Original Article

Clinical Profile, Precipitating Factors, and In-Hospital Outcomes of Patients Admitted with Acute Decompensated Heart Failure: A Prospective Observational Study

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Abstract

Background: Acute decompensated heart failure (ADHF) is a major cause of hospitalizations, and mortality and morbidity rates are high. There are limited data on patient characteristics, precipitating factors and the short-term outcomes of Indian populations. The goal of the reseach is to assess clinical profile, heart failure (HF) pheno-type, precipitating factors, and outcome of the in-hospital experience of ADHF patients. **Material and Methods:** This study is a prospective observational study of 96 consecutive adult patients who were admitted with ADHF in a tertiary care teaching hospital. Framingham criteria were used for diagnosis, and the American Heart Association guidelines for heart failure staging. Clinical data, laboratory measurements, echocardiographic data, precipitating cause and in-hospital results were collected. While $p<0.05$ was used as indication of significance, suitable parametric and non-parametric statistical tests were used. **Results:** Of note, the mean LVEF of the study population was 32.98±11.94%, and the most common phenotype was HF with reduced EF (HFrEF, 69.8%). Hypertension (55.2%) and diabetes mellitus (42.7%) were the most common comorbidities. The major etiologies were ischemic cardiomyopathy followed by hypertensive heart disease (30.2%, 26.0%). Infections (29.2%) and acute coronary syndrome (17.7%) were the most common precipitating factors. Sixty-three percent (63.5%) of the patients improved, 19.8% experienced refractory symptoms, and 16.7% passed away while hospitalized. Oxygen saturation and SBP were significantly lower while BNP was significantly higher for non-survivors. There was a strong association between mortality and AHA Stage D heart failure ($p<0.001$). **Conclusion:** ADHF has high in-hospital mortality rate, especially if there is advanced heart failure and hemodynamic compromise. HFrEF was the most prevalent phenotype and had worse outcomes. Early risk stratification and urgent appropriate management following the guidelines can lead to better short-term results.

Keywords: Acute decompensated heart failure; In-hospital mortality; B-type natriuretic peptide; Echocardiography; Risk stratification.

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Introduction

Many people with heart failure (HF) live and die as a result of the disease, and it costs a lot of money in most countries.[1,2] Even with recent advances in drug therapy and new device technologies the global burden of hospitalization for HF, especially in elderly patients, remains one of the most important in an adult population.[3,4] Acute decompensated heart failure (ADHF) is the sudden onset of or deterioration of symptoms and signs of heart failure which requires immediate hospitalisation and aggressive medical treatment. The most common cause of hospital admissions with heart failure is ADHF and tends to have poorer short- and long-term outcomes.[5,6]

Patients may present with acute pulmonary edema along with systemic congestion and/or cardiogenic shock. Recognition and risk stratification are crucial steps to rational management and optimize results.[7,8] Diagnosis of the heart failure is mostly clinical and Framingham is generally accepted as a diagnostic criterion. Current guidelines developed by the American Heart Association (AHA), American College of Cardiology (ACC) and Heart Failure Society of America (HFSA) for diagnosis and classification of HF include a thorough evaluation based on clinical, laboratory, electrocardiographic and echocardiographic assessment.[9,10]

Echocardiography has a central role in the classification of heart failure by left ventricular ejection fraction (LVEF) as heart failure with reduced ejection fraction (HFrEF), mildly reduced ejection fraction (HFmrEF) and preserved ejection fraction (HFpEF) with different pathophysiological mechanisms and therapeutic implications.[11,12] Knowing the precipitants

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(infection, arrhythmia, uncontrolled hypertension, myocardial ischemia, non-adherence to therapy, anemia, renal dysfunction) is a fundamental component because many attacks of decompensation can be prevented.[13]

Hospitalization for ACHF is known as a sentinel event in the natural history of HF. It is quite common that patients with ADHF stay for a long period in hospital, re-admission in hospital, decreased functional status and greater risk of mortality.[14] Assessment of outcomes within the hospital, such as length of the hospital stay, clinical status at discharge, New York Heart Association (NYHA) category, and adverse events are useful indicators of burden of disease and effectiveness of current management strategies.

Several international registries have done a good job describing the epidemiology and outcome of ADHF, but some of these show large regional differences in the characteristics, comorbidities, precipitating factors and treatment of patients, and so the generation of data at a regional level is warranted. Having an understanding of these factors is critical to better risk stratification, use of resources, and more precise interventions to lower hospitalizations and their adverse outcomes. For this reason, the present study was performed to explore the clinical features, precipitating causes and in-hospital outcomes of acute decompensated heart failure (ADHF) patients admitted in the tertiary care center setting.

Materials and Methods

Study Design and Participants: This was a prospective observational study, conducted in Dept. of General Medicine, TMMC&RC, for a period of 18 months after ethical clearance. Eligible consecutive adult patients (≥18 years old) with acute decompensated heart failure (ADHF) were entered into the study with written informed consent. The Framingham criteria were used for the diagnosis of ADHF and the American Heart Association (AHA) criteria were used for the heart failure staging. Excluded patients were those who had active malignancy or terminal non-cardiac illness.

Based on the formula for calculating minimum sample size: $n = Z^2P(100-P)/E^2$, where the prevalence was assumed to be 10%, the allowable error was 6%, and the 95% confidence interval (Z=1.96), the minimum sample size was 96 patients. Demographic Characteristics, Clinical History, Cardiovascular Risk Factors, Comorbidity and Precipitating Factors were noted on a proforma for clinical and diagnostic evaluation. Detailed physical examination including assessment of hemodynamic status, pulmonary congestion, peripheral edema and vital signs was done on admission.

Baseline evaluations consisted of complete blood count, renal function tests, blood electrolytes, blood glucose, electrocardiography and chest radiography. All patients had transthoracic echocardiograms done on a Philips Affinity 50C system. Patients were classified as having heart failure with reduced ejection fraction (HFrEF), mildly reduced ejection fraction (HFmrEF) or preserved ejection fraction (HFpEF) based on LVEF.

Outcome Measures: Dental patients were followed during their hospital stay. Precipitating factors and comorbidities for decompensation were recorded. The main outcomes measured were Length of Hospital Stay (LOS), New York Heart Association (NYHA) functional class at discharge, In-Hospital Adverse Events (IHAAE), and Mortality.

Statistical analysis: Data were statistically analyzed by IBM SPSS Statistics version 26.0. The continuous variables were presented as mean and standard deviation (SD) or as median (interquartile range) and categorical variables were presented as frequencies and percentage. For the comparisons among the different groups the independent-samples t-test, Mann–Whitney U test, chi-square test and Fisher's exact test were used as appropriate. Odds ratios (ORs) with 95% confidence intervals were calculated by univariate and multivariable logistic regression analyses of variables associated with adverse in-hospital outcomes.A two-sided p-value <0.05 was considered statistically significant.

Results

Baseline clinical, laboratory, and heart failure data of the study participants indicate that participants had an early diagnosis with predominantly HFrEF and low LVEF (Table 1). Table 2 shows the burden of coexisting conditions - the most prevalent being hypertension and diabetes mellitus. Table 3 shows that in-hospital outcomes were poorer in HFrEF than in the other phenotypes of heart failure. Independent predictors of in-hospital death are highlighted in Table 4: AHA Stages D HF, high BNP, low oxygen saturation, low SBP, and critical triage are all poor prognostic indicators.

The underlying etiology of ADHF is shown in graph 1, where ischemic cardiomyopathy and hypertensive heart diseases dominate. Infection, acute coronary syndrome, anemia and renal dysfunction are the main precipitating factors of decompensation and are associated with high mortality rates. Graph 3 depicts selected markers of parts of in-hospital course and the correlation with their significance for mortality, with adverse hemodynamic and biomarker profiles correlating with higher risk of mortality.

Table 1: Baseline Clinical, Laboratory and Heart Failure Characteristics (n=96)

Variable	Value
Hemoglobin (g/dL)	11.89 ± 1.96
Creatinine (mg/dL)	1.52 ± 0.67
Sodium (mEq/L)	134.22 ± 4.31
Potassium (mEq/L)	4.33 ± 0.52
BNP (pg/mL)	1264.38 ± 503.71
JVP (cm H_2O)	12.04 ± 1.82
LVEF (%)	32.98 ± 11.94
HFrEF	67 (69.8%)
HFmrEF	19 (19.8%)

HFpEF	10 (10.4%)
AHA Stage D	38 (39.6%)

Table 2: Comorbidity Burden Among ADHF Patients

Comorbidity	n (%)
Hypertension	53 (55.2)
Diabetes mellitus	41 (42.7)
CKD	28 (29.2)
CAD	18 (18.8)
PAD	17 (17.7)
Valvular disease	14 (14.6)
COPD	12 (12.5)
Others	Remaining

Table 3: Heart Failure Phenotype and In-Hospital Outcome

HF Phenotype	Improvement	Refractory	Mortality
HFrEF	37 (55.2%)	17 (25.4%)	13 (19.4%)
HFmrEF	15 (78.9%)	2 (10.5%)	2 (10.5%)
HFpEF	9 (90.0%)	0	1 (10.0%)

Table 4: Independent Clinical Predictors of In-Hospital Mortality

Variable	OR / Effect Size	p-value
AHA Stage D	OR 85.80 (4.94–1491.09)	<0.0001
SpO_2	d=0.97	0.0017
BNP	d=0.92	0.0044
Triage location	V=0.35	0.0030
SBP	d=0.48	0.0330

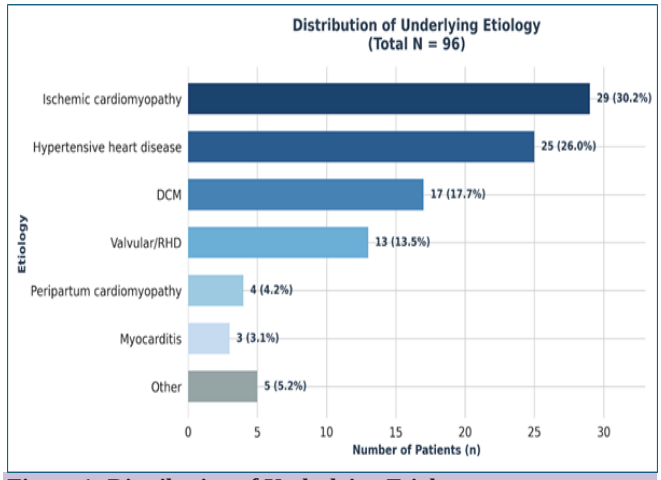

Figure 1: Distribution of Underlying Etiology

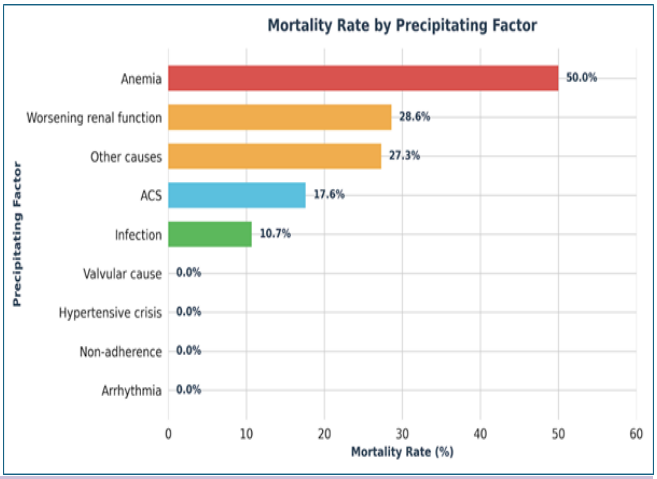

Figure 2: Precipitating Factors and Mortality Rate

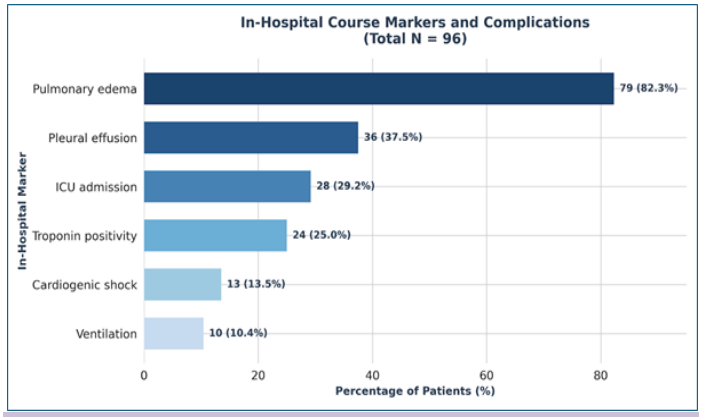

Figure 3: In-Hospital Course Markers

Discussion

In this study, the clinical profile, precipitating factors, heart failure phenotypes and in-hospital outcomes of patients admitted with acute decompensated heart failure (ADHF). The major findings were: (i) majority of patients had HFrEF (69.8 %), (ii) hypertension and diabetes mellitus are the most common comorbidities, (iii) infection and acute coronary syndrome (ACS) were important precipitating factors, and (iv) in-hospital death rate 16.7 %, with advanced heart failure stage, high BNP level, low oxygen saturation, and low SBP being associated with mortality.

The mean age of study population was similar to that reported in the Indian studies done in recent times and was slightly lower than western cohorts. Heart failure patient ages were also reported as relatively younger population compared to that in European and North American studies, suggesting demographical differences and differences in cardiovascular risk burden in LMCs as compared to other high-income

countries (Jayagopal et al.[7]) Next, hypertension (55.2%) and diabetes mellitus (42.7%) were again the most common comorbidities in our cohort, which is similar to what has been reported from the Indian registry and other recent observational studies, which have focused on the increasing role of metabolic risks in heart failure hospitalization (Jayagopal et al,[7] Huliyappa et al.[15]

Nearly 70% of admissions in the present study were for HFrEF while 19.8% and 10.4% of the admissions were for HFmrEF and HFpEF respectively. This distribution corresponds with what Kapłon-Cieślicka et al,[4] found was that there was a significant increase in the number of patients with HFrEF admitted to hospital compared with HFpEF and that hospitalized HFrEF patients tended to be more clinically severe and make more use of resources than HFpEF. Moreover, a decrease in the ejection fraction has been associated with worse patient-reported and clinical outcomes by Peters et al,[5] which we found to be true for our HFrEF trial recipients who had the highest mortality rates (19.4%) and refractory symptom burden (25.4%).

Ischemic cardiomyopathy was the most frequent etiological profile in our population (30.2%) with hypertensive heart disease (26.0%) as the second most prevalent etiological cardiovascular disease. These results are in line with the current epidemiology data that in numerous developing countries experiencing ecological transition, ischemic heart disease is the main cause of HF, especially in that setting (Yan et al.[14]) The etiological patterns observed have also been reported in the Indian population and ischemic cardiomyopathy and hypertensive heart disease are the two most common causes of ADHF admissions (Jayagopal et al,[7] Shinde et al.[13])

Infection was the common precipitating factor (29.2%), followed by ACS and treatment level of adherence. This is consistent with the observations made by Bhatia et al,[8] which suggests that the most common triggers for acute decompensation are infection, ischemic events, and medication not taken. Notably, our data showed that the highest mortality rate was among those with anemia (50%), followed by declining renal function. The results of these analyses agree with the notion that the presence of extracardiac comorbidities plays a significant influence on short-term outcomes for ADHF and worsens congestion, organ perfusion and prognosis (Arrigo et al. [1] and Ciccarelli et al.[11]).

Overall in-hospital mortality was 16.7% in the present study versus several Registry-based studies reporting rates lower than the present study. For instance, in ICCNHFR lower short-term mortality rate has been reported compared to JROAD HF (JapaneseRegistries onAcute andChronicHeartFailure) registry in Japan.[5,7] Increased mortality seen in our study might be due to more patients presenting with higher disease severity, with almost 40% of the patients in AHA stage D and about 1/3 of patients requiring CCU/ICU admission.

The key and unique finding of this study was the close relationship between AHA Stage D heart failure and mortality. These findings indicate the prognostic value of advanced heart failure, as all non-survivors were in stage D of extreme heart failure, with an odds ratio of 85.8. High-level-heart-failure (HHF) is recognized as an important driver of poor outcomes and guidelines from the ESC, AHA/ACC/HFSA recommend risk stratification and early specialist management for these patients (McDonagh et al,[2] Heidenreich et al.[3]).

We also observed significantly higher BNP levels among non-survivors. Increased BNP reflects an increased hypertrophic load on the ventricles and an activation of neurohormones, and has consistently been demonstrated to correlate with death and rehospitalization in patients with ADHF. A similar association was described by Bhatia et al,[8] who showed an important correlation between increase in natriuretic peptide and poor outcome. Also, in our population, decreased oxygen saturation and decreased systolic blood pressure had independent mortality association, emphasizing hemodynamic instability as a bad prognosis marker. This coincides with findings from the survival analysis presented by López-Vilella et al,[12] who concluded that markers of circulatory compromise were significant predictors of mortality.

In our study we found that 25% of patients were positive for troponin, however, there was no significant difference associated with mortality. This is contrary to Sreekumar et al,[9] who have shown that high troponin was significantly linked to death in ADHF. This may be explained by the fact that this difference could be due to the different sample size, patient selection and background etiological factors.

The lessons of recent research suggest that ADHF is a heterogeneous condition and that risk stratification should be based on ADHF phenotypes. Using machine-learning techniques and multi-dimensional phenotyping has led to the identification of therapeutic response-relevant patient-subsets with differing outcomes (Murray et al,[6] Anker et al.[10]).

Our study adds to the body of evidence in support of the concept of a phenotype-based approach to heart failure management in today's practice by demonstrating differences in outcomes among the patient populations in the three heart failure subgroups. Our study further underscores the need for phenotype-specific approaches to heart failure management in contemporary clinical care by demonstrating difference in outcomes across the three heart failure subgroups.

The present study has a number of limitations. It was performed in a single tertiary care centre with a relatively small number of patients and this may hamper generalisability of the results to other tertiary care centres. Second, prior to discharge, no adverse events, e.g., rechallenge, long-term mortality, were assessed. Third, number of outcome events prevented multivariable prognostic modelling. Lastly, only commonly used biomarkers were assessed and serial biomarker measurements were not conducted. Undoubtedly the study is limited but with these restrictions it serves as an important real world data about the clinical profile, precipitating factors and the short term outcome of patients who were admitted to hospital with ADHF in an Indian tertiary health care set up.

Conclusion

In this study, acute decompensated heart failure (ADHF) was linked with significant in-hospital mortality and morbidity. HFrEF was the major phenotype and the most prevalent

comorbid condition encountered was hypertension and diabetes mellitus. The main etiology was ischemic cardiomyopathy and the main precipitating factor was infections and acute coronary syndrome.

An in-hospital mortality rate of 16.7% was observed. Advanced heart failure (AHA stage D), elevated BNP level, reduced oxygen saturation and reduced systolic blood pressure were independent risk factors for death. Identifying patients early who are at high risk and achieving early and on-time adherence to guideline-directed care could lead to better clinical outcomes and fewer mortalities in the hospital setting among patients with ADHF.

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