADCHF) or new-onset acute heart failure (*de novo* AHF) based on ESC guidelines.[11] 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. Definitions of data variables in the CRF were based on the ESC guidelines of 2008 and the ACC clinical data standards of 2005.[11,12] Khat chewing was defined as chewing khat plant/leaves (*Catha edulis* containing cathionine, an amphetamine-like stimulant) within 1 month of the index admission. Idiopathic dilated cardiomyopathy was defined as a myocardial disorder in which the heart muscle is structurally and functionally abnormal (in the absence of coronary artery disease (CAD), hypertension, valvular disease, or congenital heart disease sufficient to cause the observed myocardial abnormality). HF with preserved ejection fraction (HFpEF) was defined as presence of symptoms and/or signs of HF and a left ventricular ejection fraction (LVEF) >40%.

2.1. *Statistical analyses*

Descriptive statistics were used to summarize the data. For categorical variables, frequencies and percentages were reported and differences between groups were analyzed using Pearson's chi-square test (or Fisher's exact test for cells <5). For continuous variables, mean and standard deviation were used to summarize the data while analysis was done using Student's *t*-test. For those variables that were not normally distributed, median and interquartile ranges (25th and 75th percentiles) were used to present the data while comparative analysis was performed using the nonparametric Mann–Whitney test. An *a priori* two-tailed level of significance was set at 0.05. Statistical analyses were conducted using STATA version 13.1 (STATA Corporation, College Station, TX, USA).

3. Results

A total of 47 hospitals in 7 Arabian Gulf states (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates, and Yemen) participated in the Gulf CARE project, with a total of 5005 patients enrolled. However, only 4539 met the inclusion criteria of Gulf citizens and those from the Indian subcontinent accounting for almost 92% ($n = 4157$) and 8% ($n = 382$), respectively (Table 1). The overall mean age of the cohort was 59 ± 15 years and 62% ($n = 2817$) were males. More than half of the patients (55%, $n = 2480$) presented with ADCHF while the rest (45%; $n = 2059$) had *de novo* AHF. Cardiologists were the main healthcare provider for 70% ($n = 3199$) of the patients. Comorbid conditions were common, particularly hypertension

Table 1 – Patient characteristics of the Gulf CARE cohort stratified by race.

Characteristic	All ($n = 4539$)	Indian subcontinent ($n = 382$)	Gulf citizen ($n = 4157$)	p value
Age, mean (±SD)	59 ± 15	54 ± 11	60 ± 15	<0.001
Male gender, *n* (%)	2817 (62%)	317 (83%)	2500 (60%)	<0.001
Main care provider, n (%)				
Cardiologist	3199 (70%)	326 (85%)	2873 (69%)	<0.001
Internist	1340 (30%)	56 (14%)	1284 (31%)	
BMI, kg/m^2, median (IQR)	27 (24,31)	26 (24,29)	27 (24,31)	<0.001
BMI, kg/m^2, n (%)				
<18.4	96 (2%)	3 (1%)	93 (2%)	
18.4–24.9	1401 (31%)	141 (37%)	1260 (30%)	<0.001
25.0–29.9	1703 (38%)	168 (44%)	1535 (37%)	
≥30.0	1339 (29%)	70 (18%)	1269 (31%)	
Medical history, n (%)				
Hypertension	2747 (61%)	217 (57%)	2530 (61%)	0.121
Diabetes mellitus	2236 (49%)	212 (56%)	2024 (49%)	0.011
CAD	2122 (47%)	140 (37%)	1982 (48%)	<0.001
Hyperlipidemia	1602 (35%)	120 (31%)	1482 (36%)	0.097
Smoking[a]	1003 (22%)	139 (36%)	864 (21%)	<0.001
Khat	888 (20%)	3 (1%)	885 (21%)	<0.001
CKD/dialysis	652 (14%)	58 (15%)	594 (14%)	0.633
Valvular heart disease	602 (13%)	24 (6%)	578 (14%)	<0.001
Atrial fibrillation	520 (11%)	27 (7%)	493 (12%)	0.005
Stroke/TIA	371 (8.2%)	16 (4.2%)	355 (8.5%)	0.003
PVD	197 (4.3%)	8 (2.1%)	189 (4.6%)	0.024
Alcohol[b]	14 (3%)	43 (11%)	101 (2%)	<0.001
Clinical presentation, n (%)				
Dyspnea	4441 (98%)	363 (95%)	4078 (98%)	<0.001
Basal lung crepitations	4157 (92%)	361 (95%)	3796 (91%)	0.032
Orthopnoea	3561 (78%)	283 (74%)	3278 (79%)	0.030
PND	2913 (64%)	196 (51%)	2717 (65%)	<0.001
Easy fatigability	2586 (57%)	142 (37%)	2444 (59%)	<0.001
Abdominal/lower limb swelling	2031 (45%)	92 (24%)	1939 (47%)	<0.001
Chest pain	2037 (45%)	192 (50%)	1845 (44%)	0.027
Gallop	1757 (39%)	143 (37%)	1614 (39%)	0.593
Enlarged tender liver	1290 (28%)	28 (7%)	1262 (30%)	<0.001
Type of AHF, n (%)				
De novo AHF	2059 (45%)	255 (67%)	1804 (43%)	<0.001
ADCHF	2480 (55%)	127 (33%)	2353 (57%)	

SD – standard deviation; BMI – body mass index; IQR – interquartile range; CAD – coronary artery disease; PVD – peripheral vascular disease; TIA – transient ischemic attack; CKD – chronic kidney disease; PND – paroxysmal nocturnal dyspnea; AHF – acute heart failure; ADCHF – acute decompensated chronic heart failure.
Numbers might not add up to 100% due to rounding off. Analyses were performed using Student's *t*-test, Mann–Whitney or Pearson's chi-square test, whenever appropriate.
[a] Smoking – includes chewing tobacco and/or smoking waterpipe.
[b] Alcohol – daily.

(61%; $n = 2747$), diabetes mellitus (49%; $n = 2236$), CAD (47%; $n = 2122$), and hyperlipidemia (35%; $n = 1602$). The three most common presenting signs and symptoms were dyspnea (98%; $n = 4441$), basal lung crepitations (92%; $n = 4157$), and orthopnoea (78%; $n = 3561$). On admission, the mean heart rate was 97 ± 23 and the predominant New York Heart Association (NYHA) class was III/IV (76%; $n = 3454$). The rest of the characteristics are shown in Table 1.

Indian subcontinent HF patients were generally associated with fewer comorbidities compared to Gulf citizens. They were younger (60 *vs.* 54 years; $p < 0.001$), had significantly lower proportion of patients with CAD (37% *vs.* 48%; $p < 0.001$), were khat users (1% *vs.* 21%; $p < 0.001$), and had valvular heart disease (6% *vs.* 14%; $p < 0.001$), atrial fibrillation (7% *vs.* 12%; $p < 0.001$), prior stroke/transient ischemic stroke (4.2% *vs.* 8.5%; $p < 0.001$), and peripheral vascular disease (2.1% *vs.* 4.6%; $p < 0.001$). In addition, they were also less likely to present with dyspnea (95% *vs.* 98%; $p < 0.001$), orthopnoea (74% *vs.*79%; $p = 0.030$), paroxysmal nocturnal dyspnea (51% *vs.*65%; $p < 0.001$), easy fatigability (37% *vs.*59%; $p < 0.001$), abdominal/lower limb swelling (24% *vs.* 47%; $p < 0.001$), and enlarged tender liver (7% *vs.* 30%; $p < 0.001$). However, the Indian subcontinent patients were more likely to be associated with diabetes mellitus (56% *vs.* 49%; $p < 0.001$), smoking (36% *vs.* 21%; $p < 0.001$), and alcohol consumption (11% *vs.* 2%; $p < 0.001$). Furthermore, Indian subcontinent patients were more likely to present with basal lung crepitations (95% *vs.* 91%; $p = 0.032$) and chest pain (50% *vs.* 44%; $p = 0.027$).

Table 2 shows the physical, laboratory, ECG, and echocardiography findings. Indian subcontinent patients were associated with higher baseline heart rate (102 *vs.* 96 beats/min; $p < 0.001$), systolic BP (144 *vs.*137 mmHg; $p < 0.001$), diastolic BP (87 *vs.*81 mmHg; $p < 0.001$), and lower admission serum urea (9 *vs.* 12 mmol/L; $p < 0.001$) and serum potassium

Table 2 – Physical, laboratory, ECG, and echocardiography investigations by race.

Characteristic	All ($n = 4539$)	Indian subcontinent ($n = 382$)	Gulf citizen ($n = 4157$)	p value
Physical, mean (±SD), unless specified otherwise				
HR, beats/min ($n = 4386$)	97 ± 23	102 ± 24	96 ± 23	<0.001
SBP, mmHg ($n = 4388$)	137 ± 34	144 ± 39	137 ± 34	<0.001
DBP, mmHg ($n = 4388$)	81 ± 20	87 ± 23	81 ± 19	<0.001
Raised JVP > 6 cm, n (%)	2251 (50%)	172 (45%)	2079 (50%)	0.062
Laboratory investigations, mean (±SD), unless specified otherwise				
First serum creatinine, mmol/L	130 ± 117	128 ± 102	130 ± 118	0.732
First serum urea, mmol/L	12 ± 8	9 ± 6	12 ± 9	<0.001
First serum potassium, mmol/L	4.2 (3.9–4.6)	4.1 (3.7–4.5)	4.2 (3.9–4.6)	0.002
BNP, pg/mL, median, ($n = 334$)	1300 (890–5209)	2396 (1503–5000)	1293 (890–5223)	0.370
NT-pro BNP, pg/mL, ($n = 669$)	3059 (1260–6986)	4023 (1797–7590)	2778 (1138–6891)	0.021
e-GFR, mL/min, ($n = 4476$)	64 (44–87)	70 (49–88)	63 (44–87)	0.029
Hemoglobin, g/dL	12.6 (11–14)	13.6 (12–15)	12.5 (11–14)	<0.001
Total cholesterol, mmol/L, ($n = 3268$)	4.6 (3.6–5.6)	4.4 (3.5–5.3)	4.6 (3.6–5.6)	0.155
HbA1c, % ($n = 1792$)	6.7 (5.5–8.5)	7.4 (6.0–9.8)	6.7 (5.5–8.5)	<0.001
ECG, n (%), unless specified otherwise				
Rhythm status[a]				
Sinus rhythm	3740 (82%)	328 (86%)	3412 (82%)	0.162
AF/flutter	589 (13%)	42 (11%)	547 (13%)	
CHB	59 (1.3%)	4 (1.1%)	55 (1.3%)	
Paced	68 (1.5%)	1 (0.3%)	67 (1.6%)	
SVT	24 (0.5%)	3 (0.8%)	21 (0.5%)	
Others	59 (1.3%)	4 (1.1%)	55 (1.3%)	
LV hypertrophy	1350 (30%)	116 (30%)	1234 (30%)	0.780
ST-depression/T-inversion	1987 (44%)	226 (59%)	1761 (42%)	<0.001
STEMI	474 (10%)	101 (26%)	373 (9%)	<0.001
Pathological Q waves	1061 (23%)	104 (27%)	957 (23%)	0.063
QRS duration = > 0.12 ms				
No	3616 (80%)	317 (83%)	3299 (79%)	0.006
LBBB	595 (13%)	34 (9%)	561 (14%)	
RBBB	191 (4.2%)	24 (6.3%)	167 (4.0%)	
IVCD	137 (3.0%)	7 (1.8%)	130 (3.1%)	
Echocardiography, n (%), unless specified otherwise				
LVEF, %, med (IQR) ($n = 4150$)	35 (25–45)	35 (25–40)	35 (25–45)	<0.001
LVEF > 40% ($n = 4150$)	1416 (34%)	85 (24%)	1331 (35%)	<0.001

SD – standard deviation; ECG – electrocardiography; HR – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; JVP – jugular venous pressure; BNP – B-type natriuretic peptide; NT-pro BNP – N-terminal B-type natriuretic peptide; GFR – glomerular filtration rate; AF – atrial fibrillation; CHB – complete heart block; SVT – supraventricular tachycardia; LV – left ventricular; STEMI – ST-segment elevation myocardial infarction; LBBB – left bundle branch block; RBBB – right bundle branch block; IVCD – intraventricular conduction delay; LVEF – left ventricular ejection fraction.

Analyses were performed using Student's t-test or Mann–Whitney or Pearson's chi-square or Fisher's exact tests, whenever appropriate.

[a] Percents may not add up to 100% due to rounding off.

(4.1 *vs*.4.2 mmol/L; $p = 0.002$). However, Gulf citizen patients were associated with lower, NT-pro BNP (2788 *vs*. 4023 pg/mL; $p = 0.021$), e-GFR (63 *vs*. 70 mL/min; $p = 0.029$), hemoglobin (12.5 *vs*. 13.6 g/dL; $p < 0.001$), and HbA1c (6.7 *vs*. 7.4 g/dL; $p < 0.001$), as well as lower proportion of patients with ST-depression/T-inversion (42% *vs*. 59%; $p < 0.001$) and STEMI (9% *vs*. 26%; $p < 0.001$). Furthermore, the proportion of patients with LVEF >40% was significantly lower in Indian subcontinent patients when compared to Gulf citizens (24% *vs*. 35%; $p < 0.001$).

Eighty-two percent ($n = 3740$) of the patients were in sinus rhythm with 13% demonstrating atrial fibrillation or flutter. Overall 80% ($n = 3616$) of patients had QRS duration <120 ms with only 13% ($n = 595$) of the cohort presenting with left bundle branch block (LBBB) morphology on ECG. Indian subcontinent patients were less likely to have LBBB than Gulf citizens (9% *vs*.14%; $p = 0.006$).

Table 3 presents cardiac procedures, in-hospital course, precipitating factors, etiology, and in-hospital outcomes. A total of 5.8% and 1.4% of the patients had PCI and CABG, respectively, with Indian subcontinent patients more likely to have these procedures than Gulf citizens (16% *vs*. 5%, PCI; $p < 0.001$) (3.1% *vs*. 1.3%, CABG; $p = 0.003$). The three most prevalent in-hospital events/courses included infection requiring therapy (24%), requirement of inotropes (16%) and noninvasive ventilation (NIV) (9%). Indian subcontinent patients were more likely to have NIV (16% *vs*. 9%; $p < 0.001$), cardiogenic shock (11% *vs*. 8%; $p = 0.039$), ventricular tachycardia/fibrillation requiring therapy (7.1% *vs*. 4.3%; $p = 0.014$), and be on intra-aortic balloon pump (IABP) (4.7% *vs*. 1.4%; $p < 0.001$).

The three most common precipitating causes of HF were acute coronary syndrome (ACS) (27%), noncompliance with medications (20%), and infection (15%). Indian subcontinent

Table 3 – Cardiac procedures, in-hospital course, precipitating causes, and etiology of heart failure, NYHA classification, and in-hospital outcome stratified by race.

Characteristic	All ($n = 4539$)	Indian subcontinent ($n = 382$)	Gulf citizen ($n = 4157$)	p value
Cardiac procedures, during admission, n (%)				
PCI	265 (5.8%)	63 (16%)	202 (5%)	<0.001
CABG	65 (1.4%)	12 (3.1%)	53 (1.3%)	0.003
Device therapy	111 (2.5%)	11 (2.9%)	100 (2.4%)	0.337
CRT-D	24	2	22	
CRT-P	1	0	1	
ICD	44	7	37	
PPM	42	2	40	
Valve repair/replacement	83 (1.8%)	1 (0.3%)	82 (2.0%)	0.009
In-hospital course, n (%)				
Infection requiring therapy	1100 (24%)	96 (25%)	1004 (24%)	0.669
Inotropes	728 (16%)	55 (14%)	673 (16%)	0.361
NIV	416 (9%)	62 (16%)	354 (9%)	<0.001
Intubation/ventilation	387 (8.5%)	37 (9.7%)	350 (8.4%)	0.396
Cardiogenic shock	373 (8%)	42 (11%)	331 (8%)	0.039
AFib requiring therapy	275 (6.1%)	18 (4.7%)	257 (6.2%)	0.249
Blood transfusion	231 (5.1%)	18 (4.7%)	213 (5.1%)	0.726
VT/VF requiring therapy	207 (4.6%)	27 (7.1%)	180 (4.3%)	0.014
Acute dialysis/ultrafiltration	122 (2.7%)	7 (1.8%)	115 (2.8%)	0.280
IABP	75 (1.7%)	18 (4.7%)	57 (1.4%)	<0.001
Stroke	65 (1.4%)	4 (1.1%)	61 (1.5%)	0.655
Precipitating causes of heart failure, n (%)				
Acute coronary syndrome	1235 (27%)	175 (46%)	1060 (26%)	<0.001
Noncompliance with meds	905 (20%)	52 (14%)	853 (21%)	
Infection	679 (15%)	33 (9%)	646 (16%)	
Uncontrolled hypertension	370 (8.2%)	44 (12%)	326 (7.8%)	
Uncontrolled arrhythmias	257 (5.9%)	13 (3.4%)	254 (6.1%)	
Worsening renal failure	181 (4.0%)	13 (3.4%)	168 (4.0%)	
Anemia	138 (3.0%)	6 (1.6%)	132 (3.2%)	
Etiology of heart failure[a]*, n (%)*				
Ischemic HD	2433 (54%)	250 (65%)	2183 (53%)	<0.001
Idiopathic cardiomyopathy	806 (18%)	53 (14%)	753 (18%)	
Hypertensive HD	741 (16%)	48 (13%)	693 (17%)	
Valvular HD	407 (9.0%)	19 (5.0%)	388 (9.3%)	
Pulmonary hypertension	120 (2.6%)	6 (1.6%)	114 (2.7%)	
Congenital HD	17 (0.4%)	3 (0.8%)	14 (0.3%)	
Myocarditis	14 (0.3%)	3 (0.8%)	11 (0.3%)	
NYHA classification[b] *at discharge, n (%) [n = 4542]*				
I	2229 (54%)	154 (44%)	2075 (55%)	<0.001
II	1554 (38%)	179 (51%)	1375 (37%)	
III	107 (2.6%)	13 (3.7%)	94 (2.5%)	
IV	216 (5.3%)	4 (1.1%)	212 (5.6%)	
Outcome, n (%)				
Died	296 (6.5%)	17 (4.5%)	279 (6.7%)	0.087

NYHA – New York Heart Association; PCI – percutaneous coronary intervention; CABG – coronary artery bypass graft; CRT-D – cardiac resynchronization therapy with defibrillation; CRT-P – cardiac resynchronization therapy with pacemaker; ICD – implantable cardioverter-defibrillator; PPM – permanent pacemaker; NIV – noninvasive ventilation; AFib – atrial fibrillation; VT/VF – ventricular tachycardia/ventricular fibrillation; IABP – intra-aortic balloon pump; Meds – medications; HD – heart disease.

[a] One patient had a missing etiology of heart failure.

[b] For NYHA classification, analytics excluded those that died ($n = 296$; 6.5%) as well as those that left against medical advice ($n = 137$; 3.0%) (LAMA) ($n = 433 = 4539 - 4106$). Analyses were performed using Pearson's chi-square or Fisher's exact tests, whenever appropriate.

patients were more likely to be associated with ACS (46% *vs.* 26%; $p < 0.001$) and uncontrolled hypertension (12% *vs.* 7.8%; $p < 0.001$) while Gulf citizens were more likely to be associated with noncompliance with medications (21% *vs.* 14%; $p < 0.001$) and infection (16% *vs.* 9%; $p < 0.001$) as precipitating causes of HF. The three most prevalent etiologies of HF were CAD (54%), idiopathic cardiomyopathy (18%), and hypertensive heart disease (HHD) (16%). Valvular heart disease, as an etiology, accounted for 9% ($n = 407$) of the patients.

Table 4 outlines discharge medications of the Gulf CARE cohort. Among the discharged medications, and besides aspirin (81%) and statins (72%), the most prescribed medications were diuretics (94%), angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ACEIs/ARB) (79%), beta-blockers (71%), and aldosterone antagonists (44%). Indian subcontinent patients were more likely to be prescribed aspirin (86% *vs.* 81%; $p = 0.015$), clopidogrel (57% *vs.* 36%; $p < 0.001$), and statin (83% *vs.* 71%; $p < 0.001$) while Gulf citizens

Table 4 – Discharge medications of the Gulf CARE cohort stratified by race.

Medications at discharge[a]	All ($n = 4106$)	Indian subcontinent ($n = 350$)	Gulf citizen ($n = 3756$)	p value
Diuretics	3862 (94%)	322 (92%)	3540 (94%)	0.089
Aldosterone antagonist	1800 (44%)	121 (35%)	1679 (45%)	<0.001
ACEI	2510 (61%)	215 (61%)	2295 (61%)	0.905
ARB	723 (18%)	39 (11%)	684 (18%)	0.001
Beta-blocker	2925 (71%)	251 (72%)	2674 (71%)	0.837
Digoxin	1045 (25%)	86 (25%)	959 (26%)	0.693
Nitrates	1583 (39%)	136 (39%)	1447 (39%)	0.903
Hydralazine	292 (7.1%)	30 (8.6%)	262 (7.0%)	0.267
Aspirin	3344 (81%)	302 (86%)	3042 (81%)	0.015
Clopidogrel	1538 (37%)	200 (57%)	1338 (36%)	<0.001
Statin	2955 (72%)	290 (83%)	2665 (71%)	<0.001
CCB	623 (15%)	53 (15%)	570 (15%)	0.987
Anticoagulant	751 (18%)	51 (15%)	700 (19%)	0.060
Anti-arrhythmic	195 (4.8%)	15 (4.3%)	180 (4.8%)	0.670
Ivabradine	201 (4.9%)	19 (5.4%)	182 (4.9%)	0.629

ACEI – angiotensin converting enzyme inhibitor; ARB – angiotensin receptor blocker; CCB – calcium channel blocker.
[a] Medications at discharge excluded those that died ($n = 296$; 6.5%) as well as those that left against medical advice ($n = 137$; 3.0%) (LAMA) ($n = 433 = 4539 - 4106$). Analyses were performed using Pearson's chi-square.

were likely to be prescribed aldosterone antagonist (45% *vs.* 35%; $p < 0.001$) and ARB (18% *vs.* 11%; $p < 0.001$).

Table 5 shows follow-up data at 3 and 12 months. Follow-up status was complete in 98.5% of patients at 3 and 12 months. At 3-month follow-up, Indian subcontinent patients were less likely to be hospitalized for HF (15.1% *vs.* 20.5%; $p < 0.001$). They were more likely to undergo CABG (7.4% *vs.* 3.3%; $p < 0.001$) but less likely to have device therapy (0.4% *vs.* 1.1%; $p = 0.024$) when compared to Gulf citizens. Importantly, Indian subcontinent patients were less likely to die compared to Gulf citizens (7.6% *vs.* 13.7%; $p = 0.003$). Over the 12-month follow-up period, Indian subcontinent patients were associated with lower hospitalization rate for HF (18.8% *vs.* 23.7%; $p < 0.001$) but higher use of device therapy (1.9% *vs.* 1.5%; $p < 0.001$) and the procedure, CABG (9.2% *vs.* 6.3%; $p < 0.001$) when compared with Gulf citizens. Furthermore, Indian subcontinent patients were associated with lower all-cause mortality when compared to Gulf citizens (17.1% *vs.* 22.8%; $p < 0.001$).

Table 5 – Gulf CARE follow-up, 3- and 12-month outcomes by race ($n = 5005$).

Outcome	All ($n = 4539$)	Indian subcontinent ($n = 382$)	Gulf citizen ($n = 4157$)	p value
3-month outcomes				
Losses to follow-up, *n* (%)	65 (1.4%)	5 (1.3%)	60 (1.4%)	0.832
Hospitalization for HF	903 (18.0%)	414 (15.1%)	489 (20.5%)	<0.001
LOS, median (IQR), days	6 (4–10)	6 (4–9)	6 (4–10)	0.942
CABG	258 (5.2%)	169 (7.4%)	89 (3.3%)	<0.001
Device therapy	40 (0.8%)	9 (0.4%)	31 (1.1%)	0.024
CRT-D	10	1	9	
ICD	20	5	15	
PPM	10	3	7	
Died	597 (13.2%)	29 (7.6%)	568 (13.7%)	0.003
12-month outcomes				
Losses to follow-up, *n* (%)	76 (1.5%)	39 (1.7%)	37 (1.4%)	0.303
Hospitalization for HF	1075 (21.5%)	427 (18.8%)	648 (23.7%)	<0.001
LOS, median (IQR), days	6 (3–10)	5 (3–8)	6 (4–11)	<0.001
CABG	380 (7.6%)	209 (9.2%)	171 (6.3%)	<0.001
Device therapy	82 (1.6%)	42 (1.9%)	40 (1.5%)	<0.001
CRT-D	13	72	11	
ICD	34	13	21	
PPM	34	27	7	
CRT-P	1	0	1	
Died	1012 (20.2%)	390 (17.1%)	622 (22.8%)	<0.001

HF – heart failure; LOS – length of hospital stay; IQR – interquartile range; CRT-D – cardiac resynchronization therapy with defibrillation; ICD – implantable cardioverter-defibrillator; PPM – permanent pacemaker; CRT-P – cardiac resynchronization therapy with pacemaker; CABG – coronary artery bypass graft.
Mortality was cumulative also including those that died in hospital. Analyses were performed using Mann–Whitney or Pearson's chi-square test, whenever appropriate.

4. Discussion

The present study is the first multinational multicenter prospective study to compare clinical characteristics and long-term prognosis of AHF patients from Middle East Arab population and Indian subcontinent, residing in the Middle East. The results of this study demonstrate that AHF patients from this region are a decade younger than Western patients with high prevalence of ischemic heart disease and diabetes, and a higher preponderance to AHF with reduced ejection fraction. Middle East Arabs were associated with higher rates of HF risk factors. In-hospital mortality was similar, but 3-month and 12-month mortalities were high in the Middle East group.

Even though, the Middle Eastern Arab patients were older compared to Indian subcontinent patients (60 *vs.* 54 years), both were a decade younger than the Western population (70 years).[13,14] In the African AHF registry, mean age was 52 years.[15] This onset of AHF at early age in both Middle East and Indian subcontinent patients may be due to overall younger population in the region, as well as higher prevalence of cardiac risk factors at a younger age that was noted in previous HF registries from Qatar and Saudi Arabia.[8,16] Another factor for younger age of Indian subcontinent patients could be due to presence of a younger expatriate workforce residing in the Middle East, specifically blue-collar workers.

When compared to the Western population, it is well known that South Asian HF patients are having lower body mass index, past CAD, or myocardial infarction, and were more often diabetic, and were less often smokers and alcohol consumers.[4–7,17,18] However, in this study, Indian subcontinent patients were more likely to be smokers, alcohol consumers, and less obese with high prevalence of diabetes mellitus compared to Middle East patients. Smoking and alcohol consumption is high among Indian subcontinent patients possibly due to presence of young workers deprived of family presence in their country of work. Diabetes mellitus was high among those from the Indian subcontinent and Middle East cohorts at 56% and 49%, respectively. The burden of diabetes mellitus in the Middle East countries is highest among all nations (23 *vs.* 8% global prevalence) As per International Diabetic Federation statistics,[19] diabetic patients are increasingly prone for HF with many factors contributing to HF, such as severe diffuse multivessel CAD, recurrent myocardial infarction, and diabetic cardiomyopathy with both systolic and diastolic dysfunction.[20]

In this study, hypertension was the commonest risk factor in both cohorts, but Middle East patients had increasingly higher prevalence of CAD, obesity, valvular heart disease, atrial fibrillation, and khat chewing. This indicates that Middle East HF patients are at higher risk for HF than the Indian subcontinent patients. In a recent population-based study, among individuals without cardiovascular disease, higher BMI was found to have an independent, linear association with subclinical myocardial injury, as assessed by hs-cTnT levels and provided complementary prognostic information regarding the risk of incident HF.[21] It is presumed that Indian subcontinent patients generally have high prevalence of valvular heart disease due to high incidence of rheumatic fever in that region, but this study shows that significant number of Middle East valvular heart disease patients present with AHF even though the etiology data of valvular heart disease was not collected. In a systemic review of global burden of AF, it was observed that AF occurrence is related to increasing age, presence of valvular heart disease, and ethnicity.[22] Added to this, there is high prevalence of khat chewing, which is an amphetamine-like stimulant, which can cause euphoria, hypertension, myocardial infarction, and dilated cardiomyopathy. In a Gulf acute coronary syndrome registry analysis, khat chewing was an independent risk factor for in-hospital mortality, recurrent ischemia, and HF.[23] All these indicate that countries in this region are undergoing fast epidemiological transition and are facing the double burden of traditional cardiac risk factors, as well as nontraditional risk factors for HF in this region like khat chewing.

In the Indian subcontinent patients, ischemic heart disease as etiology and ACS as precipitating factor were more common, as well as STEMI-precipitating AHF. As noted in this registry, ischemic etiology is the commonest etiology of HF in the American and European registries, except in the African registry.[13–15] In this study, Indian subcontinent patients when compared to Middle East HF patients had more occurrence of ACS, specifically ST-elevation MI.[24] Large studies have documented higher incidence of ST-elevation MI among South Asians.[24,25] Also, younger age patients are known to present more frequently with ST-elevation MI.[26–28] This may be the main reason for Indian subcontinent patients presenting more with de novo AHF.

Another important finding from this registry is that Indian subcontinent patients presented more with AHF with reduced ejection fraction (76%) compared to Middle East patients (65%), which is similar to European registry, but more that the American registry.[13,14] In both cohorts, this high prevalence of left ventricular systolic dysfunction may be due to high prevalence of ischemic heart disease, ACS, especially STEMI, as well as underlying diabetic cardiomyopathy or khat chewing (in Middle East patients). In this study, NT-pro-BNP level was found to be significantly higher in Indian subcontinent patients when compared to Middle East patients. This finding has been noted before in a study where Asian and black patients with HF had higher BNP levels at admission compared with white and Hispanic patients.[29] BNP levels at admission provided prognostic value for in-hospital mortality and hospital LOS irrespective of race/ethnicity.[29]

With regard to treatment there were no significant differences in discharge medications, except for aldosterone antagonists, which were used more in Middle East patients, and antiplatelet/statin therapy, which were used more in Indian subcontinent patients. Although, Indian subcontinent patients had more HFrEF, aldosterone use was suboptimal. However, even though overall cardiac procedures were less in the entire registry, Indian subcontinent patients received more PCI or CABG. This may be due to higher occurrence of ACS/STEMI in these patients, as well as because they were younger. It has been noted in few studies, as well as in the Indian CREATE ACS registry, that younger patients with STEMI receive more frequently evidence-based therapies compared

with patients with unstable angina and non-ST-elevation MI.[28] Noncompliance to medications was noted more with Middle East patients, which may be due to racial disparities in health literacy, as noted in a study.[30]

In-hospital mortality was 6.5% in both cohorts with no difference, but 3-month and 12-month hospitalization and mortality was significantly high among Middle East Arabs when compared to Indian subcontinent patients. These disparities may be attributable to poorer outpatient management following discharge, as there was high prevalence of precipitating factors, noncompliance to medications, and underutilization of cardiac procedures and lack of specialist HF clinics in the region. The Indian subcontinent patients, as noted in this study, have cardiologist as main care provider and may have followed-up with cardiologist in private clinics resulting in better care, and a few of them fly to their own country for procedures and come back. This underscores need for aggressive outpatient management of HF patients post-discharge from hospital and setting up of specialist HF clinics in the region for Middle East patients.

4.1. *Limitations*

There are several limitations in this study. As with any registry study, confounding or unknown variables could have influenced the results. The Indian subcontinent patients were those working and residing in the Middle East, and thus the results are not necessarily generalizable to the entire South Asian countries. Indian subcontinent patients were predominantly men who were compared with Middle East Arab men and women. Majority of the Indian subcontinent patients are ''blue collar'' workers who may not self-report some of risk factors, which may have led to inaccuracies in reporting. Echocardiographic interpretation was at the discretion of the echo cardiographer performing the study; no centralized evaluation was done. Reasons for underusage of procedures were not known in this study.

5. Conclusions

AHF patients from this region are a decade younger than Western patients with high prevalence of ischemic heart disease, diabetes mellitus, and a higher preponderance to AHF with reduced ejection fraction. Middle East Arabs were associated with higher rates of HF risk factors. In-hospital mortality was similar, but 3-month and 12-month mortalities were high in the Middle East group. There is an urgent need to prevent/control ischemic heart disease and diabetes to reduce HF burden among those in both groups, as well as the need for setting up HF clinics for better postdischarge management of HF patients.

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Conflicts of interest

The authors have none to declare.

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