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Presentation and Management of Acute Decompensated Heart Failure in a Tertiary Care Hospital in Kerala, India

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Abstract

Background: Heart failure (HF) is one of the leading causes of morbidity and mortality in people over 60years of age. There are a multitude of causes that lead to HF depending on one's age, demographics and other co-morbidities. Even though several population-based and hospital-based studies exists, the epidemiology of acute decompensated heart failure (ADHF) have been poorly described. A reliable means for estimation of heart failure is lacking in India because of the absence of a proper surveillance.

Methods and Results: Data from 104 patients admitted with ADHF from a single tertiary hospital in India during March 2020 to February 2021 was analyzed. Mean age was 68.62±11.79 years and almost half of the population were females. The most common etiology of HF in the population was ischemic heart disease (IHD), followed by hypertensive heart disease (HTHD). Total in-hospital mortality during initial admission was 8.7% and the composite of mortality and hospitalization for HF (HHF) was higher in patients with IHD (64%). CKD stage 3b or more, SGOT > 50 and LVEF <30% was associated with significant number of rehospitalization and death within 1 month. Adherence to GDTM was noted to be 55.4% during discharge and 64.5% during 1-month follow-up. GDTM with triple drug therapy was shown to reduce mortality and HHF within 1 month to 14.8% while it rises to 80% when none of the drugs are used.

Conclusions: An LVEF < 30% was identified as an independent predictor of mortality and rehospitalization for HF. The prevalence of HFpEF was noted to be higher in females. A higher mortality was noted for patients of IHD with HFrEF. Almost half of the patients

of HFrEF received guideline directed medical therapy. Those who received GDMT had lower 30-day mortality and/or rehospitalization for heart failure compared to those who did not.

Keywords: Acute decompensated heart failure, Failure registry, Heart Failure, Left ventricular ejection fraction, Mortality and rehospitalization in HF, HFrEF, HFpEF

Introduction

Heart failure (HF) is one of the leading causes of morbidity and mortality in people over 60 years of age. With an aging and rapidly expanding population, the prevalence of HF is rising substantially in India causing increased mortality and morbidity.

The causes of HF vary and is dependent on a variety of factors like age, demographics and co-morbidities. Several population-based and hospital-based studies have been conducted in different parts of the world and its epidemiology has been well described[1,2,3,4,5,6]. Unfortunately, there has been very few reports on presentation and management of heart failure from India. Partly this is due to absence of a proper surveillance program for HF. Management of HF has been largely as per the guidelines from European Society of Cardiology (ESC) and American College of Cardiology (ACC). However, these guidelines are based on evidence from western patients and may not be relevant in HF care in a vast country like India with its unique challenges. Hence there is an urgent need to develop a surveillance system to analyze the clinical presentation, management and outcome of patients admitted with heart failure in India.

Registry studies are observational studies which provide detailed information about the patients with a particular condition enabling systematic comparison and analysis across various centers[7]. Registries help to understand the differences in clinical practice and patient outcomes across various centers and to identify the targets for improvements. The data generated can be used by health authorities for development of policies and implementation of strategies for improvement of care.[8]

Institutional level cardiac disease registries will pave a pathway to establish a national registry and a single data repository in a developing country like India. Heart failure registries have proved to be valuable for improving treatment modalities and outcomes in Indian patients with HF.[9,10] Several studies on presentation and management of HF has been carried out recently in different parts of India .[11,12,13,14,15] But results from these studies vary considerably, reflecting the cultural diversity of India and differences in the prevalence of risk factors for HF. Hence, there is a need for more registries studying HF at regional and institutional levels. The present study was undertaken as an institutional level HF registry in Thrissur, Kerala to compare the presentation, management and outcomes of HF with other regions of Kerala and rest of India.

Methods

This was a prospective observational study of patients admitted with a diagnosis of acute decompensated heart failure (ADHF) from March 2020 to February 2021 at the Department of Cardiology, Mother Hospital, Thrissur, India. The diagnosis of HF was based on the Framingham's criteria[16]. All adult patients (age >18years) admitted with ADHF to the cardiac intensive care unit were enrolled after getting informed consent. Information about the presenting symptoms, history of pre-existing disease conditions and risk factors, findings on physical examination, laboratory investigations including biomarkers, EKG, chest x ray, details of procedures and interventions, treatment strategies and in-

hospital outcomes were carefully recorded using a structured questionnaire.

Those on treatment or told to have diabetes in the past were classified as having diabetes. Those on treatment for hypertension or told to have high blood pressure in the past were considered to have hypertension. Those who gave history of consuming alcohol at least once during the past year were considered positive for alcohol intake and those who have smoked at least once during the past month were classified as smokers.

An underlying etiology of HF was identified in all the study participants. When there were more than one identifiable etiological factors, most important cause was taken as the etiology. Patients with a history of angina or previous acute coronary syndrome (ACS) and those who presented with HF and had features of ACS were considered to have ischemic heart disease (IHD). Those with no evidence of coronary artery disease (CAD) and having LV dysfunction (EF $\leq$ 40%) and / or global hypokinesia on echocardiogram were classified under dilated cardiomyopathy (DCM). Those with no evidence of CAD, but having history of high blood pressure (BP) along with diastolic dysfunction and features of left ventricular hypertrophy (LVH) were classified as hypertensive heart disease (HTHD). Those having LVH, with asymmetric septal thickening and no evidence of hypertension were classified as hypertrophic cardiomyopathy (HCM). Those with evidence of valve disease and heart disease at birth were classified under valvular heart disease (VHD) and congenital heart disease (CHD) respectively.

Echocardiographic evaluation was done in all study subjects and LVEF was estimated using the Teicholz method[17],[18]. Heart failure was divided basically into two types as either HF with reduced EF (HFrEF) if LVEF is $\leq$40% and HF with preserved EF (HFpEF) if LVEF is >40% as per the ACCF/AHA guideline 2013[19] and its 2017 focused update[20]. Guideline directed medical therapy (GDMT) was defined as the combination of angiotensin converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB)/angiotensin receptor neprilysin inhibitor (ARNI), beta blockers (BB) and mineralocorticoid receptor antagonist (MRA). We have not included SGLT2 inhibitors (SGLT2i) in this study.

Discharged patients were followed-up at 30 days at the hospital outpatient department. Information about those who missed follow-up visit was collected by telephonic contact. The study was approved by the Institutional review board (IRB) of Mother Hospital with the approval number ECR-199.

Statistical methods

All the data collected were coded and entered in Microsoft Excel sheet which was re-checked and analyzed using SPSS statistical software version 22. Quantitative variables were summarized using mean and standard deviation. Categorical variables were represented using frequency and percentage. Independent sample t test was used for comparing continuous variable between groups. Pearson Chi-square test and Fisher's Exact test were used for comparing categorical variables between groups. A p value of <0.05 was considered statistically significant

In hospital and 1-month mortalities were estimated as proportions (no of deaths/total registered patients). Composite of mortality and heart failure hospitalization was used for risk factor analysis. A binary logistic regression analysis was used to determine factors affecting mortality and heart failure re-hospitalizations.

The final model included demographic variables (age, sex and financial status), type of HF (HFrEF or HFpEF), baseline comorbidities (diabetes, hypertension, pulmonary disease, stroke), etiology of HF, behavioral risk factors (alcohol, tobacco use), EF, serum creatinine and guideline-based treatment status.

Results

Socio-demographic details

From March 2020 to February 2021, 106 patients were admitted to the cardiology critical care unit (CCU) with a diagnosis of ADHF. Two patients were referred to another hospital at the request of patients / relatives and hence a total of 104 patients were included in the study. Table 1 shows the socio-demographic details of the patients. Mean age was 68.62±11.79 years and almost three fourth of the study population were elderly (60 years or more). Half of the population were females. The average duration of hospitalization was 4.23±2.09 days. Almost one third of the patients were in the below poverty line (BPL) category and most patients were uninsured or had no government aid.

Parameters	Total (N = 104)
Age in years, mean (SD)	68.42 ± 11.79
Duration of hospitalization, mean (SD)	4.23 ± 2.09 days
Age Groups, n (%)	
<60 years	22 (21.2)
≥60 years	82 (78.8)
Gender, n (%)	
Females	51 (49)
Males	53 (51)
Financial status, n (%)	
APL	69 (66.3)
BPL	35 (33.7)
Health insurance status, n (%)	
Government Aided	10 (9.6)
Private	9 (8.7)
Uninsured	85 (81.7)

Table 1: Socio-demographic characteristics of the study population

SD: standard deviation; APL: above poverty line; BPL: below poverty line.

Clinical characteristics

Among the study participants, more than two third had HFrEF (LVEF ≦ 40%) and nearly one third had HFpEF (LVEF > 40%). About one fifth of patients had an EF above 50% and one quarter had an EF < 30%. Majority of the patients had diabetes (71.2%) and hypertension (65.4%). Around 40% of the patients had chronic kidney disease (CKD) and 13.5% had atrial fibrillation (AF) (Table 2).

We looked at the differences in clinical characteristics of patients with HFrEF and HFpEF. There was no significant difference in the mean age of the patients between these two groups (68.43 ± 11.79 years vs 68.63 ± 11.53 years respectively; P value = 0.795). However more women presented with HFpEF than men (62.5% vs 37.5%) while more men presented with HFrEF than women (57.0% vs 43.0%). (p value = 0.058). There were no differences in the prevalence of CKD, diabetes, hypertension, atrial fibrillation, anemia, alcohol use or smoking between subjects with HFrEF and HFpEF. Tachycardia was more frequent in HFrEF than HFpEF (41.7% vs 62.5%, p value = 0.016). Elevation of serum cardiac troponins was more common in HFrEF than HFpEF. (66.7% vs 38.2%; p value=0.016)

With respect to etiology of heart failure, IHD accounted for the majority of cases of heart failure (61.5%), followed by HTHD and DCM. VHD, HCM and CHD were infrequent causes of HF. However, IHD was more frequent in HFrEF than HFpEF (73.6% vs 34.4% p value < 0.001) and HTHD was more frequent in HFpEF (40.6% vs 2.8%, p value <0.001). In fact, in HFpEF,

HTHD was more common than IHD as an etiologic factor. (86.6% vs 17.2%, p value <0.001).

Characteristics	Total Subjects (N=104)	HFrEF 72 (69.2%)	HFpEF 32 (30.8%)	P value
Mean Age (years)	68.42 ± 11.79	68.63 ± 11.53	67.97 ± 12.53	0.795
Female	51 (49)	31 (43.0)	20 (62.5)	0.058
Male	53 (51)	41 (57.0)	12 (37.5)	
Risk factors and comorbidities, n (%)				
T2DM	74 (71.2)	51(70.8)	23(71.9)	0.914
HTN	68 (65.4)	47(65.3)	21(65.6)	0.973
Alcohol use (current)*	12 (11.5)	11(15.2)	1(3.1)	0.073
Smoking (current)*	9 (8.6)	8 (11.1)	1 (3.1)	0.181
Anemia (Hb<10 gm%)	22 (21.2)	13 (18.1)	9 (28.1)	0.246
CKD (eGFR < 45)	42 (40.4)	29 (40.3)	13 (40.6)	0.973
AF	14 (13.5)	8 (11.1)	6 (18.8)	0.292
Clinical features, n (%)				
Tachycardia	51 (49)	41(56.9)	10 (31.3)	0.016*
Mean SpO2	88.90 ± 9.21	87.97 ± 9.29	91.00 ± 8.79	0.122
Elevated Troponins	48 (46.2)	38(66.7)	10(38.5)	0.016*
Etiology, n (%)				
Ischemic Heart Disease (IHD)	64(61.5)	53(73.6)	11(34.4)	<0.001
Hypertensive Heart Disease (HTHD)	15(14.4)	2 (2.8)	13 (40.6)	<0.001
Nonischemic Dilated Cardiomyopathy (DCM)	13(12.5)	13 (18.1)	0	0.008*
Valvular Heart Disease (VHD)	8(7.7)	4(5.6)	4(12.5)	0.247
Hypertrophic cardiomyopathy (HCM)	2(1.9)	0	2(6.3)	0.093
Congenital Heart Disease (CHD)	1(1)	0	1	0.308

Table 2: Clinical characteristics of study participants with respect to type of heart failure

T2DM: Type 2 diabetes mellitus; HTN: Hypertension; Current alcohol use defined by those with history of consuming alcohol at least once during the past year; Current smoker defined by those who have smoked at least once during the past month; Hb: Hemoglobin; eGFR: estimated glomerular filtration rate; AF: Atrial fibrillation.

Medical therapy

On admission more than half of the patients were already on aspirin and nearly 50% of them on clopidogrel, RAAS blockers and Beta blockers. Almost all patients received diuretics, most of them were prescribed dual antiplatelet drugs and around two third of the patients were given ACEI/ARB, betablockers and nitrates. There was no significant drop in the usage of these medications at one month follow up (Table 3).

Table 3: Medical treatment: in-hospital and at one month follow up.

Drugs	In-hospital n(%) (N=104)	At one month follow up n(%) (N=91)
Diuretics	103(99)	87(95.6)
ACEI/ARB	70(67.3)	73(80.2)
ARNI	2(1.9)	5(5.5)
Beta blockers	70(67.3)	71(78)
MRA	56(53.8)	55(60.4)
Digoxin	23(22.1)	22(24.2)
Hydralazine	9(8.7)	9(9.9)
Nitrates	70(67.3)	56(61.5)
Antiplatelets	96(92.3)	77(84.6)
Amiodarone	13(12.5)	8(8.8)

We also looked at the proportion of patients with HFrEF who GDMT with a combination of ACE/ARB/ARNI,

BB and MRA, during hospital stay, at discharge and at one month follow up (Figure 1).

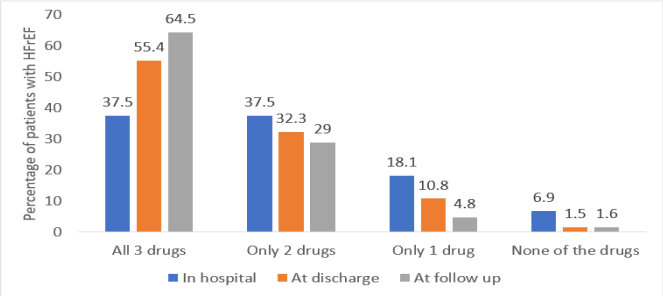

Figure 1: Use of GDMT in patients with HFrEF

Mortality and rehospitalization

The in-hospital mortality rate was 8.7%, and one-month mortality was 12.5% (Figure 2). Rehospitalization for HF (HHF) was observed in 16 subjects (11.5%), out of which 4 died. The composite of one-month HHF and mortality was 24%.

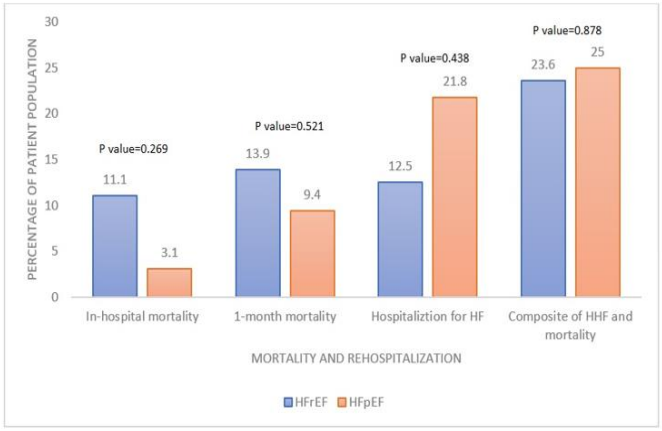

Figure 2: Mortality in-hospital and at one month follow up, HHF and composite of mortality and HHF.

The p value comparing mortality and hospitalization among patients with HFrEF and HFpEF is mentioned on top of each section. HFrEF: heart failure with reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; HHF: hospitalization for heart failure.

We looked at the factors predicting the risk of death or re-hospitalization for heart failure (Table 5). Elderly age, hospitalization for more than 5 days, rales more than 50% lung base, elevated JVP, low SpO2, high SGOT, CKD, and LVEF < 30% were significant risk factors.

Characteristics	Total Subjects (N=104)	Composite of death or HHF within 1month, n (%)	P value
Age 60 and above	82 (78.8)	24 (29.3)	0.016*
Female gender	51 (49)	15 (29.4)	0.208
Hospitalization > 5 days	23 (22.1)	9 (39.1)	0.050*
Previous ACS	44 (42.3)	12 (27.3)	0.509
H/o CKD	20 (19.2)	6 (30.0)	0.488
T2DM	74 (71.2)	17 (23.0)	0.690
HTN	68 (65.4)	18 (26.5)	0.973
Rales >50% lung bases	49 (47.1)	18 (36.7)	0.004*
High JVP	86 (82.7)	24 (27.9)	0.044*
Tachycardia	51 (49)	11 (21.6)	0.563
High SBP	85 (81.7)	18 (21.2)	0.149
SpO2 < 88%	35 (33.7)	15 (42.9%)	0.001*
High SGOT (>50)	14 (32.6)	6 (75.0)	0.005*
CKD (eGFR < 45)	42 (40.4)	16 (38.1)	0.006*
HFrEF	72 (69.2)	17 (23.6)	0.878
HFpEF	32 (30.8)	8 (25.0)	0.878
LVEF <30%	28 (26.9)	11 (39.3)	0.027

Table 4: Factors predicting risk of death or re-hospitalization for Heart Failure

ACS: acute coronary syndrome; CKD: chronic kidney disease; T2DM: type2 diabetes mellitus; HTN: hypertension; JVP: jugular venous pressure; SBP: systolic blood pressure; SGOT: serum glutamate ornithine transferase; eGFR: estimated glomerular filtration rate; HFrEF: heart failure with reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; LVEF: left ventricular ejection fraction.

Binary logistic regression analysis showed that LVEF < 30% and Basal crepitation of >50% of lung fields were independent predictors of mortality and hospitalization within one month (p value=0.007 and 0.011 respectively) (Table 5).

Table 5: Factors associated with re-hospitalization or death within 1 month – Binary Logistic regression

Variable	P value	Hazard ratios	95% confidence interval	
			Lower	Upper
Age group	0.068	0.128	0.014	1.164
CKD 3b and above	0.235	0.515	0.172	1.539
Duration of hospitalization	0.085	0.347	0.104	1.15
Orthopnea	0.563	0.584	0.094	3.609
Basal creps >50%	0.007*	0.219	0.072	0.665
LVEF <30%	0.011*	0.230	0.074	0.719
Constant	0.999	9.307		

We assessed the impact of the use of GDMT for HFrEF (combination of ACEI/ARB/ARNI, BB and MRA). We found significant reduction in the mortality and rehospitalization at one month with the use of dual or triple drug therapy compared with single or no drug therapy. (44.4% vs 16.6%; p value=0.016) (Figure 3).

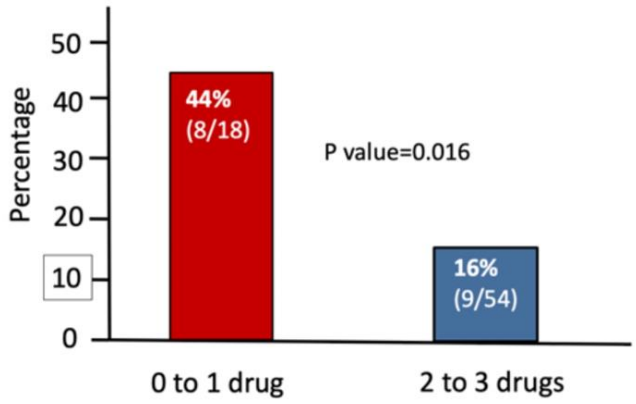

Figure 3: GDMT in HFrEF: composite of death and HHF in one month

Figure depicting the impact of GDMT in preventing death and hospitalization for heart failure in patients with HFrEF. A significant reduction in mortality and was observed with the use of double or triple drug therapy compared to single or no drug therapy with a p value of 0.016. GDMT: guideline directed medical therapy; HFrEF: heart failure with reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction.

Discussion

In this prospective observational study which included 104 patients with HF, we found that the mean age of presentation was 68.4 ± 11.8 years which was similar to other Indian registries of heart failure [11,14,15, 21]. However, our heart failure population was comparatively 4 to 5 years younger when compared to HF registries from developed countries [1,2,3,22]. Likewise, the proportion of patients with HFpEF was only 30% which was similar to other Indian registries, but lower than those from developed countries [1,2,3].

Like international registries, we also observed a higher prevalence of co-morbidities in heart failure, with the prevalence of diabetes being significantly higher in our study (71.2%).

The most important cause of heart failure was IHD, consistent with other studies. However, upon separate analysis, we found that most important cause of HFpEF was HTHD and not IHD.

Our study revealed a substantially higher rate of prescription of medications for heart failure compared to two large heart failure registries published from Kerala. Proportion of heart failure patients who received ACE inhibitors/ARB/ARNI, BB and MRA in our study were 69.2%, 67.3% and 53.8% respectively. In contrast, the figures for in-hospital treatment with these drugs in the Kerala Heart failure registry 48.7%, 59.7% and 45.4% respectively and in the Trivandrum Heart failure registry, they were 38.6%, 58.2% and 45.9% respectively.

Compared to previous studies from India, our study demonstrated a higher usage of GDMT in HFrEF, with

almost 55% of patients on all three medications at discharge and 65% at one month follow up. This contrasts with only 25% of patients in Trivandrum Heart Failure Registry and 28% in Kerala Heart Failure registry who received GDMT. This could be attributed to the urban location of the hospital, better financial status of the patients (as only 33% were below poverty line) and the time period of our study when the treatment strategies for HFrEF were more well established

Our study highlights the high mortality and re-hospitalization rates of patients with heart failure (24% in our study). The in-hospital mortality in our study population was 8.7%, compared to 8.5% in the Trivandrum Heart Failure Registry and 7% in the Kerala Heart Failure Registry. We found that elderly age, prolonged hospital stays, elevated JVP, more than 50% crepitations over lung base, CKD, elevated liver enzymes, low SPO2, and EF less than 30% predicted higher risk for mortality and re-hospitalization at one month. There were no differences attributable to sex, or type of heart failure. However, on logistic regression analysis, only very low EF (<30%) and prolonged hospital stay were found to be significant factors. These findings need to be interpreted cautiously since our sample size was very small.

We analyzed the benefits of GDMT in preventing cardiovascular death and HHF in patients with HFrEF. Mortality and HHF consistently remained lower in patients who were initiated on either all three drugs or at least two drugs of GDMT compared to those who were initiated on only one or none (p value = 0.016). The composite of mortality and HHF rate was significantly higher (44%) in those who received none or only one of the drugs, while it was substantially lower (16%) in those who received at least 2 or more.

Strengths and Limitations

Our study stands out as one of the very few single-center registries on heart failure in India. We believe that such single center studies can aid in identifying regional variations in clinical practice, eventually leading to national registries on heart failure management. We had excellent follow up and the study has highlighted the high re-hospitalization rate in HF. The major limitation of the study is the small sample size and hence our findings may not represent the true picture of HF management in the region. One month follow up is probably not sufficient to assess the impact of management strategies in heart failure. We did not record drug doses which could show challenges in achieving maximum tolerated dose of proven therapies. Lastly, SGLT2 inhibitors, which are advocated in the new guidelines are not used in this population and ARNI is prescribed very rarely.

Conclusions

Our study had a higher proportion of females and elderly population, shorter hospital stays, and a greater usage of GDMT at discharge and one-month follow-up.

Patients hospitalized with HF in our study are mostly elderly, equally distributed among males and females and have a high prevalence of IHD. The prevalence of HFpEF was noted to be higher in females with a relatively higher prevalence of HTHD, which was higher as compared to other HF studies form India. Additionally, a longer in-hospital stay during the initial admission predicted mortality and one month hospitalization as compared to other reports. An LVEF < 30% was identified as an independent predictor of mortality and rehospitalization for HF.

Almost half of the patients of HFrEF received guideline directed medical therapy and it was associated with a

lower mortality and rehospitalization for HF. The study shows that all patients admitted with HFrEF, should be started on GDMT with all three drugs (ACEI/ARB/ARNI, BB, MRA) at the earliest unless contraindicated, to prevent early rehospitalization and HF mortality.

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