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ORIGINAL RESEARCH ARTICLE

Impact of diabetes on mortality and rehospitalization in acute heart failure patients stratified by ejection fraction

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Abstract

Aims The aim of this study is to determine the impact of diabetes mellitus on all-cause mortality and rehospitalization rates at 3 months and at 1 year in patients admitted with acute heart failure (AHF) stratified by left ventricular ejection fraction (EF).

Methods and results We analysed consecutive patients admitted to 47 hospitals in seven Middle Eastern countries (Saudi Arabia, Oman, Yemen, Kuwait, United Arab Emirates, Qatar, and Bahrain) with AHF from February to November 2012 with AHF who were enrolled in Gulf CARE, a multinational registry of patients with heart failure (HF). AHF patients were stratified into three groups: HF patients with reduced (EF) (HFrEF) ($<$40%), HF with mid-range EF (HFmrEF) (40–49%), and HF patients with preserved EF (HFpEF) ($\geq$50%). Analyses were performed using univariate and multivariate statistical techniques. The mean age of the cohort was 59 ± 15 years (ranging from 18 to 99 years), and 63% (n = 2887) of the patients were males. A total of 2258 (49%) AHF patients had diabetes mellitus. The mean EF was 37 ± 14%. A reduced EF was observed in 2683 patients (59%), whereas 962 patients (21%) had mid-range and 932 patients (20%) had preserved EF. Multivariable analyses demonstrated no significant differences in all-cause mortality between diabetics and non-diabetics in all the three types of HF; at 3 months follow-up: HFrEF [adjusted odds ratio (aOR), 1.30; 95% confidence interval (CI): 0.94–1.80; P = 0.119], HFmrEF (aOR, 0.98; 95% CI: 0.51–1.87; P = 0.952), and HFpEF (aOR, 0.69; 95% CI: 0.38–1.26; P = 0.225); and at 12-months follow-up: HFrEF (aOR, 1.25; 95% CI: 0.97–1.62; P = 0.080), HFmrEF (aOR, 1.07; 95% CI: 0.68–1.68; P = 0.783), and HFpEF (aOR, 1.07; 95% CI: 0.67–1.72; P = 0.779). There were also no significant differences in rehospitalization rates between diabetics and non-diabetics in all the three types of HF; at 3 months follow-up: HFrEF (aOR, 0.94; 95% CI: 0.74–1.19; P = 0.581), HFmrEF (aOR, 0.82; 95% CI: 0.53–1.26; P = 0.369), and HFpEF (aOR, 1.06; 95% CI: 0.64–1.78; P = 0.812); and at 12-months follow-up: HFrEF (aOR, 0.93; 95% CI: 0.73–1.17; P = 0.524), HFmrEF (aOR, 0.81; 95% CI: 0.56–1.17; P = 0.257), and HFpEF (aOR, 1.29; 95% CI: 0.82–2.05; P = 0.271).

Conclusions There were no significant differences in 3 and 12 months all-cause mortality as well as rehospitalization rates between diabetics and non-diabetic patients in all the three types of AHF patients stratified by left ventricular ejection fraction.

Keywords Heart failure; Diabetes mellitus; Mortality; Middle East; Readmission

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Introduction

Heart failure (HF) is associated with increasing incidence of diabetes in view of its insulin resistant state.[1] Prevalence of type 2 diabetes mellitus (T2DM) remains almost the same in both HF with reduced ejection fraction (EF) (HFrEF) and HF with preserved EF (HFpEF).[2] The prevalence of diabetes mellitus in congestive heart failure ranges between 11% and 28%.[3] Diabetes along with racial difference and age also plays an important role in the management of HF.[4] Most of the major trials have shown that the treatment of HF should remain the same irrespective of the presence of T2DM.[5] Diabetes in HF is an independent predictor of mortality and frequent hospitalizations. Incidence of HF in diabetic patients is reported to be twice the rate when compared with those without diabetes.[6] Rate of readmissions is noted relatively high in HF patients with T2DM.[7] Early diagnosis and proper treatment plan are important to achieve favourable short-term and long-term outcomes. Anti-diabetic medications increase the metabolic risk and thereby increase the rate of mortality and HF-related hospitalizations in all patients irrespective of the presence of HF.[8] Systematic reviews and meta-analyses have identified age, duration of DM, renal failure, and coronary artery disease (CAD) as independent risk factors for developing HF in diabetic patients.[9]

There is scant information on the epidemiology of HF in diabetic patients in the Arabian Gulf. The aim of this study was to determine the impact of diabetes mellitus on all-cause mortality and rehospitalization rates at 3 months and at 1 year in patients admitted with acute heart failure (AHF) stratified by left ventricular ejection fraction in the Arabian Gulf.

Methods

Gulf CARE is a prospective, multicenter, multinational registry of AHF patients admitted to 47 hospitals in seven Middle Eastern countries (Kuwait, Oman, Qatar, United Arab Emirates, Bahrain, Saudi Arabia, and Yemen).[10] The registry is listed in clinicaltrials.gov (number NCT01467973). Baseline and admission-based variables on demographic, co-morbidities, behavioural risk factors, clinical presentation, investigations, including medication history, and in-hospital outcomes were captured. Follow-up for all-cause mortality and rehospitalization was carried out telephonically at 3 months and either telephonically or through out-patient clinic visits at 1 year.

Data entry was carried out online using a custom designed electronic case-record form at the Gulf CARE website (www.gulfcare.org). Institutional or national ethical committee or review board approvals were obtained. Trained abstractors collected the data from medical records at each participating site, and this information was recorded using an electronic case-record form. Importantly, registry participation did not require any alteration of treatment or hospital care, and entry of the data into the registry was not contingent on the use of any particular therapeutic agent or treatment regimen.

Definition of heart failure

Acute heart failure (AHF) was defined according to the European Society of Cardiology[11] as the rapid onset of symptoms and signs secondary to abnormal cardiac function, including (i) symptoms (dyspnoea at rest or on exercise, fatigue, tiredness, and ankle swelling), (ii) signs (tachycardia, tachypnoea, elevated jugular venous pressure, pulmonary rales, pleural effusion, hepatomegaly, and peripheral oedema), and (iii) objective evidence of structural or functional abnormality of the heart at rest (third heart sound, murmurs, cardiomegaly, abnormal echocardiogram, and raised natriuretic peptide concentration). AHF was further classified as either acute decompensated chronic heart failure (ADCHF) or new-onset acute HF (de novo AHF) on the basis of European Society of Cardiology guidelines. ADCHF was defined as the worsening of HF in patients with a previous diagnosis or hospitalization for HF. De novo AHF was defined as AHF in patients with no history of HF.[12]

HFrEF was diagnosed when patients with symptoms and signs of HF had a measured EF $<$40%. HF with mid-range EF (HFmrEF) was diagnosed when patients with symptoms and signs of HF had a measured EF between 40% and 49%. HFpEF was diagnosed when patients with symptoms and signs of HF had a measured EF between $\geq$50%.[13–15]

Patients with HF who were discharged from the emergency room without admission were excluded from the registry. Patients with no available record of EF were also excluded from the analysis.

Data variables

Coronary artery disease (CAD) was diagnosed if any of the following conditions were present: at least one major epicardial coronary artery determined by coronary angiography to have $>$70% obstruction, history of myocardial infarction associated with wall motion abnormality seen on echocardiography or gated blood pool imaging, and/or stress testing (with or without imaging) results that are diagnostic of CAD. Hypertension was defined when any of the following

conditions were present: untreated systolic blood pressure >160 mmHg or diastolic blood pressure >105 mmHg for at least 3 months and/or hypertension requiring at least two drugs for control for ≥5 years.[16]

Type 2 diabetes was diagnosed on the basis of fasting plasma glucose levels ≥126 mg/dL (7.0 mmol/L), 2 h plasma glucose levels (2 h PG) ≥200 mg/dL (11.1 mmol/L) during oral glucose tolerance test, and HbA1c ≥6.5% (48 mmol/mol).[17]

Statistical analysis

Descriptive statistics were used to summarize the data. For categorical variables, frequencies and percentages were reported. Differences between groups were analysed using Pearson's χ^2 test. For continuous variables, mean and standard deviation were used to summarize the data while analysis was performed using Student's *t*-test.

Multivariable logistic regression models, utilizing the simultaneous method, were performed to evaluate the impact of HF (HFrEF, HFmrEF, and HFpEF) on all-cause mortality and rehospitalization (primary outcomes) at 3 months and at 1 year post-hospital discharge. The multivariate logistic models were adjusted for age, gender, body mass index, smoking, khatt chewing, peripheral vascular disease, hypertension, diabetes mellitus, prior stroke/transient ischaemic attack, systolic blood pressure, diastolic blood pressure, serum creatinine, in-hospital percutaneous coronary intervention or coronary artery bypass graft, admission diagnosis, New York Heart Association class, in-hospital course (included non-invasive ventilation, intubation/ventilation, cardiogenic shock, inotropes, intra-aortic balloon pump, acute dialysis/ultrafiltration, atrial fibrillation requiring therapy, major bleeding, blood transfusion, stroke, and systemic infection requiring therapy), and discharged medications [diuretics, digoxin, oral nitrates, CCBs, beta blockers, aldosterone antagonist, ACEIs, ARBs, aspirin, and I_f channel blocker (ivabradine)].

The goodness of fit of the multivariable logistic model was examined using the Hosmer and Lemeshow goodness-of-fit statistic. Based on the χ^2 distribution, a Hosmer and Lemeshow statistic with a $P > 0.05$ is considered a good fit. The discriminatory power of the logistic model was assessed by the area under the receiver operating characteristics curve also known as *C*-index. A model with perfect discriminative ability has a *C*-index of 1.0; an index of 0.5 provides no better discrimination than chance. Models with area under the receiver operating characteristics curve of >0.7 are preferred. An a priori two-tailed level of significance was set at $P < 0.05$. Statistical analyses were conducted using STATA version 13.1 (STATA Corporation, College Station, TX, USA).

Results

A total of 4457 HF patients with a diagnosis of AHF were recruited to the study; 63% (n = 2887) of the patients were male. The mean age was 59 ± 15 years, ranging from 18 to 99 years. Forty-nine percent (n = 2258) of the patients had diabetes mellitus. A total of 2762 (60%) had CAD, 2783 (61%) patients had hypertension, and 1646 (36%) patients had known dyslipidaemia. Atrial fibrillation was observed in 559 patients (12%), and chronic kidney disease or those requiring dialysis was observed in 670 (15%) patients.

The mean EF of the cohort was 37 ± 14%. A reduced EF (<40%) was observed in 2683 patients (59%), whereas 962 patients (21%) had mid-range (40–49%) EF while 932 patients (20%) had preserved EF (≥50%). At hospital discharge, the aetiology of HF was recorded as being acute coronary syndrome in 1259 (28%) patients, primary cardiomyopathy in 854 (19%) patients, hypertensive heart disease in 697 (15%) patients, primary valve pathology in 441 (9.6%) patients, and pulmonary hypertension in 116 (2.5%) patients. The median duration of hospitalization was 7 (4–10) days. The overall in-hospital mortality was 5.2% (n = 236).

Acute heart failure (AHF) diabetic patients were older (63 vs. 55 years; $P < 0.001$) with higher body mass index (30 vs. 27 kg/m^2; $P < 0.001$) but less likely to be male (60% vs. 66%; $P < 0.001$), smokers (18% vs. 26%; $P < 0.001$), khatt users (9.3% vs. 28%; $P < 0.001$), and alcohol consumers (3.0% vs. 4.1%; $P = 0.032$). AHF diabetic patients were also more likely to present with CAD (73% vs. 48%; $P < 0.001$), peripheral vascular disease (7.2% vs. 1.6%; $P < 0.001$), stroke/transient ischaemic attack (11% vs. 5.0%; $P < 0.001$), hypertension (82% vs. 41%; $P < 0.001$), dyslipidaemia (54% vs. 18%; $P < 0.001$), chronic kidney disease/dialysis (23% vs. 6.3%; $P < 0.001$), sleep apnoea requiring therapy (3.2% vs. 0.8%; $P < 0.001$), and ADCHF type (60% vs. 51%; $P < 0.001$). They were also associated with higher serum creatinine (143 vs. 117 μmol/L; $P < 0.001$) and systolic blood pressure (142 vs. 132 mmHg; $P < 0.001$). There were no significant differences mean left ventricular ejection fraction between diabetics and non-diabetics (37% vs. 37%; $P = 0.259$); however, diabetics were less likely to be associated with HFrEF compared with non-diabetics (56% vs. 61%; $P = 0.002$). Other clinical characteristics are outlined in *Table 1*.

At hospital discharge, diabetic patients were less likely to receive aldosterone antagonists (36% vs. 53%; $P < 0.001$), digoxin (20% vs. 33%; $P < 0.001$), beta blockers (71% vs. 74%; $P < 0.001$), and angiotensin-converting-enzyme inhibitors (57% vs. 66%; $P < 0.001$) but more likely to receive ivabradine (7.0% vs. 3.6%; $P < 0.001$) and angiotensin

Table 1 Patient characteristics of the Gulf CARE cohort stratified by diabetes mellitus (DM) (N = 4577)

Characteristic, n (%) unless specified otherwise	All (N = 4577)	DM		P-value
		No (n = 2319)	Yes (n = 2258)	
Demographic				
Age, mean ± SD, years	59 ± 15	55 ± 17	63 ± 11	<0.001
Male gender	2887 (63%)	1525 (66%)	1362 (60%)	<0.001
Smoking	1020 (22%)	607 (26%)	413 (18%)	<0.001
Khatt	849 (19%)	639 (28%)	210 (9.3%)	<0.001
Alcohol	163 (3.6%)	96 (4.1%)	67 (3.0%)	0.032
BMI, mean ± SD, kg/m^2	28 ± 6	27 ± 6	30 ± 7	<0.001
Medical history				
CAD	2762 (60%)	1104 (48%)	1658 (73%)	<0.001
PVD	201 (4.4%)	38 (1.6%)	163 (7.2%)	<0.001
Afib	559 (12%)	285 (12%)	274 (12%)	0.873
Stroke/TIA	370 (8.1%)	116 (5.0%)	254 (11%)	<0.001
Hypertension	2783 (61%)	940 (41%)	1843 (82%)	<0.001
Dyslipidaemia	1646 (36%)	418 (18%)	1228 (54%)	<0.001
CKD/dialysis	670 (15%)	145 (6.3%)	525 (23%)	<0.001
Sleep apnoea with therapy	90 (2.0%)	18 (0.8%)	72 (3.2%)	<0.001
Vulvular heart disease	644 (14%)	398 (17%)	246 (11%)	<0.001
Clinical presentation				
Dyspnoea	4484 (98%)	2270 (98%)	2214 (98%)	0.694
Orthopnoea	3609 (79%)	1849 (80%)	1760 (78%)	0.139
Abd/lower limb swelling	2054 (45%)	1077 (46%)	977 (43%)	0.031
Weight gain	1225 (27%)	703 (30%)	522 (23%)	<0.001
Chest pain	2045 (45%)	1013 (44%)	1032 (46%)	0.169
Palpitation	1427 (31%)	858 (37%)	569 (25%)	<0.001
Easy fatiguability	2605 (57%)	1416 (61%)	1189 (53%)	<0.001
Ascites	653 (14%)	370 (16%)	283 (13%)	0.001
Enlarged tender liver	1244 (27%)	870 (38%)	374 (17%)	<0.001
Gallop	1730 (38%)	1014 (44%)	716 (32%)	<0.001
Basal lung crepitations	4217 (92%)	2138 (92%)	2079 (92%)	0.878
BG, mean ± SD, mmol/L	9.7 ± 5.8	7.0 ± 3.1	12.6 ± 6.6	<0.001
Crea, mean ± SD, μmol/L	130 ± 116	117 ± 107	143 ± 124	<0.001
SBP, mean ± SD, mmHg	137 ± 34	132 ± 33	142 ± 33	<0.001
Signs of pleural effusion	843 (18%)	489 (21%)	354 (16%)	<0.001
Heart failure type				
AHF	2047 (45%)	1147 (49%)	900 (40%)	<0.001
ADCHF	2530 (55%)	1172 (51%)	1358 (60%)	
ECG				
Sinus status				0.003
Sinus rhythm	3749 (82%)	1858 (80%)	1891 (84%)	
Afib/flutter	628 (14%)	358 (15%)	270 (12%)	
CHB	49 (1.1%)	30 (1.3%)	19 (0.8%)	
Paced	68 (1.5%)	27 (1.2%)	41 (1.8%)	
SVT	26 (0.6%)	14 (0.6%)	12 (0.5%)	
Others	57 (1.3%)	32 (1.4%)	25 (1.1%)	
LV hypertrophy	1434 (31%)	737 (32%)	697 (31%)	0.506
ST-depression/T-inversion	2053 (45%)	940 (41%)	1113 (41%)	<0.001
STEMI	487 (11%)	255 (11%)	232 (10%)	0.429
Pathological Q waves	1110 (24%)	487 (21%)	623 (28%)	<0.001
QRS duration ≥ 0.12 msec				0.256
No	3602 (79%)	1813 (78%)	1789 (79%)	
LBBB	616 (13%)	330 (14%)	286 (13%)	
RBBB	211 (4.6%)	109 (4.7%)	102 (4.5%)	
IVCD	148 (3.2%)	67 (2.9%)	81 (3.6%)	
Echocardiography				
LVEF, mean ± SD, %	37 ± 14	37 ± 14	37 ± 13	0.259
HFrEF	2683 (59%)	1415 (61%)	1268 (56%)	
HFmrEF	962 (21%)	447 (19%)	515 (23%)	0.002
HFpEF	932 (20%)	457 (20%)	475 (21%)	

Percentages might not add up to 100% due to rounding off. Analyses were performed using Student's t-test or Pearson's χ^2 test, whenever appropriate.

SD, standard deviation; smoking, includes chewing tobacco and/or smoking water-pipe; alcohol, drinking daily; BMI, body mass index; kg, kilogram; CAD, coronary artery disease; PVD, peripheral vascular disease; Afib, atrial fibrillation; TIA, transient ischaemic attack; CKD, chronic kidney disease; Abd, abdominal; BG, baseline admission blood glucose; Crea, creatinine; SBP, systolic blood pressure; AHF, acute new-onset heart failure; ADCHF, acute decompensated chronic heart failure; ECG, electrocardiography; 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, intra ventricular conduction delay; LVEF, LV ejection fraction; HFrEF, heart failure (HF) with reduced ejection fraction (EF) (<40%); HFmrEF, HF with mid-range EF (40–49%); HFpEF, HF with preserved EF (≥50%).

receptor blockers (57% vs. 66%; $P < 0.001$). Other pre-admission and discharged medications are shown in *Table 2*.

As shown in *Table 3*, there were no significant differences in cumulative all-cause mortality and rehospitalization rates, neither at 3 months nor at 1 year follow-up, in all the three types of HF (all *P*-values were >0.05).

Discussion

The data extracted from GULF CARE registry demonstrated that there were no significant differences in 3 and 12 months all-cause mortality as well as rehospitalization rates between diabetics and non-diabetic patients in all the three types of AHF patients stratified by left ventricular ejection fraction in the Arabian Gulf. The findings are contrary to many studies that have shown poor outcomes in those HF patients with elevated HbA1c.[18] A moderate difference between HFrEF and HFpEF diabetic patients in terms of in-hospital mortality has been observed.[19] Interestingly, young diabetic HF patients have also been reported to have higher risk ratio for mortality.[20] An observational study had suggested that optimal glycaemic control, blood pressure control, and the addition of ACE inhibitors in the treatment regimen may reduce the mortality risk in HF patients.[21,22] CAD and renal impairment have also been reported to increase the risk of mortality in HF.[23]

International data have reported up to 40% incidence of diabetes in AHF patients and 25% in chronic HF patients.[24] In our study, an incidence of 49% of diabetes mellitus has been observed in AHF patients in the Arabian Gulf. In the setting of HF and diabetes, many randomized controlled trials have shown no benefits with strict glycaemic control.[25] In the CHARM trial, the cardiovascular mortality and rate of

Table 2 Pre-admission and discharge medications of the Gulf CARE cohort stratified by diabetes mellitus (DM) (*N* = 4577)

Medication, *n* (%)	All (*N* = 4577)	DM		*P*-value
		No (*n* = 2319)	Yes (*n* = 2258)	
Pre-admission				
Diuretics	2643 (58%)	1175 (51%)	1468 (65%)	<0.001
Aldosterone antagonist	784 (17%)	406 (18%)	378 (17%)	0.491
Digoxin	798 (17%)	461 (20%)	337 (15%)	<0.001
Nitrates	1208 (26%)	425 (18%)	783 (35%)	<0.001
CCB	589 (13%)	158 (6.8%)	431 (19%)	<0.001
Hydralazine	201 (4.4%)	43 (1.9%)	158 (7.0%)	<0.001
Aspirin	2863 (63%)	1167 (50%)	1696 (75%)	<0.001
Clopidogrel	883 (19%)	281 (12%)	602 (27%)	<0.001
Statin	2,350 (51%)	789 (34%)	1561 (69%)	<0.001
Oral anticoagulant	571 (12%)	312 (13%)	259 (11%)	0.042
Ivabradine	108 (2.4%)	32 (1.4%)	76 (3.4%)	<0.001
Anti-arrhythmic	117 (2.6%)	50 (2.2%)	67 (3.0%)	0.082
Beta blocker	2061 (45%)	859 (37%)	1202 (53%)	<0.001
ACEI	1993 (44%)	978 (42%)	1015 (45%)	0.058
ARB	589 (13%)	184 (7.9%)	405 (18%)	<0.001
UFH/LMWH	210 (4.6%)	86 (3.7%)	124 (5.5%)	0.004
At discharge[a]				
Diuretics	3970 (94%)	2000 (93%)	1970 (95%)	0.073
Aldosterone antagonist	1885 (45%)	1141 (53%)	744 (36%)	<0.001
Digoxin	1109 (26%)	701 (33%)	408 (20%)	<0.001
Nitrates	1619 (38%)	604 (28%)	1015 (49%)	<0.001
CCB	637 (15%)	185 (8.6%)	451 (22%)	<0.001
Hydralazine	309 (7.3%)	86 (4.0%)	223 (11%)	<0.001
Aspirin	3454 (82%)	1628 (76%)	1826 (88%)	<0.001
Clopidogrel	1608 (38%)	657 (31%)	951 (46%)	<0.001
Statin	3064 (73%)	1271 (59%)	1793 (86%)	<0.001
Oral anticoagulant	816 (19%)	479 (22%)	337 (16%)	<0.001
Ivabradine	223 (5.3%)	78 (3.6%)	145 (7.0%)	<0.001
Anti-arrhythmic	207 (4.9%)	100 (4.7%)	107 (5.2%)	0.476
Beta blocker	3067 (73%)	1586 (74%)	1481 (71%)	0.036
ACEI	2606 (62%)	1418 (66%)	1188 (57%)	<0.001
ARB	720 (17%)	319 (15%)	401 (19%)	<0.001
UFH/LMWH	153 (3.6%)	58 (2.7%)	95 (4.6%)	0.001

Analyses were performed using Pearson's χ^2 test.
CCB, calcium channel blocker; ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; UFH, unfractionated heparin; LMWH, low molecular weight heparin.
[a]Medications at discharge excluded those that died (*n* = 236; 5.16%) as well as those that left against medical advice (*n* = 122; 2.67%) (LAMA) (*N* = 4219).

Table 3 Impact of diabetes mellitus on mortality and rehospitalization rates (at 3 months and at 1 year follow-up) by multiple logistic regression stratified by left ventricular ejection fraction (LVEF) (N = 4577)

	Mortality				Rehospitalization			
Outcome	aOR [95% CI]	*aP*-value	HL	ROC	aOR [95% CI]	*aP*-value	HL	ROC
3 months								
HFrEF (n = 2683)	1.30 [0.94–1.80]	0.119	0.042	0.79	0.94 [0.74–1.19]	0.581	0.390	0.62
HFmrEF (n = 962)	0.98 [0.51–1.87]	0.952	0.020	0.79	0.82 [0.53–1.26]	0.369	0.322	0.73
HFpEF (n = 932)	0.69 [0.38–1.26]	0.225	0.101	0.81	1.06 [0.64–1.78]	0.812	0.545	0.70
12 months								
HFrEF (n = 2683)	1.25 [0.97–1.62]	0.080	0.292	0.76	0.93 [0.73–1.17]	0.524	0.864	0.62
HFmrEF (n = 962)	1.07 [0.68–1.68]	0.783	0.527	0.75	0.81 [0.56–1.17]	0.257	0.357	0.63
HFpEF (n = 932)	1.07 [0.67–1.72]	0.779	0.482	0.75	1.29 [0.82–2.05]	0.271	0.161	0.65

Multivariate analyses were conducted using logistic regression model utilizing stepwise-backwards elimination method adjusting for age, gender, smoking, khatt use, alcohol, body mass index, coronary artery disease, peripheral vascular disease, prior stroke/transient ischaemic attack, hypertension, dyslipidaemia, chronic kidney disease or dialysis, sleep apnoea requiring therapy, vulvular heart disease, abdominal lower limb swelling, weight gain, serum creatinine, systolic blood pressure on admission, admission blood glucose, sinus status, prior medications (diuretics, digoxin, oral nitrates, calcium channel blockers, beta blocker, aldosterone antagonist, angiotensin-converting-enzyme inhibitor, angiotensin receptor blocker, aspirin, clopidogrel, and ivabradine) for the in-hospital model while for the 3 and 12 months logistic models, medications at hospital discharge were used
aOR, adjusted odds ratio; a*P*-value, adjusted *P*-value; CI, confidence interval; HL, Hosmer and Lemeshow *P*-value; ROC, area under the receiver operating curve also known as c-statistic; HFrEF, heart failure (HF) with reduced ejection fraction (EF) (<40%); HFmrEF, HF with mid-range EF (40-49%); HFpEF, HF with preserved EF (≥50%).

hospitalizations were found higher with HFpEF than HFrEF.[26] The ALLHAT trial has shown that diabetes mellitus had a two-fold rise in risk for HF hospitalizations as well as mortality.[27] The Framingham Heart study has shown a 34% mortality at 1 year for diabetic patients who were diagnosed to have HF.[28] The SOLVD trial also demonstrated higher rates of hospitalizations, mortality in asymptomatic ischaemic cardiomyopathy patients with diabetes.[29] The Framingham study has shown that the rate of incidence of HF was five-fold higher in women and 2.4-fold higher in men with diabetes.[30] Incidence of diabetes was found to be 67% in AHF patients with cardiorenal anaemia syndrome in Gulf Care registry.[31] A new risk calculator for HFrEF (https://www.hfriskcalc.in/) has been suggested.[32]

A community-based study showed that advanced NYHA class was associated with higher incidence of diabetes.[33] A Scottish retrospective study has shown that South Asians had a higher rate of HF hospitalizations and death than Caucasians.[34] In the SOLVD trial, African Americans with HFrEF were at higher risk of developing AHF compared with Whites.[35] A study evaluating diabetic cardiomyopathy showed diabetes in Blacks were associated with reduced end diastolic volume and stroke volume with an increased left ventricular mass.[36] In the Middle East, AHF patients were a decade younger when compared with those in the Western world.[37] A systemic review has shown that the use of metformin was associated with a 13% reduction in readmissions for HF in diabetic patients.[38] Another study has shown metformin to be associated with a reduction in mortality and major adverse cardiovascular events.[39] The DECLARE-TIMI 58 trial has demonstrated that diabetic HF patients will benefit with dapagliflozin treatment in terms of reduced all-cause mortality and cardiovascular death in HFrEF. Furthermore, there was also a noted reduction in HF-related hospitalizations in both HFrEF and HFpEF patients.[40] SGLT2 inhibitors were associated with reductions in HF hospitalizations in diabetic patients.[41] The SAVOR-TIMI 53 trial has shown that saxagliptin increases the risk of HF hospitalizations.[42] Newer molecules, neprilysin inhibitors, have shown nepho protective and anti-diabetic effects.[43] In our study, we found that diabetics has no impact on mortality or rehospitalization rates at 3 months or at 12 months in all the types of HF.

The limitation of this study is its nature of being a registry, which may have introduced bias through confounding by variables not controlled for or measured (such as iron levels and history of chronic anaemia). In some countries, only a few hospitals took part in the registry; hence, the results might not entirely generalizable. Reasons for underuse of medications or procedures were not known in this study. The recording of natriuretic peptides was optional as not all countries routinely measure them. Echocardiographic interpretation was at the discretion of the person performing the study; no centralized evaluation was performed. Patients' renal function at discharge is unknown, and there are no data regarding the frequency of patients with improvement of renal function. This study did not record the cognitive status and the disability status in patients with stroke, which obviously have a major impact on morbidity and mortality and only 1 year mortality. Mortality rates at 3 months and at 1 year follow-up were only recorded without the specification of the exact date of death of each patient, and hence, the Kaplan–Meier curves could not have been performed. Finally, because this was HF registry, diabetic medications were not routinely captured. Future studies need to overcome these limitations.

Conclusions

There were no significant differences in 3 and 12 months all-cause mortality and rehospitalization rates between diabetics and non-diabetic patients in all the three types of AHF stratified by left ventricular ejection fraction.

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Conflict of interest

The authors declare that they have no competing interests.

Author Contributions

M.A.J. participated in analysis and manuscript preparation. R. R. participated in data analysis and manuscript preparation. I. A.Z. did the statistical analysis and manuscript review. R.D. participated in the data analysis and drafting of manuscript. B.B. participated in data acquisition and manuscript preparation. All authors had access to data and take responsibility for the integrity of data and the accuracy of data analysis. All authors have read and approved the manuscript.

Availability of data and materials

There are no ethics restrictions preventing the sharing of the raw data.

Statement

The present submission (ESCHF-19-00101) does not have significant overlap with the previous ones (ESCHF-18-00056R3: Incidence and impact of cardiorenal anaemia syndrome on all-cause mortality in acute heart failure patients stratified by left ventricular ejection fraction in the Middle East and ESCHF-18-00214R2: "One-Year Outcome of Acute Heart Failure Patients with Reduced, Mid-Range and Preserved Ejection Fraction"), and the previous published submission has been adequately cited.

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