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CURRENT TRENDS OF TREATMENT AND OUTCOME OF PATIENTS WITH HEART FAILURE AT TERTIARY CARE CENTRE: A HOSPITAL BASED STUDY IN EASTERN NEPAL

Sahadeb Prasad Dhungana[1*], Kunjang Sherpa[1], Prahlad Karki[2] and Sanjib Kumar Sharma[2]

[1]Senior Resident, [2]Professor, Division of Cardiology,
Department of Internal Medicine, B.P. Koirala Institute of Health Sciences, Dharan, Nepal.

*Corresponding Author: Dr. Sahadeb Prasad Dhungana

Senior Resident, Department of Internal Medicine, B.P. Koirala Institute of Health Sciences, Dharan, Nepal.

ABSTRACT

There is limited information on current trends of treatment and in-hospital outcome of patients with heart failure from Nepalese population. This is a prospective longitudinal study on 160 consecutive patients with New York Heart Association (NYHA) class III or IV symptoms of heart failure admitted from June 2015 to June 2016 at B.P. Koirala Institute of Health Sciences, Nepal. Mean age was 53.5 years. About one third of the cohort had hypertension and 20.6% had diabetes mellitus. Common precipitating factors for admission were non-compliance to drugs, atrial fibrillation, chest infection, uncontrolled hypertension, severe anemia, pregnancy and hypothyroidism. Ischemic cardiomyopathy, rheumatic heart disease, dilated cardiomyopathy, hypertensive heart disease, peripartum cardiomyopathy were common etiologies constituting 25%, 21.8%, 10.6%, 7.5%, 6.9% of cases respectively. At discharge, 86.2% patients were prescribed diuretics, 65.6% angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, 50% beta-blockers, 24.4% digoxin. Twenty patients died at hospital and they were of older age, had refractory symptoms, severe systolic dysfunction, had de novo heart failure due to acute coronary syndrome, severe rheumatic valvular heart disease. The mean length of hospital stay was 5.5 ± 3.5 days. Nineteen left against medical advice due to poor prognosis and socioeconomic reason. Fifteen patients were referred for valve replacement. Majority were discharged with improvement in symptoms and sleep quality. Heart failure is associated with significant morbidity and mortality because of associated comorbidities and underuse of proven therapy. Improvement in use of proven therapy, prompt diagnosis and treatment of precipitating factors are the key for better outcome.

KEYWORDS: Heart failure, In-hospital outcome, treatment.

INTRODUCTION

Heart failure is a common clinical syndrome caused by a variety of cardiac conditions that impairs the ability of the ventricle to fill with or eject blood[1] At least 50% of patients have systolic heart failure with a low ejection fraction.[2] The prevalence and severity of diastolic dysfunction increases with age and the development of diastolic dysfunction is associated with an increased risk of heart failure.[3] The factors that promote the fluid retention and precipitate overt heart failure are similar in patients with systolic and diastolic heart failure.[4]

The goals of treatment are the reduction in symptoms, a decrease in number of hospital admissions and prevention of premature death. The main stay of treatment is lifestyle modifications and pharmacologic therapy. Implantable devices and surgery may be required in selective patients. Angiotensin-converting enzyme inhibitors (ACEIs), beta-blockers(BBs) and spironolactone have been documented to improve clinical status and survival of patients with heart failure.[5] Diuretic therapy results in favorable effects on cardiac preload and afterload with improvement in LV performance.[6] Mortality and morbidity after symptomatic heart failure is high although variable rates have been reported which could be due to differences in disease severity and appropriate use of medical therapy.

The number of patients with heart failure is increasing in developing countries, as result of western type lifestyle, ageing of the population and still a high burden of rheumatic heart disease. Considering the paucity of data on heart failure in Nepal, this study was conducted to explore the current trends of medications prescribed for heart failure and its impact on outcome in hospital setting.

MATERIALS AND METHODS
This is a prospective longitudinal study. Total of 160 consecutive patients (age ≥16 years) with diagnosis of heart failure who were admitted from June 2015 to June 2016 at division of cardiology, internal medicine ward of B.P. Koirala Institute of Health Sciences (BPKIHS), Nepal were included in the study. The aim was to evaluate the current trends of treatment and its outcome in patients with heart failure. This also looked at the effect of treatment on quality of life [objective improvement in NYHA class and subject improvement in sleep quality] at the time of discharge and the impact of co-morbidities and other organs dysfunction on treatment pattern and outcome. All patients admitted with diagnosis of heart failure with reduced or preserved ejection fraction (NYHA functional class III/IV) based on Framingham Criteria and echocardiographic assessment were included..

Clinical variables noted on admission were age, gender, underlying etiology of heart failure, co-morbidities and medications used by the patient. In addition, improvement in symptoms reflected by change in NYHA class was noted to assess the quality of life at the time of discharge. Outcome of treatment was assessed by mortality during hospitalization, number of cases who left against medical advice, number of referrals to other center, improvement in NYHA class and sleep quality at the time of discharge and other organs dysfunction due to heart failure.

The serum electrolyte, hemoglobin, renal function tests, electrocardiographic and echocardiographic parameters were assessed. Ethical approval was obtained from institutional review committee (IRC) prior to starting the study. Collected data were entered in Microsoft excel 2007 and converted into SPSS 21 version. For descriptive statistics: percentage, mean, standard deviation, median, Interquartile range was calculated. Graphical and tabular presentation was made as necessary.

RESULTS
A total of 160 consecutive patients were included. This constituted 8.2 % of the total number of medical admissions during this period. There were 89 women (55.6%) and 71 men (44.4%). The mean age of the cohort was 53.5 (range 16-90) years. Fifty nine (36.9%) patients were current cigarette smokers and 20 (12.5%) had a significant history of alcohol consumption. About one third 47 (29.4%) of patients was being treated for hypertension. The overall prevalence of diabetes mellitus was 33 (20.6%). Among the underlying co-morbidities, 110 (68.8%) were anemic, 46 (28.7%) had underlying coronary artery disease, 14(8.8%) had chronic kidney disease, 21(13.1%) had acute kidney injury at the time of admission, 5(3.1%) were under treatment for chronic obstructive pulmonary disease. Clinical characteristics of patients with heart failure are summarized in Table 1.

Table 1: Clinical characteristics of patients with heart failure (n=160).

Age in year (mean and range)	53.5 (16-90)
Male	71 (44.4%)
Female	89 (55.6%)
Heart rate in bpm (mean and range)	94.15 (60-160)
Tachycardia (Heart rate >100 bpm)	49 (30.6%)
Blood pressure in mmHg(Mean and Range)	
Systolic	112.46 (60-210)
Diastolic	72 (40-100)
Presenting symptoms at admission	
Dyspnea (NYHA class) IV	124(77.5%)
III	36 (22.6%)
Palpitation	20 (12.5%)
Fatiguability	98 (61.2%)
Clinical signs	
Raised JVP	107 (66.9%)
Crackles	146 (91.3%)
Edema	125 (78.1%)
Risk factors and Co-morbidities	
Anemia	110 (68.8%),
Hypertension	47 (29.4%)
Type 2 diabetes mellitus	33 (20.6%)
Chronic kidney disease	14 (8.8%)
Coronary artery disease	46 (28.7%)
Smoking	59 (36.9%)
Alcohol consumption	20 (12.5%)
Chronic obstructive pulmonary disease	5 (3.1%)

The common precipitating factors for HF were progressive course of the disease 70 (43.7%), non-compliance with drugs 30 (18.7%), atrial fibrillation (AF) with fast ventricular rate 22(13.7%), chest infection 12 (7.5%), uncontrolled hypertension 10(6.25%), severe anemia 9(5.6%), pregnancy 6(3.75%) and hypothyroidism 4(2.5%). Of note, there was only 10(6.3%) case of acute myocardial infarction who presented with de novo heart failure. Among the abnormal ECG findings, 49(30.6%) had atril fibrillation, LV hypertrophy was observed in 40(25%) of patients, Electrocardiography and Echocardiography features of

patients with heart failure are shown in Table 5. Figure 1 shows the etiological risk factors for HF in the cohort. Ischemic cardiomyopathy, rheumatic heart disease, dilated cardiomyopathy, Peripartum cardiomyopathy, Hypertensive heart disease were the common risk factors for HF in the cohort constituting 40(25%), 35(21.8%), 17(10.6%), 11(6.9%), 12(7.5%) of cases respectively. Other causes of HF in the cohort included congenital heart diseases (6.25%), alcohol related cardiomyopathy (5%), pericardial diseases (3.1%), cor pulmonale (3.1%), sclerodegenerative aortic stenosis (2.5%), tachycardia induced cardiomyopathy (1.8%).
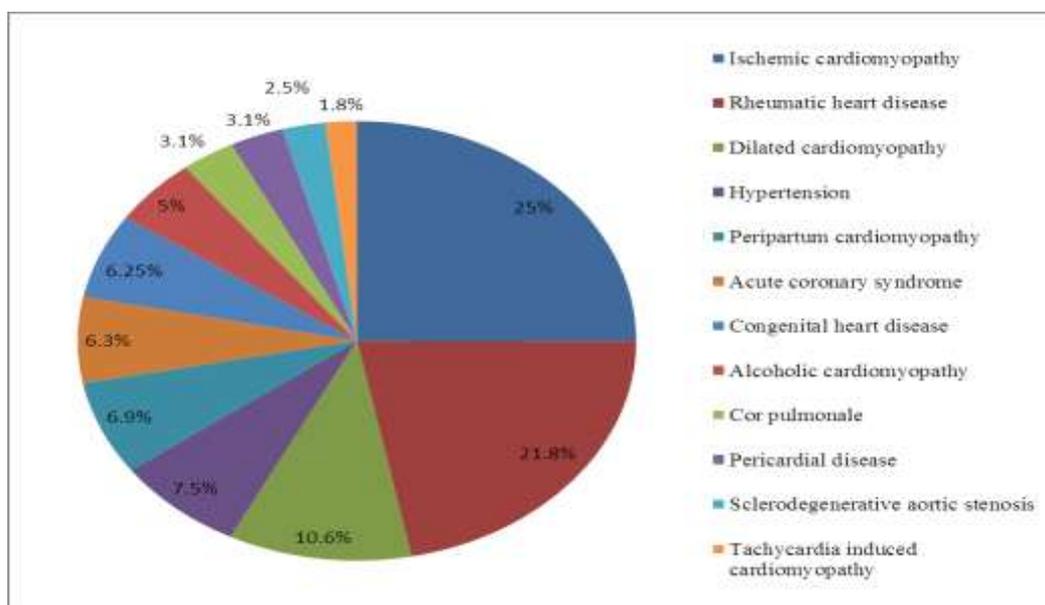

Figure 1: Etiologies of heart failure (n=160).

On admission, 137(85.6%), 78(48.7%), 21(13.1%), and 39(24.4%) patients were prescribed diuretic agents, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and digitalis, respectively. Inotropic

agents, antithrombotics (Warfarin, Aspirin), antiarrhythmic agent (Amiodarone), nitrates (intravenous glyceryl trinitrate) were prescribed for 45(28.1%), 78(48.7%), 8(5%), 5(3.1%) subjects respectively.

Table 2: Individual drugs used in patients with heart failure (n=160).

Drug class	Drug	No. of patients
Diuretics	Furosemide	96 (60%)
	Torsemide	38 (23.7%)
	Metolazone	3 (1.9%)
ACEI	Enalapril	43 (26.8%)
	Ramipril	23 (14.3%)
ARBs	Losartan	21(13.1%)
Beta blockers	Metoprolol	52 (32.5)
	Carvedilol	15 (9.3%)
	Bisoprolol	1 (0.6%)
Glycosides	Digoxin	39 (24.4%)
Aldosterone antagonist	Spironolactone	78 (48.7%)
Nitrates	NTG	5 (3.1%)
Inotropic agents	Dobutamine	23 (14.4%)
	Dopamine	18 (11.3%)
	Noradrenaline	4 (2.5%)
Antithrombotics	Warfarin	20 (12.5%)
	Aspirin	58 (36.3%)
Antiarrhythmics	Amiodarone	8(5%)

Table 3: Different drugs combination used in patients with heart failure (n=160).

Diuretics	29(18.1%)
Diuretics + ACEI/ARBs	51(31.8%)
Diuretics + BBs	26 (16.2%)
Diuretics + ACEI+BB	32 (20%)
Diuretics +ACEI+BB+AA	22(13.7%)

ACE: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor bloker,
BB: Beta blocker.

Table 4: Outcome of patients with heart failure (n=160).

Mean duration of hospital stay	5.5 ± 3.5 days
Improvement in NYHA class	121 (75.6%)
IV to I	11 (6.9%)
IV to II	81 (50.6%)
IV to III	29 (18.1%)
Quality of sleep (subjective)	
Improved	113(70.6%)
Status quo	35 (21.9%)
Died	20 (12.5%)
Left against medical advice	19 (11.9%)
Referred to other centre	15(9.4%)
Discharged with improvement	121(75.6%)
Organs dysfunction	
Acute kidney injury	21 (13.1%)
Hepatitis	12 (7.5%)
Stroke	5 (3.1%)
Pulmonary embolism	2 (1.2 %)
Electrolytes imbalance	
Hyponatremia	58(36.3%)
Hypernatremia	15(9.4%)
Hypokalemia	15(9.4%)
Hyperkalemia	17(10.6%)

Table 5: Electrographic and Echocardiographic findings of patients with heart failure (n=160).

Electrocardiogrphic findings		Echocardiographic findings	
Heart rate (bpm)		LVEF	
Normal (60-100)	111(69.3%)	Normal	40 (25%)
Tachycardia (>100)	49 (30.6%)	Reduced	120 (75%)
Rhythm		PASP	
Sinus	123(76.9%)	Normal	22(13.8%)
AF	37(23.1%)	Mild to moderate	115 (71.9%)
		Severe	23(14.4%)
RBBB	8(5%)	RV dysfunction	39 (24.4%)
LBBB	14(8.8%)	MR	84(52.5%)
LVH	40(25%)	LVDD	132 (82.5%)

HR: Heart rate, AF: Atrial fibrillation, RBBB: right bundle branch block, LBBB: Left bundle branch block, LVH: Left ventricular hypertrophy, LVEF: Left ventricular ejection fraction, PASP: Pulmonary artery systolic pressure, RV: Right ventricle, MR: Mitral regurgitation, LVDD: Left ventricular diastolic dysfunction.

At the time of discharge, 138 patients (86.2%) were prescribed diuretic agents, 105(65.6%) angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, 39(24.4%) digoxin, 80(50%) beta-blockers. Ancillary medications used during the course of admission were aspirin in 58(36.3%), Warfarin in 20 (12.5%), calcium channel blockers (Amlodipine or Diltiazem) in 22 (13.7%), antihyperglycemic agents in 33(20.6%), thiazide diuretic agents in 7(4.3%), and amiodarone in 5 (3.1%). Combination of drugs prescribed at the time of discharge is shown in Table 3.

In-hospital outcomes
In hospital outcome of patients is depicted in Table 4. Twenty patients died during the course of admission. Causes of death were progressive pump failure 9 (45%), refractory pulmonary edema due to severe rheumatic mitral valve diseases 7(35%) and sudden death possibly

due to arrhythmia 4 (20%). Those who died were of older age, had refractory NYHA class IV symptoms, severe LV systolic dysfunction, had de novo heart failure due to ACS, severe rheumatic valvular heart disease. The mean overall length of hospital stay was 5.5 ± 3.5 days (range 3 -12 days). Nineteen (11.9%) left against medical advice due to poor prognosis and socioeconomic reason. Fifteen (9.4%) of patients were referred to other tertiary centre for valve replacement who had symptomatic severe rheumatic mitral and aortic valve diseases. Majority of patients 121(75.6%) were discharged with improvement in symptoms in terms of NYHA class. With regard to sleep quality, 113(70.6%) had subjective improvement without need for extra pillows during sleep.

DISCUSSION
About 1 to 2% of the population in developed countries suffers from heart failure and its prevalence rises with age.[2] In our study, 45% of patients were of age more than 60 years. At least 50% patients have systolic dysfunction[2] and one third of all patients have diastolic dysfunction with normal ejection fraction.[7] In our cohort, majority of patients (75%) had systolic dysfunction and 25% had heart failure with preserved ejection fraction probably due to underdiagnosis of diastolic heart failure. Coronary heart disease (CHD) is the most common cause of heart failure in developed countries. CHD may be contributing factor in patients with heart failure of other causes[8] and sometimes it may be overlooked. A retrospective analysis by Dubey et al[9] in Nepal found that CHD accounted for 36.5% patients with heart failure. In our study, 31.3% of patients had CHD either presenting as ischemic cardiomyopathy or acute coronary syndrome with pump failure. In developing countries, rheumatic heart disease is a common problem.[10] Likewise, 21.8% of our patients had severe rheumatic valvular lesion in the form of mitral stenosis or regurgitation followed by aortic stenosis or regurgitation. They presented at earlier age compared to other causes of heart failure. Dilated cardiomyopathy (DCM) is characterized by dilation and impaired contraction of ventricles and may or may not develop overt heart failure.[11] All our patients (10.6%) of DCM had severe biventricular systolic dysfunction. Peripartum cardiomyopathy (PPCMP) is a rare that occurs in late pregnancy and the early postpartum period and it needs to rule out the other causes of cardiomyopathy.[12] In our study, 6.9% of patients were labelled as PPCMP based on the temporal relationship of LV dysfunction with peripartum period. Although hypertension is a common problem, it is rarely a sole cause of cardiac damage leading to heart failure.[13] About 7.5 % of our patients had severe uncontrolled hypertension presenting with features of heart failure at admission and majority had normal systolic function. Sclero-degenerative disease of the aortic valve is the most common valvular cause of heart failure in the developed world.[14] In contrary, only 2.5% of our patient had sclerodegenerative severe aortic stenosis leading to

severe systolic dysfunction. Cardiomyopathy may occur with chronic tachycardias with ventricular rates of 130 to 200 beats/ minute and the rate of tachycardia may correlate with the degree of left ventricular dysfunction.[15] of three patients with chronic tachycardia in our study, two had incessant ectopic atrial tachycardia and one had right ventricular outflow tract tachycardia as the cause of LV dysfunction.

The heart failure symptoms and signs are nonspecific and must be evaluated in the context of clinical circumstances.[16] In our study, 61% patients complained of easy fatiguability, 78% had leg edema, 67% had raised JVP and 91% had basal lungs crackles.

The goals of heart failure therapy are reduction of morbidity and mortality. Diuretic therapy results in favorable effects on both cardiac preload and afterload with improvement in LV performance.[16] Eighty six percent of our patients were prescribed diuretics at the time of admission except those who had hypotension or cardiogenic shock requiring inotropic support. Majority received loop diuretics (Furosemeide or Torsemide in combination with Spironolactone). Angiotensin-converting enzyme inhibitors, beta-blockers, and spironolactone have been documented to improve clinical status and survival of patients with heart failure.[5] The proven effects of ACE inhibition to prolong survival in NYHA class II through IV patients support their use as first-line agents in the management of chronic heart failure.[18,19] Only 65.6% of our patients were prescribed ACEI or ARBs at the time of discharge owing to lower range of blood pressure or fear of worsening renal function. Similarly, only 50% of patients were started on beta blockers due to fear of decompensation or failure to achieve euvolemic state. We noted underuse of disease-modifying drugs such as beta-blockers, ACEI or ARBs and no prescription of combined hydralazine and isosorbide probably due to unavailability of this drug in our country. Although the use of BBs, ACEIs or ARBs have improved than previous years as study done in Kathmandu valley by Baskota et al[20] in 2006 showed even more restricted use of these therapies. In contrary, the use of spironolactone was more liberal. No good evidence are identified for the benefit of diuretics, ACE inhibitors,[21] beta blockers, aldosterone antagonists or calcium antagonists in patients with preserved ejection fraction. Diuretics are often used to reduce and prevent fluid overload. Similarly, all our patients were prescribed loop diuretic agents along with antihypertensive drugs.

Mortality and morbidity after symptomatic heart failure is very high although variable rates have been reported.[22] Patients with heart failure report high levels of frustration with progressive loss of functional capacity, social isolation and the stresses of monitoring a complex medical regimen. Though NYHA functional class is the most dominant predictor among somatic variables, the major determinants of reduced quality of

life are unknown.[23] Late presentations was common in our population with all patients presented with NYHA class III or IV symptoms probably due lack of awareness or easy approach to health care facility. Overall mortality in our study was 12.5% compared with 3.8% to 6.7% in high-income countries.[24, 25] Causes of death were progressive pump failure, refractory pulmonary edema due to severe rheumatic mitral valve diseases, and sudden death possibly due to arrhythmia. Those who died were of older age, had refractory NYHA class IV symptoms, severe LV systolic dysfunction, had de novo heart failure due to ACS, severe rheumatic valvular heart disease. The mean overall length of hospital stay was 5.5 ± 3.5 days (range 3 to 12 days) which is similar to lengths of stay reported in high-income countries (4 to 7 days).[24] Nineteen (11.9%) left against medical advice due to poor prognosis and socioeconomic reason. Fifteen (9.4%) of patients were referred to other tertiary centre for valve replacement who had symptomatic severe rheumatic mitral and aortic valve diseases. Majority of patients 121(75.6%) were discharged with improvement in symptoms in terms of NYHA class. With regard to sleep quality, 70.6% had subjective improvement without need for extra pillows during sleep. Some of the possible reasons for underuse of standard medications for HF in our cohort may include poor awareness of these therapies for HF among physicians, high cost of multidrugs therapy and the late presentation and severity of HF in our subjects which may prohibit the use of all proven therapies. Many physicians are still not comfortable commencing beta-blockers or combined hydralazine and isosorbide in severely ill patients with HF. There are some limitations in this study. This was hospital based study in limited number of patients with short in-hospital follow up and represents severely symptomatic cohort only. Diagnosis of ischemic heart disease was based on history, risk factors, wall motion abnormality in echocardiography and may not be perfect because lack of coronary angiography in all cases. Assessment of sleep quality was subjective and no objective tool was used.

Heart failure is a common problem and associated with significant morbidity and mortality because of associated various comorbidities and underuse of proven therapy like beta blockers, ACE inhibitors and ARBs. Improved compliance to drugs, prevention of coronary and rheumatic heart disease, prompt diagnosis and treatment of precipitation factors are the key for better outcome. Special focus should be given to minimize the risk factors for coronary artery disease and prevention of rheumatic heart disease which is still a major health problem in Nepal.

CONFLICT OF INTEREST: No.

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