Original Article

Acute decompensated heart failure in a North Indian community hospital: Demographics, clinical characteristics, comorbidities and adherence to therapy

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ABSTRACT

Background: Acute decompensated heart failure (ADHF) is a growing public health problem in the community. Limited and often contradictory data are available from small studies published from India. Objective of this study was to report clinical characteristics, outcome, and discharge treatment strategies of these patients from a single community hospital.

Methods: In this observational prospective study from a multispeciality community hospital from North India, data were collected to include demographics, clinical characteristics, management strategies, and prognosis in 428 patients with ADHF admitted for more than two consecutive years (January 2017 through December 2018).

Results: The study included 428 patients (mean age 61 ± 14 years) of whom 59% were male. ADHF with reduced left ventricular ejection fraction (HFrEF) was present in 77% subjects; Preserved (≥50%) and midrange ejection fraction (41−49%) with ADHF was observed in 12% and 11% patients, respectively. Ischemic etiology was noticed in 69% of the population. Prior myocardial revascularisation was observed in 47% of all and in 71% of those with ischemic heart disease. Major comorbidities included type 2 diabetes mellitus (60.7%), arterial hypertension (51%), anemia (54%), chronic kidney disease (29%), atrial fibrillation (16%), and hypothyroidism (9%). Mean hospital stay was 4.5 ± 3.2 days (inter-quartile range: 2−9 days). In-hospital mortality was 8.4% (36 patients) and there were additional 17% deaths over 6 months after discharge. At-discharge medication in those with HFrEF included anti−renin−angiotensin agents (57%), beta-adrenergic receptor blocking agents in 53%, mineralocorticoid receptor antagonists in 34%, ivabradine in 21%, and digoxin in 5%. Angiotensin−neprilysin inhibitor was prescribed to 21% patients at discharge. Ferric carboxymaltose use was in 7.5% of all despite a high prevalence of anemia (54%). Vaccination status at discharge was not available in majority.

Conclusion: The commonest cause of ADHF presenting to this community hospital was HFrEF of ischemic etiology. It is associated with significant in-hospital mortality. There is substantial under-use of guideline-recommended chronic heart failure therapies at hospital discharge. These data provide useful information which can be used to improve patient care and formulate future strategies for management of ADHF.

Acute decompensated heart failure (ADHF) is a syndrome of sudden worsening of pre-existing heart failure (HF) or new onset HF with cardiorespiratory compromise. It is the commonest reason for hospitalization in the elderly in the Western world.[1] Limited data are available about HF or ADHF in India.[2–7] Epidemiology of ADHF has definitely changed from 1949 when Vakil first described demographics of these patients in a study of 1281 subjects admitted with the diagnosis of HF.[2] Hypertension−coronary artery disease was the main etiology (31%), followed by rheumatic heart disease (29%), syphilis (12%), and pulmonary causes (8%). In a small study of 125 patients of ADHF admitted in a public hospital in Nagpur,[3] rheumatic heart disease was the dominant etiology (52.8%) followed by hypertension−coronary artery disease (28%). In a contemporary study of 90 patients with ADHF reported from a tertiary referral center from North India,[5] ischemic etiology accounted for 54% cases and rheumatic heart disease in 10.8% and

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in-hospital mortality of 31%. In the largest registry of ADHF reported from Kerala, 72% of 1205 patients (mean age 61 years) had underlying ischemic heart disease and an in-hospital mortality of 8.5%.[6] In a National Heart Failure registry initiated by the Indian College of Cardiology, ischemic etiology accounted for 58% of 1005 patients with a mean age of 61 years and in-hospital mortality of 8.8%.[7] Significant observation of both registries is the high prevalence of HF with reduced ejection fraction (74% and 72%, respectively). Both these registries are from South India with very limited data from the North. We initiated the present study to understand demographic and clinical characteristics, underlying comorbidities, hospital outcome and treatment strategies in a typical North Indian hospital.

1. Methods

1.1. Design of the study

We prospectively enrolled consecutive patients with ADHF admitted to our cardiology unit in the hospital-based observational and prospective registry during a two-year study period (January 2017 through December 2018). Inclusion criteria were acute cardiorespiratory compromise of cardiac origin with elevated natriuretic peptides. Patients were enrolled if they were hospitalized for episodes of new or worsening HF without any differentiation between the two types of acute HF. The patients with primary diagnosis of acute coronary syndrome, shock, pulmonary embolism, septicemia, infective endocarditis, acute stroke, known rheumatic heart disease, congenital heart disease, known prior cor pulmonale and dengue fever were excluded from this registry. Consecutive patients were enrolled. Patients who were <18 years old and who refused consent were excluded. Entry in the study was not contingent on the use of any particular therapeutic agent or treatment regimen. Patients were followed up for 6 months after discharge for major adverse events, including death and rehospitalization by telephonic contacts. The protocol was approved by the institutional ethics committee.

1.2. Definitions

In the presence of any documented history of myocardial infarction, unstable angina or stable angina supported by prior coronary revascularisation or significant obstructive coronary artery disease, ischemic heart disease was considered the primary etiology. Hypertension was considered as causative if it was sustained and treated for before admission, uncontrolled ($\geq$140/90 mmHg), and had evidence of other complications such as left ventricular hypertrophy on electrocardiography, and there was no prior myocardial infarction. Dilated cardiomyopathy was considered the main etiology if symptoms coexisted with left ventricular systolic dysfunction, in the absence of ischemic heart disease, hypertension, and other possible causes. Diabetes was considered a comorbidity if the patients were previously diagnosed with a label of diabetes and were on antidiabetic drugs. In-hospital hyperglycemia alone or glycated hemoglobin obtained during hospital stay was not considered for definition of diabetes. Chronic kidney disease was defined as estimated glomerular filtration rate (by MDRD formula) of <60 ml/min/1.73 M^2 at discharge time. Anemia was defined by hemoglobin level <12 gm% in females and <13 gm% in males. ADHF was categorized as heart failure with reduced ejection fraction (HFrEF) if echocardiographic left ventricular ejection fraction (LVEF) was $\leq$40% on admission. The patients with LVEF $\geq$50% with evidence of cardiac structural or functional abnormality and elevated natriuretic peptides (brain natriuretic peptide (BNP) > 100 pg/mL or Nt-Pro BNP > 300 pg/mL) were labeled HF

with preserved ejection fraction (HFpEF). In the remaining wherein LVEF was 41—49%, HFmrEF (midrange LVEF with HF) was considered as the subtype.

1.3. Data collection

Data were directly collected from medical records for all clinical variables related to HF and treatment, including clinical variables such as functional class, metabolic parameters, treatment details, and course in hospital. Follow-up data were collected during scheduled outpatient department visits in the HF clinic. We contacted patients who did not come for follow-up in the HF clinic via telephone to ascertain medication use, rehospitalization, and death status. For each case enrolled, data collected include[1] demography[2] cause of HF[3], precipitating factors[4], comorbidities[5], complications.[6] Hospital outcome[7] discharge medications[8] and 6-month post-discharge follow-up.

1.4. Statistical analysis

Data are reported as mean ($\pm$standard deviation) for continuous variables and proportions (percentages) of patients for categorical variables. Tests of differences in treatment and patient characteristics between the two cohorts were performed using Student's t-tests for continuous variables and the χ^2 or Fisher's exact tests for categorical variables. A p value of <0.05 was considered significant.

1.5. Observations

A total of 428 patients with first admission of ADHF (age$\geq$ 18 years) whose diagnosis was adjudicated by clinical criteria, electrocardiography, echocardiography, and natriuretic peptides were included in this study over a period of two years (January 2017 through December 2018). There were 251 male (58.6%) and 177 female (41.4%) patients with a mean age of 61 $\pm$ 14 years (range 27—90 years). The patients were treated by individual physicians with no specific protocol. As this was an observational study, no attempt was made to change the prevailing practice and no guidelines were prescribed. All patients were treated by intravenous diuretics and inotropes were used in 112 (24.8%) patients. Mean hospital stay was 4.5 $\pm$ 3.2 days (range: 2—9 days). Thirty-six patients (8.5%) died during the hospital stay (male 23, female 13, mean age: 71 $\pm$ 13 years). Mean LVEF of the entire population was 33 $\pm$ 12% (range: 15—62, Fig. 1). Quantitative ejection fraction data were not available in 5 patients. Mean estimated glomerular filtration rate was 53 $\pm$ 27.8 mL/min/1.73 M^2 (range: 7—132, $n = 422$, Fig. 2). Mean hemoglobin concentration was 11.6 $\pm$ 2.6 Gm % (range: 3.9—15.3 Gm). Ischemic etiology was observed in 294 patients (68.9%), nonischemic ADHF was seen in 113 patients (26.4%), and nonrheumatic primary valvular heart disease (largely degenerative aortic valve stenosis or mitral regurgitation) was noted in 21 (4.91%) patients (Fig. 3). Comorbidities other than ischemic heart disease recorded were type 2 diabetes mellitus in 260 patients (60.7%), arterial hypertension in 232 (54%), chronic kidney disease in 122 (29%), atrial fibrillation in 71 (16%), and hypothyroidism in 39 (9%). Atrial fibrillation was twice more frequent in females (23% vs 12%, $p < 0.05$, Table 1), whereas hypothyroidism was four times more common in females (4% vs 16%, $p < 0.05$). Tobacco use was reported in 54 men (21%) and none of the women. Left bundle branch block was observed in 58 patients (11.4%), whereas right bundle branch block was seen in 18 patients (4%). Implantable converter-defibrillators with or without resynchronization therapy were previously implanted in 43 (10%) patients. One hundred forty-three (33.5%) patients had prior percutaneous coronary interventions and 61 (14%) had prior bypass surgery. Of those
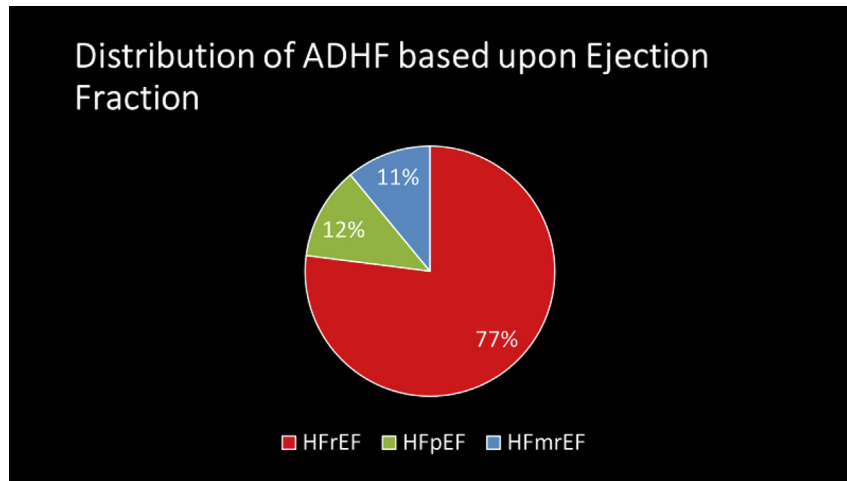
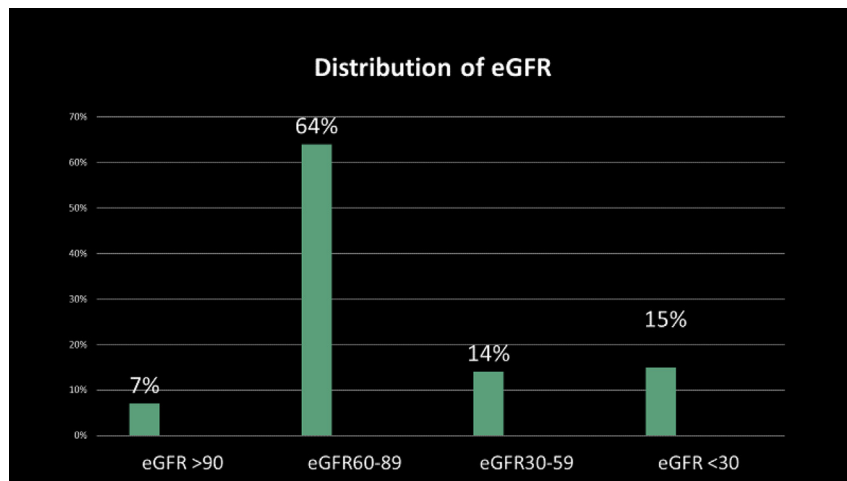**Fig. 1.** Frequency of ADHF by left ventricular ejection fraction. ADHF, acute decompensated heart failure.

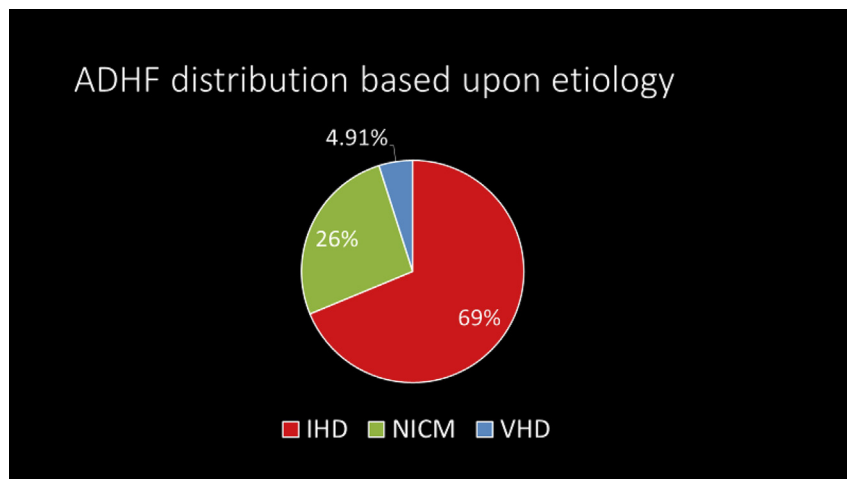**Fig. 2.** Estimated glomerular filtration rate in the entire cohort.

Fig. 3. ADHF frequency based upon etiological diagnosis. IHD, ischemic heart disease, NICM, nonischemic cardiomyopathy; VHD, primary valvular heart disease; ADHF, acute decompensated heart failure.

Table 1
Comorbidity analysis.

Risk factor	Number	%
Diabetes mellitus	260	60.7%
Hypertension	232	54%
CKD	122	29%
Atrial fibrillation	71	16%
Hypothyroidism	39	9%

CKD, chronic kidney disease.

with ischemic heart disease, 71% had prior coronary revascularisation. Anemia was detected in 231 patients (54%) but intravenous ferric carboxymaltose was used in 31 (7%) patients before discharge. However iron studies were performed in only 28 patients. Specific pharmacotherapy was initiated in patients after stabilization but data about this were collected at or just before discharge. At discharge, anti−renin−angiotensin−aldosterone system (anti−RAAS) drugs were prescribed to 186 of 326 HFrEF patients (57%); angiotensin−neprilysin inhibitor was the commonest discharge anti-RAAS agent ($n = 67$, 21%) followed by angiotensin-receptor blocking agents in 65 (19.9%) and angiotensin-converting enzyme inhibitors in 54 (15.6%) patients. Beta-receptor blocking drugs were prescribed to 175 of 326 patients (53.7%). Mineralocorticoid receptor antagonists (spironolactone or eplerenone) were received by 111 (34%) patients with HFrEF and 41 (41%) of 97 patients with HFpEF and HFmrEF. Ivabradine at discharge was advised to 69 (20.86%) patients with HFrEF (Table 2). Digoxin use at discharge was in 20 patients (4.91%). Optimal guidelines-recommended therapy that included anti-RAAS agents, beta-blockers, and mineralocorticoid receptor antagonists was prescribed to 108 (33%) patients. three hundred ninety-two patients were discharged alive of which 67 (17%) died by six months. However, detailed longitudinal records are not available. Amongst those who died in the hospital (ischemic etiology in 83%, non-ischemic 17%), only seven (17%) had documented arrhythmic deaths. Postdischarge medication use was slightly altered with an additional 4% patients prescribed angiotensin−neprilysin inhibitor and an additional 19% patients were prescribed mineralocorticoid receptor antagonists. Frequency of beta-adrenergic receptor blockers use was unchanged.

2. Discussion

Given the unmet needs concerning acute HF in India, prospective observational data are important as these provide real-world information on epidemiology of this clinical syndrome. Regional and ethnical differences in the epidemiology, clinical characteristics, and outcome of patients hospitalized for ADHF require attention. Gaps in knowledge, clinical practice, physician's attitude, training and preparedness of the health-care systems can be assessed at regional levels. This analysis of 428 consecutive patients with ADHF from a single community hospital of north India represents the largest prospective contemporary database. The study

Table 2
Guidelines-recommended drug therapy at discharge.

Therapeutic agent	Number	%
Anti-RAAS	186	57% (HFrEF)
Beta-blockers	175	53% (HFrEF)
MRA	111	(34%)
Ivabradine	69	20.9% (HFrEF)
Digoxin	20	4.91%

HFrEF, heart failure with reduced ejection fraction; anti−RAAS, anti-−renin−angiotensin−aldosterone system.

confirms previous observations of two multicentric studies from South India[6,7] and provides new insights into the current management strategies, lacunae and epidemiology. Our study reiterates that HFrEF of ischemic etiology (77%) is the dominant type of ADHF in north India (the other phenotypes being uncommon), the patients are relatively younger and type 2 diabetes mellitus is the major associated comorbidity. Higher CKD prevalence despite younger age may be partly related to higher prevalence of diabetes mellitus. Our data provide additional demographics, clinical characteristics, and outcome information. There is growing trend toward use of newer pharmacotherapy at discharge (particularly ARNI) although guidelines-recommended therapy is still underused. Inspite of younger age of our patients, in-hospital mortality is more than twice of that reported from the western world.[9]

Compared with Trivandrum Heart Failure registry[6] from Kerala which had design similar to our study but was multicentric, we noticed striking similarities and some differences. Age range, comorbidities, etiology, and in-hospital mortality were similar in both studies. However, our study had more female patients, shorter hospital stay, greater utilization of myocardial revascularisation procedures, more device implantations, and more often guidelines-mandated therapy at discharge. These differences probably represent urban location of this hospital and also temporally distinct periods of the studies. There is also great similarity between our study and preliminary results of the Indian College of Cardiology National Heart Failure registry of 1005 patients.[7] A recent large single-center study of ambulatory HFrEF from North India shows similar age range, risk factors and etiology but much lower female patient representation, low incidence of atrial fibrillation and better renal function despite similar LVEF.[8] With regard to gender representation, our study is closer to ADHERE,[9] ESC registry,[10] Japanese ATTEND registry[11] and Korean ADHF registry.[12] However, it is noteworthy that patients admitted with HF do not have significant differences in South and North India despite several differing health-care system, social, cultural, and educational aspects.[6−8]

The AFAR study[5] from India is unique in many respects. It is an acute HF registry of 90 patients from a tertiary medical center. The study had all the patients with ADHF-HFrEF but with a very high in-hospital mortality of 31% and further 26% mortality 6 months after discharge in a relatively younger patient population who did not have high comorbidity burden. These patients probably represent a distinct phenotype of acutely sick inotrope-requiring patients who prefer to go to a tertiary care center expecting benefit from mechanical circulatory devices or listing for heart transplantation. The data reported in this study are very different compared to that from this study and those from the Trivandrum Heart failure registry and National Heart failure registry.[7,8] It is noteworthy that despite very sick population, frequency of guideline-mandated discharge medications was high. In a recent small study of ADHF from the Western India, HFpEF was present in >40% cases and overall in-hospital mortality was 21%.[13]

Prevalence of HF in India is unknown. Based upon the global prevalence of HF in 2% of adult population, some authors have estimated that India has about 20 million patients with HF.[14,15] ADHF is a sentinel event in vulnerable phase with important prognostic implications. Presuming an ADHF incidence of 20% amongst those who have HF, nearly four million patients every year seek readmission or have de novo ADHF.[16] This presumption does not take in account the issue of health-care access in the community which is heterogenous and variable throughout the Indian landscape. Its prognosis is dismal with average survival less than two years even in more developed economies.[17] Regardless of ejection fraction, ADHF is related to progressive rise in cardiac filling pressures owing to aggravating or precipitating factors. The

concerns during ADHF should include thorough decongestion and stabilization of fluid balance, identification and management of exacerbating factors, and titration of neurohormonal antagonists for long-term benefit. It is unlikely that all patients at discharge would be on neurohumoral modulator therapy because of concerns regarding hypotension, worsening renal dysfunction, and hemodynamic instability. A figure of 53—57% seen in this study may be suboptimal but is quite realistic with a scope for upward improvement. Simultaneous attention to optimizing the management of comorbid medical illness, including diabetes, anemia, chronic kidney disease, atrial fibrillation, and hypothyroidism should also get priority to reduce noncardiovascular rehospitalizations. ADHF as shown in this study is truly a multidisciplinary syndrome needing attention from several specialists. Observations of this study underscore the need for a more comprehensive approach in patients with ADHF that can coordinate care of these aspects for preventing long-term morbidity and mortality.

3. Limitations

This prospective database is not a clinical trial but an observational registry. As such, there are no treatment requirements, randomization, or longitudinal follow-up. Patients were entered in the registry only once on first admission and subsequent admissions were not included. Hence impact of readmissions was not studied. After-discharge patient status was not be assessed thoroughly in all the patients although telephonic status of live or dead and medication adherence was obtained. The data are observational, and the analysis is largely at discharge. In addition, the results may be influenced by assessment and treatment regimens that are not standardized and vary by physicians's choices. The data presented apply to those patients with on-admission measurement of LVEF. Lack of precise universal definition of ADHF makes this study open to criticism. However, the aim of this 2-year prospective study was to analyze the trends in clinical practice using this broad definition of ADHF.

Conflict of interest

The authors have none to declare.

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