

Original article

## Association of Non-Cardiac Comorbidities with the Outcomes of Admitting Acute heart failure Patients Tripoli, Libya

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### Abstract

The patients with Acute heart failure (AHF) usually present with multiple interrelated comorbidities. These comorbidities play a major role in determining the prognosis and outcome of AHF patients, as well as affecting the management. Our study aimed to describe the Effect of the presence of non-cardiac comorbidities on the outcomes of the admitting patients with AHF in Tripoli University Hospital. From Jan- Oct 2022 we carried out this descriptive cross-sectional study in the cardiac department and cardiac care unit in Tripoli University Hospital. A self-constructed questionnaire was designed to collect the data from medical records, and then the data was analyzed by using SPSS version 20. 140 were enrolled in this study. The patients were 102 (72.9%) males and 38 (27.1%) females, their mean age was 60.08 yrs.  $\pm$  SD 12.9. 128 patients (91.4%) were presented in the decompensated stage of their previous heart failure status and 5 (3,6%) presented as cardiogenic shock. Non-compliance to treatment was the leading aggravating cause for decompensation with a percentage of 31.4% followed by infection at 29.2 %, and atrial fibrillation in 12.1% of the cases. Almost all enrolled patients had multiple comorbidities only 8 (5.7%) had no comorbidities Those comorbidities include D.M in 84 patients (60%), anemia in 17 patients (12.1%), chronic kidney disease (CKD) in 43 patients (30.7%) and chronic obstructive pulmonary disease (COPD) 4 (2.9%). Regarding treatment, only 10.7% of our patients were on the guidelines-directed medical therapy of heart failure (GDMT) in their discharge to home, According to the patient outcomes in this study 14 (10%) of patients needed advanced management, 12 (8.6%) died. The rest of the 114 (81.4%) responded to standard medical management mainly diuretics and GDMT. This study showed a significant statistical correlation between CKD and the worse outcomes with a (p-value = 0.055) and between cardiogenic shock and in-hospital mortality with a (p-value = 0.057). Our patients were relatively young, mostly male, with a high prevalence of D.M, , more acute on chronic heart failure than denevo cases, and lower use of GDMT use, The presence of comorbidities, especially CKD as well as the presence of cardiogenic shock, are associated with increases the risk of in-hospital mortality.

### Introduction

Acute heart failure is defined as a rapid or gradual onset of symptoms and/or signs of heart failure, severe enough for the patient to seek urgent medical attention, leading to unplanned hospital admission or an emergency department visit [1], despite the advance in the management in the last decade, it still carries a high mortality rate, with In-hospital mortality ranging from (4% to 10%) [2,3], with post-discharge 1-year mortality reached up to 25-30% [4,5]. The In-hospital mortality rate is more frequently observed in those with new-onset HF [2], but have lower post-discharge mortality rates compared with those with acute decompensation of chronic HF [6,7].

Heart failure is a disease of aging, so most of the patients have one or more comorbidities which play a major role in determining the prognosis and outcome of them, as well as affecting the management [8]. Non-cardiac Comorbidities such as anemia, Diabetes Mellitus, chronic obstructive pulmonary disease (COPD), and renal impairments are common findings in patients with acute heart failure, iron deficiency anemia which is defined by ferritin levels  $<100 \mu\text{g/ml}$  or ferritin in the range of  $100\text{--}300 \mu\text{g/l}$  with a

transferrin saturation <20% has a high prevalence rate in acute decompensated heart failure where it can reach up to 80% in the first days after admission [9] the presence of anemia is considered an independent prognostic predictor in heart failure patients [10], associated with recurrent admission, increasing cardiovascular and all-cause mortality [11].

Heart failure patients with Diabetes Mellitus have worse prognosis compared with Nondiabetic heart failure patients, its prevalence in heart failure patients ranges between (30 % - 45 %) [12] it has been well documented that cardiovascular and all cause mortality increased in the patients with diabetes [13] mortality reached to 37% in diabetic patients with heart failure [14].

Chronic kidney disease (CKD) is a progressive process where the estimated glomerular filtration rate (eGFR) is reduced (< 60 ml/min/1.73 m<sup>2</sup>), or albuminuria, or both, for at least three months [15], presence of CKD is associated with the development and progression of cardiovascular disease (CVD) and its outcomes [16,17], and increasing prevalence of heart failure [18], Coexisting (CKD) and heart failure doubles the risk of all-cause mortality [19], Up to 50% of patients with either a preserved or reduced ejection fraction have (CKD) [20]. The reduced (eGFR) carries higher adverse outcomes than a reduction in left ventricular ejection fraction in heart failure [21]. In patients with acute heart failure in addition to CKD patients may develop worsening renal function (WRF) during hospitalization with different pathophysiological mechanisms. The definition of worsening renal function (WRF) is an increase of serum creatinine levels during hospitalization ( $\geq 0.3$  mg/dl). As the kidneys receive about 20–25% of cardiac output, which will be reduced in patients with AHF leading to a reduction in renal perfusion, in addition to the side effect of some drugs used in the management of AHF all contribute to worsen the renal function (WRF), several factors contribute to worsen outcomes in AHF patients in addition to the reduced (eGFR) such as electrolyte imbalance especially hyperkalemia which is associated with poor prognosis [22,23].

COPD has similar symptoms with acute heart failure leading to confounding appropriate diagnosis. It may lead to wrong therapy or under usage of beneficial therapy like  $\beta$ -blockers, although the use of cardio-selective versus  $\beta$ -blocker in these patients can be used safely in COPD patients [24]. This study aims to identify the effect of the presence of non-cardiac comorbidities on the outcome of patients admitted with AHF, and to ensure future concentration on these comorbidities aiming to improve HF patient outcomes in all public health institutions in Libya, especially in the absence of sufficient data in this area.

## Methods

### **Study design and setting**

A descriptive cross-sectional study of patients admitted with the diagnosis of AHF either a new-onset HF or decompensation of chronic established HF. It was carried out in the main teaching hospital in Tripoli/Libya, Tripoli University Hospital, from (Jan- Oct 2022). A self-constructed questionnaire was designed to collect the data from medical records. The confidentiality of the data has been kept at all levels of the study.

### **Inclusion and exclusion criteria**

Our inclusion criteria were Libyan patients >18 years of age, admitted with a diagnosis of AHF. Our exclusion criteria were: non-Libyan patients, younger patients than 18 years old and those with no established diagnosis of heart failure.

### **Data collection procedure**

Admission-based variables data on demographics, etiology, precipitating factors, primary diagnoses, non-cardiac co-morbidities, clinical presentation, hospital admission patterns, and in-hospital outcome were collected from medical records. Data were analyzed by using IBM SPSS version 20 (IBM Corp., Armonk, NY, United States). Descriptive statistics were used to present all results.

### **Non-cardiac Comorbidities**

We analyzed the effect of four major Non-cardiac comorbidities in the analysis: diabetes mellitus (DM), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), and anemia. DM was defined according to medical records or baseline laboratory results (i.e., HbA<sub>1c</sub>  $\geq 6.5\%$ ). CKD was defined on laboratory results (estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m<sup>2</sup>), and anemia was defined according to laboratory results of ferritin levels <100  $\mu\text{g/ml}$  or ferritin in the range of 100–300  $\mu\text{g/l}$  but a transferrin saturation <20%, COPD was diagnosed based on medical record documentation (discharge diagnosis, or follow up notes).

## Results

This research paper presents the results of a comprehensive study on acute heart failure with non-cardiac comorbidities. A total of 140 Libyan consecutive patients with an established diagnosis of acute heart failure who were admitted to the cardiac ward or coronary care unit (CCU) at TUH were enrolled in this study.

102 (72.9%) of the patients were males and 38 (27.1%) were females, their mean age was 60.08 yrs.  $\pm$  SD 12.9, the minimum age was 27 yrs. and the maximum age was 94 yrs. The primary diagnoses of the HF patients were also analyzed. Among the cases, 7 cases (5 %) diagnosed as de novo heart failure, indicating the occurrence of HF as a new and independent condition. 5 cases (3.6%) of the patients admitted in cardiogenic shock, and The majority of patients, accounting for 128 cases (91.4%), were diagnosed with acute decompensation of the chronic heart (ADHF) emphasizing the prevalence of this condition. Non-compliance to treatment was the leading aggravating factor for decompensation with a percentage of 31.4% followed by infection at 29.2 %, and Atrial Fibrillation in 12.1% of the cases.

The distribution of ejection fraction (EF) among the AHF patients was examined. It was found that the majority of patients, accounting for 121 cases (86.4%), had an EF of less than 40%. A smaller proportion, 16 cases (11.4%), fell within the range of 41% to 50%. Only a minority, comprising 3 cases (2.1%) of the patients, had an EF greater than 50%. These findings based on EF reflect the underdiagnosis of HFPEF. Additionally, the study investigated the hospital admission locations for HF patients. The majority of patients, 125 cases (89.3%), were admitted to the cardiac ward, indicating the significance of specialized cardiac care in managing HF. A smaller proportion, 15 cases (10.7%), required intensive care and were admitted to the CCU.

Regarding treatment on admissions, we found 79.28% of the total numbers of our patients were taking frusemide, 75% on ACE or ARBS, 70.7% on B blockers, 62% on Aldactone, and only 27.8% on SGLT2 inhibitors, 14.2% on Entresto, and only 10.7% of our patients were on the guidelines directed medical therapy of heart failure GDMT. Regarding the adherence of the patients to the GDMT based on the EF, we found that 35% of the HFrEF patients were on the 4 GDMT, 60% on the 3 pillars of the GDMT, 89% on 2 pillars of GDMT, and 94% of them were on 1 pillar For the HFmREF patients only 12.5% were on SGLT 2 inhibitors ( which according to the ESC guidelines of heart failure is considered as class I recommendation). No patients were on ARNI, 18.7% received MRA (class two recommendation), and for the HFpEF patients 66.6% were on SGLT2 inhibitors (class 1 recommendation), 66.6% were on MRA (class 2 recommendation) and no patients were on ARNI (class 2 recommendation). In addition to HF-specific findings, the study investigated co-existing non-cardiac conditions among the patients. Almost all enrolled patients had multiple comorbidities only 8 (5.7%) had no comorbidities. DM was observed in 84 (60 %) of the cases, CKD was prevalent in 43 (30.7%) of the patients. Anemia was present in 17 (12.1%) of the patients. COPD was found in 4 (2.9%) of the cases. Furthermore, the research examined the outcomes of HF patients. It was found that a significant proportion, 114 cases (81.4%), of patients, responded to medical treatment, A smaller percentage, 14 cases (10 %), required advanced management which was Cardiac Resynchronized therapy Defibrillator (CRTD), suggesting the complexity and severity of their condition. Unfortunately, 12 cases (8.6%) of the patients die. Regarding the details of the dead patients, 11 of them (91.7%) had an EF of < 40%, 9 (75%) had DM, 3 (25%) had anemia and 6 (50%) had CKD with a (p-value = 0.055).

Overall, this study provide clear idearegarding the types of heart failure , hospital admission patterns, patient treatment, co-existing non-cardiac conditions, and patient outcomes among HF patients. These findings enhance our understanding of HF, facilitate tailored treatment strategies, and pave the way for further research to improve patient care and outcomes of the patients.

**Table 1. Socio-demographic characteristics of HF patients, TUH, 2022**

Character	No.	%
Gender		
Male	102	72.9%
Female	38	27.1%
Age		
25- 45 years	21	15%
46-65 years	72	51.4%
66-85 years	45	32.2%
$\geq$ 68 years	2	1.4%

**Table 2. Clinical characteristics of HF patients, TUH, 2022**

Character	No.	%
<b>Primary diagnoses</b>		
Newly diagnosed heart failure	7	5%
Cardiogenic shock	5	3.6%
Acute decompensation of chronic heart failure( ADHF)	128	91.4%
<b>EF</b>		
Less than 40%	121	86.5%
41% to 50%	16	11.4%
More than 50%	3	2.1%
<b>Hospital admission patterns</b>		
Cardiac ward	125	89.3%
CCU	15	10.7%
<b>Patient treatment</b>		
Furosemide	11	79.28%
ACE or ARBS	105	75%
B blockers	99	70.7%
Aldactone	87	62%
SGLT2 inhibitors	39	27.8%
Entresto	20	14.2%
On the guidelines directed medical therapy GDMT	15	10.7%
<b>Co-existing non-cardiac conditions</b>		
DM	84	60 %
CKD	43	30.7%
Anemia	17	12.1%
COPD	4	2.9%
No comorbidities	8	5.7%
<b>Patient outcomes</b>		
Recovered	114	81.4%
Require advanced management	14	10 %
Death	12	8.6%

## Discussion

This study is unique as it is the first of its type to be conducted in Libya. Despite the small number of Exposed patients in this study ( 140 ), however, it gives a general view of the Libyan situation, we found that the male gender was the predominant gender by a ratio of (72.9%) similar to that found by Dr. Hassanein M and his colleagues [25], T Abdurashidova and his colleagues [26], higher than that observed by Dr. Khalid F AlHabib and his colleagues [27], Umut Kocabaş and his colleagues [28] and differ from the result of Dr. Masho Tigabe and his colleagues [29], as well as (ADHERE) study [34] where the predominant gender was female, Dr. Albertino Damasceno and his colleagues found 50% of their admitting AHF patients were female [30],

The mean age for our patients was 60.08 years which is relatively younger than expected. Since heart failure is a disease of old [31], our finding was similar to that in central Asia [26], the Gulf area [27], Subsahara Africa [28], and Egypt [25], younger than the European Union [34,35,36] USA [34], and older than African survey [30], our explanation for that is the high prevalence of CAD risk factors among young and middle-aged Libyan people and unhealthy lifestyles in Libya as that was noted in heart failure registries from the Middle East[37,38]. more studies are needed to know the cause.

Most of the admitting patients ( 91.4% ) were presented with decompensated status ADHF, and only 5% presented for the first time ( de --novo), this finding is different from what was previously reported in other studies[29,32,33] where the majority of admitted patients were newly diagnosed heart failure patients, this finding needs more studies to know the reason.

Non-compliance to treatment was the leading aggravating factor for decompensation with a percentage of 31.4% followed by infection at 29.2 %, and Atrial Fibrillation in 12.1% of the cases, these findings were due to the lack of medical insurance for our heart failure patients and expensive cost for most of the guidelines directed medical therapy, in comparing with other studies in, Ethiopia [29], Uganda [32], Turkish HF registry [43].

86.4% of our patients had EF < 40% (HF<sub>r</sub>EF), and only 2.1% had EF > 50% ( HF<sub>p</sub>EF), which reflects our underdiagnosis of HF<sub>p</sub>EF cases. IHD was the main etiology of AHF in 45,7 % of the total number of our patients, our result was similar to that in the European Registry [36], USA Registry [34], followed by

Nonischemic cardiomyopathy in 22.8%, Systemic Arterial Hypertension in 19.2 %, Valvular Heart Disease in 7.4%, and 5% had Tachyarrhythmia as an Etiology.

94.7% of our patients had Noncardiac comorbidities. our result was higher than that seen in USA[42], Europe[43], and Sub-Sahara African countries [30], Regarding the prevalence of Non-cardiac comorbidities among AHF-admitting patients we found Diabetes Mellitus was the commonest comorbidity followed by Chronic kidney disease, Anemia, and lastly COPD, in comparison with other similar studies DM was the commonest in the Gulf registry of AHF cases [39], China [40]. Anemia was the commonest comorbidities in another study [41].

Only 10.7% of the total number of our patients were on GDMT 35% of the HFrEF patients were on the 4 GDMT, 60% on the 3 pillars of the GDMT, 89% on 2 pillars of GDMT, and 94% of them were on 1 pillor For the HFpREF patients only 12.5% were on SGLT 2 inhibitors (which according to the ESC guidelines of heart failure is considered as calssI recommendation) , and no patients were on ARNI, 18.7% were received MRA (calss two recommendation), and for the HFpEF patients 66,6% were on SGLT2 inhoibitors (Class 1 recommendation), 66.6% were on MRA (class 2 recommendation) and no patients were on ARNI (class 2 recommendation), these findings reflecting the underadherence of our heart failure patients to these treatments mainly due to the high costs of these treatments and unfortunately, these medications are not prescribed by many doctors, these finding necessitated the importance of the presence of medical insurance for the patients, and the need for improvement of education programmes for our practicing physiciants , these results were lower than that in Gulf area [44], Turkey [45], real world Meta-Analysis [46] and similar to Canadian study [47].

Unfortunately, (8.6%) of the patients died in the hospital. Our mortality rate was higher than that observed in Sub-Saharan countries [30] and Egypt [48], lower than that observed in Ethiopia [29], and similar to that observed in Turkey [28], this research showed a significant correlation between the presence of CKD and the patient's worse outcomes (p-value = 0.055) and between the presentation with cardiogenic shock and in-hospital mortality (p-value = 0.057) similar to that observed in an Egyptian study [49].

## Conclusion

Our patients were relatively young, mostly male, with a high prevalence of ischemic heart disease, reduced ejection fraction, majority of the patients presented with decompensated status of their heart failure, and a lower rate of GDMT use. The presence of comorbidities, especially chronic kidney diseases, as well as the presence of cardiogenic shock, increases the risk of in-hospital mortality. More efforts, and organized preventive programs to control the non-cardiac comorbidities among heart failure patients to improve their outcomes.

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## Conflicts of Interest

The authors declare no conflict of interest.

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### المستخلص

عادةً ما يعاني مرضى قصور القلب الحاد من أمراض مصاحبة متعددة ومتراصة. تلعب هذه الأمراض المصاحبة دورًا رئيسيًا في تحديد تشخيص ونتائج مرضى قصور القلب الحاد، فضلاً عن التأثير على الإدارة. هدفت دراستنا إلى وصف تأثير وجود أمراض مصاحبة غير قلبية على نتائج المرضى الذين يتم قبولهم في مستشفى طرابلس الجامعي بسبب قصور القلب الحاد. من يناير إلى أكتوبر 2022 أجرينا هذه الدراسة المقطعية الوصفية في قسم القلب ووحدة العناية القلبية في مستشفى طرابلس الجامعي. تم تصميم استبيان تم إنشاؤه ذاتيًا لجمع البيانات من السجلات الطبية، ثم تم تحليل البيانات باستخدام برنامج SPSS الإصدار 20. تم تسجيل 140 مريضًا في هذه الدراسة. كان المرضى 102 (72.9%) من الذكور و 38 (27.1%) من الإناث، وكان متوسط أعمارهم 60.08 سنة. ± الانحراف المعياري 12.9. كان 128 مريضًا (91.4%) في مرحلة عدم التعويض من حالة قصور القلب السابقة لديهم و 5 (3.6%) كانوا مصابين بصدمة قلبية. كان عدم الامتثال للعلاج هو السبب الرئيسي. المتفاقم لعدم التعويض بنسبة 31.4% يليه العدوى بنسبة 29.2% والرجفان الأذيني في 12.1% من الحالات. كان لدى جميع المرضى المسجلين تقريبًا أمراض مصاحبة متعددة ولم يكن لدى 8 فقط (5.7%) أمراض مصاحبة. تشمل هذه الأمراض المصاحبة مرض السكري في 84 مريضًا (60%) وفقر الدم في 17 مريضًا (12.1%) ومرض الكلى المزمن (CKD) في 43 مريضًا (30.7%) ومرض الانسداد الرئوي المزمن. (COPD) 4 (2.9%) فيما يتعلق بالعلاج، كان 10.7% فقط من مرضانا على العلاج الطبي الموجه للمبادئ التوجيهية لقصور القلب (GDMT) عند خروجهم إلى المنزل، ووفقًا لنتائج المرضى في هذه الدراسة، احتاج 14 (10%) من المرضى إلى إدارة متقدمة، وتوفي 12 (8.6%). واستجاب باقي المرضى البالغ عددهم 114 (81.4%) للعلاج الطبي القياسي بشكل أساسي مدرات البول والعلاج الطبي الموجه للمبادئ التوجيهية. أظهرت هذه الدراسة وجود ارتباط إحصائي كبير بين مرض الكلى المزمن والنتائج الأسوأ مع (القيمة الاحتمالية = 0.055). وبين الصدمة القلبية والوفيات داخل المستشفى مع (القيمة الاحتمالية = 0.057). كان مرضانا صغارًا نسبيًا، ومعظمهم من الذكور، مع انتشار مرتفع لمرض السكري، وأكثر حدة في قصور القلب المزمن من حالات دينيفو، واستخدام أقل لاستخدام العلاج الطبي الموجه للمبادئ التوجيهية، ويرتبط وجود الأمراض المصاحبة، وخاصة مرض الكلى المزمن وكذلك وجود الصدمة القلبية، بزيادة خطر الوفاة داخل المستشفى.