Original Article

Heart Failure Etiologies, Management and Short-term Outcomes in Hospitalized and Clinic-Based Patients in India

Rajeev Gupta[1], Vaibhav Grover[2], Krishna kumar Sharma[3], Bhawani S Mishra[4], Sanjeeb Roy[5], Ajeet Bana[6]

[1]Chairman Academic Research Development Unit, Rajasthan University of Health Sciences, Jaipur, [2,3,4]Research fellow, [5]Senior Consultant, Cardiology , [6]Chairman CTVS Cardiac Surgery Fortis Escorts Hospital, Jaipur, Rajasthan, India

ABSTRACT

Introduction: Heart failure epidemiology has been very poorly studied in India.There are only limited studies that have evaluated etiologies and outcomes. The aim of this study was to determine etiologies and management of heart failure in hospital and clinic-based patients.

Methodology: Successive patients presenting to a tertiary care hospital with acute decompensated heart failure (ADHF, n=102) and stable heart failure (SHF, n=179) were enrolled. Etiology of heart failure was diagnosed using clinical examination and echocardiography. Both the groups were followed for 90 days. Descriptive statistics are presented.

Results: Etiologies of heart failure in ADHF v/s SHF patients, respectively, was coronary heart disease 50.0 v/s 53.6%, hypertension 27.4 v/s 15.1%, dilated cardiomyopathy 16.7 v/s 7.3%, rheumatic heart disease 4.9 v/s 14.0%, and hypertrophic cardiomyopathy 1.0 v/s 7.3%. Heart failure with normal ejection fraction was in 23 ADHF (22.5%) and 2 SHF (1.1%) patients. In-hospital treatments included diuretics, nitrates, angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), mineralocorticoid receptor antagonists (MRA), digoxin, anticoagulants, vasodilators and vasopressors. In-hospital mortality in ADHF was 10.3% (n=11). At discharge significantly greater numbers of patients with ADHF v/s SHF were on loop-diuretics (95.5 v/s 78.2%), antiplatelets (74.4 v/s 64.2%) and antiarrhythmics/ivabradine (23.3 v/s 6.1%) while lesser were on thiazides (1.5 v/s 9.5%), MRA (33.4 v/s 43.0%), ACEI/ARB (34.5 v/s 76.0%) and beta-blockers (33.4 v/s 45.8%) ($p<0.05$). 90-day mortality in ADHF was 26.7% (n=24) and in SHF 6.7% (n=7) ($p<0.01$).

Conclusions: Coronary and hypertensive heart diseases are important causes of heart failure at a tertiary-care hospital in India. Rheumatic heart disease and primary cardiomyopathies are also present in significant proportion. In ADHF patients there is low use of evidence-based therapies (ACEI/ARBs, beta-blockers) and short-term mortality is high.

INTRODUCTION

Heart failure is an emerging clinical and public health problem in India and many other low and lower-middle income countries.[1] Global Burden of Diseases Study (2010) reported that heart failure leads to more than 300,000 deaths annually.[2] Majority of these deaths occur in high-income countries where the prevalence of this condition is increasing.[3] This is due to a combination of population aging, better management of heart failure risk factors such as hypertension and better management of acute coronary events. In low- and lower-middle income countries decline in incidence of rheumatic fever and nutritional and infective causes of cardiomyopathies has led to greater proportion of heart failure with ischemic heart disease and hypertension.[1,4] Heart failure is classified as heart failure with reduced ejection fraction (HFrEF) and with normal or preserved ejection fraction (HFnEF).[5] Although there is a significant overlap in etiologies of these two conditions, the latter is characterized by greater frequency of acute presentation and inferior outcomes.[5] Minnesota Heart Study reported that while long-term mortality from HFrEF declined over a 20 year period from 1980 to 2000, that from HFnEF did not.[6] Heart failure has also been classified as acute

decompensated heart failure (ADHF) and chronic stable heart failure (SHF).[4,5] Although management strategies in the two groups are similar, etiologies and short-term prognosis could be different. ADHF is characterized by equal distribution of HFrEF and HFnEF while SHF is characterized by greater prevalence of HFrEF.[6,8] In heart failure patients, use of angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), mineralocorticoid receptor antagonists (MRA) and beta-blockers has significantly decreased mortality.[5,9]

Heart failure epidemiology has been very poorly studied in India.[1] There are only limited studies that have evaluated etiologies and outcomes.[10,11] Hospital-based studies in 1950s and 1960s reported a substantial burden of infective heart diseases including rheumatic heart disease (RHD) and syphilis.[12-15] A recent study from Orissa has reported continuing problem of RHD.[16] High mortality from heart failure has been reported from all over the world.[9] In India, a clinic-based prospective study in early 1980s reported 3-year mortality of more than 60%.[17] This was similar to international studies before advent of better therapies with ACEI and beta-blockers.[4] A significant burden of HFnEF was reported in hospitalized patients with heart failure.[18] Prevalence and types of heart failure in hospitalized or clinic-based patients with heart failure has not been well studied in recent years.[19] Therefore, to determine etiologies, management practices as well as in-hospital and 3-month outcomes in hospitalized and clinic-based patients with heart failure of diverse etiologies we performed a prospective registry.

METHODS

Successive patients presenting to a tertiary care non-government hospital with acute decompensated heart failure and presenting to an out-patient clinic with stable heart failure during a 12-month period from January to December 2012 were enrolled. Institutional research review board approved the study. Consent to use the patient data were obtained from hospital administration and informed consent was obtained from each patient. All the data were anonymized before analysis. Diagnosis of heart failure was confirmed by clinical examination and echocardiography in both groups of patients. For confirmation of the heart failure diagnosis in ADHF patients with chronic lung diseases or other comorbidities, serum NT-pro brain-related natriuretic peptide (NT-proBNP) levels were estimated. Details of in-hospital acute management in ADHF patients were obtained prospectively from the first day of admission to discharge. In clinic-based SHF patients, the details of diagnosis and medical treatment were recorded. Active follow-up of all patients was performed and details of medical treatment and outcomes were obtained at 90+15 days. We could obtain management details of all surviving individuals by either face-to-face interview or telephonically. Events were locally adjudicated.

Statistical analysis: Descriptive statistics are reported. Chi-square test was used to compare significance of inter-group differences, p values <0.05 were considered significant.

RESULTS

We enrolled 102 patients with acute decompensated heart failure (ADHF) and 179 with stable heart failure (SHF). There was significantly greater proportion of men (70.6%) than women (29.4%) in the study cohort. The mean age in ADHF was men 65.4±14.6 and women 64.0±16.0 and in SHF was men 71.0±9.0 and women 61.2±17.8 years. Etiologies and risk factors are reported in table 1.

Also, the application of health promoting bacteria for therapeutic purpose is one of the strongest emerging fields. Shift in the paradigm of the treatment from specific bacteria elimination to alteration of the bacterial ecology

Among hospitalized ADHF v/s clinic based SHF patients coronary heart disease was in 50.0 v/s 53.6%, hypertension in 27.4 v/s 15.1%, primary dilated cardiomyopathy in 16.7 v/s 7.3%, rheumatic heart disease in 4.9 v/s 14.0% and hypertrophic cardiomyopathy in 1.0 v/s 7.3%. Echocardiography was performed in all patients to confirm the diagnosis while serum NTproBNP estimation was performed in 12/102 hospitalized patients. Prevalence of HFnEF was 23 (22.5%) in ADHF and 2 (1.1%) in SHF.

Medical treatment among hospitalized patients with ADHF included oxygen therapy, injectable diuretics, nitrates, inotropes (digoxin, milrinone) and vasopressors (dopamine, dobutamine, noradrenaline) as required. Other drugs were diuretics (loop diuretics, thiazides), ACEI, ARB, MRA, beta-blockers, antiplatelet drugs, antiarrhythmics and Ivabradine. The in-hospital oral medications, discharge medications and 90-day medications in ADHF patients and baseline and 90-day medications in clinic-based SHF patients are shown in table 2.

Table 1: Clinical characteristics, etiological diagnoses and risk factors of heart failure in the study subjects

Etiology	Total (n=281)	Hospital based ADHF (n=102)	Clinical based SHF (n=179)	χ^2 test p value
Etiologies	151 (53.7)	51 (50.0)	100 (53.6)	0.343
Coronary heart disease	55 (19.6)	28 (27.4)	27 (15.1)	0.009
Hypertension	30 (10.7)	5 (4.9)	25 (14.0)	0.018
Rheumatic heart disease	30 (10.7)	17 (16.7)	13 (7.3)	0.014
Dilated cardiomyopathy	14 (4.9)	1 (1.0)	13 (7.3)	0.019
Hypertrophic cardiomyopathy	1 (0.4)	-	1 (0.6)	-
Pericardial diseases				
Risk factors	77 (27.4)	35 (34.3)	42 (23.4)	0.049
Smoking/tobacco use	16 (5.7)	6 (5.9)	10 (5.6)	0.110
Alcohol abuse	142 (50.5)	62 (60.8)	80 (44.7)	0.009
Hypertension	101 (35.9)	52 (51.0)	49 (27.4)	<0.001
Diabetes	39 (13.9)	19 (18.6)	20 (11.7)	0.081
COPD				

Numbers in parentheses are percent. ADHF- acute decompensated heart failure; SHF- stable heart failure

Table 2: Pharmacotherapy for in-hospital and clinic-based heart failure patients

Drug therapy	Hospital based ADHF In-hospital (n=102)	At-discharge (n=90)	At-90 days (n=66)	Clinic based SHF Clinic based (n=179)	At-90 days (n=97)
Loop diuretics	94(92.2)	86(95.5)	58(87.8)	140(78.2)	72(74.2)
Thiazide diuretics	8(7.8)	-	2(1.5)	17(9.5)	11(11.3)
Anti-aldosterone	34(33.3)	31(33.4)	11(16.7)	77(43.0)	47(48.5)
Digoxin	35(34.3)	26(28.9)	7(10.6)	57(31.8)	32(33.0)
ACE inhibitors	29(28.4)	27(30.0)	28(42.4)	63(35.2)	33(34.0)
ARBs	5(4.9)	4(4.4)	3(4.5)	73(40.8)	33(34.0)
ACE inhibitors/ARB	34(33.3)	31(34.4)	31(46.9)	136(76.0)	66(78.0)
Beta-blockers	34(33.3)	31(33.4)	32(48.5)	82(45.8)	44(45.4)
Dihydropyridine CCB	23(22.5)	18(20.0)	(9.1)	36(20.1)	19(19.6)
Nitrates	29(28.4)	29(32.2)	13(19.6)	55(30.7)	21(21.6)
Aspirin/clopidogrel	80(82.4)	67(74.4)	44(66.7)	115(64.2)	59(60.8)
Anticoagulants	55(53.9)	10(11.1)	2(3.0)	16(8.9)	14(14.4)
Antiarrthymic drugs, ivabradine	33(32.4)	21(23.3)	3(4.5)	11(6.1)	14(14.4)

ADHF acute decompensated heart failure; SHF stable heart failure; ACE angiotensin converting enzyme; ARB angiotensin receptor blocker; CCB calcium channel blockers

At discharge significantly greater numbers of patients with ADHF v/s SHF were on loop-diuretics (95.5 v/s 78.2%), antiplatelets (74.4 v/s 64.2%) and antiarrhythmics or ivabradine (23.3 v/s 6.1%) while lesser number of ADHF patients were on thiazides (1.5 v/s 9.5%), anti-aldosterone (33.4 v/s 43.0%), ACE inhibitors (30.0 v/s 35.2%), ARBs (4.5 v/s 40.8%), any ACE inhibitor or ARB (34.5 v/s 76.0%) and beta-blockers (33.4 v/s 45.8%) ($p<0.05$). Use of digoxin (28.9 v/s 31.8%), nitrates (32.2 v/s 30.7%) and anticoagulants (11.1 v/s 8.9%) was similar. At 90 days, treatment details of 90 ADHF and 97 SHF patients was available. At 90 days, in

ADHF v/s SHF patients there was a significantly greater use of diuretics, lower use of MRA, ACEI/ARB, digoxin, anticoagulants, antiarrhythmics and ivabradine and similar use of beta blockers (Table 2).

The in-hospital mortality in ADHF patients was 10.3% (11/102 patients). Causes of death included refractory hypotension, intractable dyspnea, arrhythmias or infection. At 90 days the mortality in ADHF was 26.7% (n=24) while in SHF was 6.7% (n=7) (p<0.01) (Figure 1).

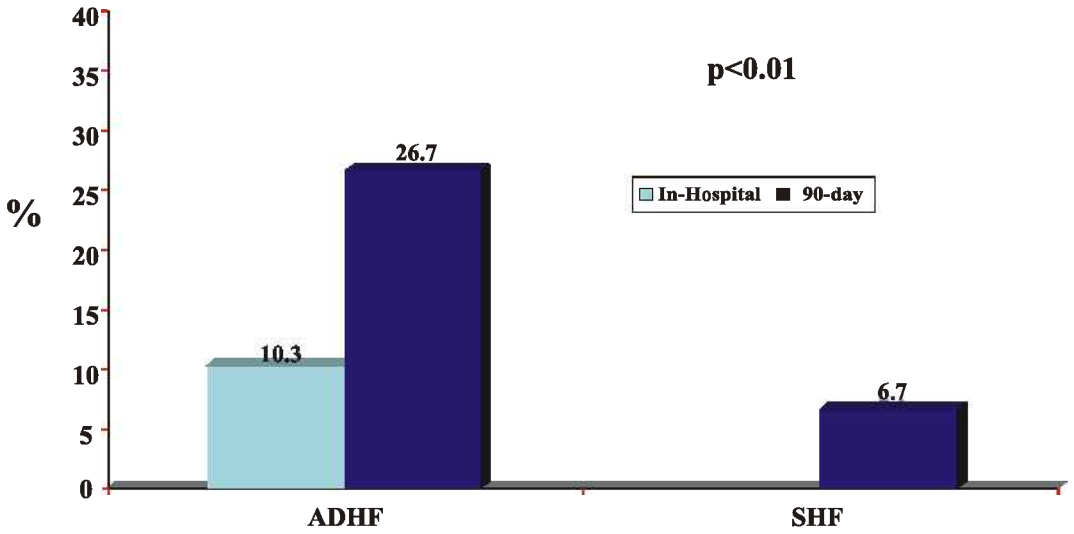

Figure 1: Six months cumulative mortality.

This registry shows that coronary heart disease and hypertension are the most important causes of heart failure and HFnEF is present in significant proportions in acute heart failure. Profile of stable patients with heart failure is different and apart from coronary and hypertensive heart disease, cardiomyopathy and rheumatic heart disease are also present in significant proportions. The study also shows a high short-term mortality of acute decompensated heart failure. Low use of evidence based heart failure therapy, especially RAAS (renin angiotensin aldosterone system) blockers and beta-blockers is observed in both ADHF and SHF patients. Previous studies from India have reported significant burden of RHD as a cause of heart failure. Epidemiological evidence suggests that this condition is still an important clinical problem,[16] although importance of RHD as a cause of heart failure in India needs larger studies in socioeconomically diverse hospitals. ' A pivotal study of heart failure in India in 1940s reported that important causes of heart failure were RHD, syphilitic heart disease and hypertension.[12] Sapru reviewed the hospital-based data on admissions and diagnoses in the country from 1940's to 1970's.[14] In 1950's and 1960's more than 50% of all admissions to government hospitals in the country were due to RHD and only a few were due to coronary and other hypertensive heart diseases. The trend changed in 1970s and coronary and hypertensive heart diseases have gained importance.[15] The present study is one of the first from the country that has reported that more than 70% patients with ADHF as well as clinic-based SHF patients have heart failure due to coronary and hypertensive heart diseases. Recently published Trivandrum Heart Failure Registry (n=1205) has also reported that 72% of cases of hospitalized heart failure had ischemic heart disease, 13% had dilated cardiomyopathy and 8% had rheumatic heart disease.[10] Similar findings are reported in the Indian cohort of INTERCHF study. These findings are also similar to studies from most parts of the world [4-8,18].[6-9, 21] Studies from high-income countries have reported that more than 90% of heart failure is due to coronary and hypertensive heart diseases.[22] A review reported that in US, while 62% of 43,444 patients had ischemic heart disease as cause of heart failure, hypertension was present in half of the rest.[23] These findings are similar to our study where hypertensive heart disease is an important cause of heart failure (Table 1). High prevalence of HFnEF in the hospitalized ADHF patients in the present study is similar to the high-income countries.[7] However, our data are obtained from a non-government private hospital and may not be regionally or nationally representative.

Low use of evidence based protective therapies such as ACEI/ARB, MRA and beta blockers in patients with ADHF is observed in the present study. Similar findings have been reported from ADHERE registry and NCDR-PINNACLE program in the US.[7,8] In ADHERE registry use of ACEI or ARB varied from 50-90% in different hospitals[7] while PINNACLE program[8] reported their use in 40-100%. In the present study, while the use of ACE inhibitors or ARBs is low in acutely decompensated patients with heart failure, there is a trend of progressive increase in their use so at the end of three months 47% of patients were receiving them. Use of ACEI/ARBs is very high (76%) in the stable CHF patient group in the present study and similar to studies from developed countries.[8] A slightly lower use could also be due to high presence of RHD in the stable heart failure patients where their use has not been recommended by guidelines.[5] Low use of beta-blockers in ADHF reflects greater number of elderly patients with multiple co-morbidities. However, their use increased over the three month period in this group from 33% to 48% (Table 2). Low use of beta-blockers in stable HF patients is an area of concern, however. Use of other drug classes such as nitrates, antiplatelet drugs, anticoagulants and antiarrhythmics is similar to previous reports.[7,8]

High mortality in ADHF patients is observed in the present study (Figure 1). This is similar to the previous reports from other countries[5] including the US[6] and Trivandrum Heart Failure Registry[10] in India. Mortality in SHF is very low and is much lower than previous reportsfrom India.[17] A larger study which includes patients with varying grades of ADHF is multiple hospitals of the country is required to truly assess heart failure outcomes in the country. The present data from a tertiary care hospital may suggest either a referral or selection bias.

Other limitations of the study include a small sample size, study limited to one hospital and a short follow-up duration.

CONCLUSION

This study shows that pattern of heart failure is changing in India with emergence of coronary heart disease and hypertension as important causes of ADHF as well as stable HF. Rheumatic heart disease continues to be an important issue, especially in clinics. This situation is similar to Latin America where a combination of degenerative and infective causes of heart failure is still prevalent.[21] There is a need for better management of these patients with greater use of evidence based therapies in these patients.[9,24] Epidemic of heart failure in low income countries needs population wide strategies for cardiovascular risk factor prevention (smoking/tobacco control, and promotion of healthy diet and physical activity) and individualized strategies for better risk factor control (hypertension, hypercholesterolemia and diabetes) to prevent the epidemic of coronary heart disease and hypertension. Continuing challenge of RHD needs focus on social determinants of health.

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Corresponding Author

Dr Rajeev Gupta, 16 Hospital Road, Jaipur, 302001, Rajasthan, India.

email: rajeevgg@gmail.com