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Original Research Article

Clinical Profile and Short-term Outcome of Heart Failure Patients in a Tertiary Hospital in Kaski, Nepal: A Cross-sectional Study

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ABSTRACT:

Introduction: Heart failure is one of the leading causes of hospitalization. The aim of this study was to evaluate the epidemio-clinical profile and short-term outcome of hospitalized heart failure patients in a tertiary care hospital. **Methods:** This descriptive cross-sectional study was conducted at Pokhara Academy of Health Sciences, Kaski, Nepal from October 1, 2021 to January 31, 2022. All the hospitalized heart failure patients aged 18 years or above were included. Relevant history, examination, laboratory and pertinent findings were noted. Descriptive statistics were used for qualitative and quantitative data. Paired t-test was used for comparison of pre-and post-hospitalization data. A p-value <0.05 was taken for statistical significance. **Results:** There were a total of 116 patients (65.5% females) with a mean age of 64.20 ± 16.35 years. Most of them had shortness of breath (97.4%) and orthopnea (72.4%) and presented with pedal/sacral edema (81.9%) and bilateral basal crepitations (69.8%) in the chest. Heart failure with preserved ejection fraction was the most prevalent (61.2%) type and dilated cardiomyopathy (27.6%) was the commonest etiology of heart failure. The median duration of hospitalization was five days and the in-hospital mortality was 2.6%. Loop diuretics and vasodilators (angiotensin-converting enzyme inhibitor/angiotensin receptor blocker) were the most commonly used medications. **Conclusions:** Dilated cardiomyopathy was the most common etiology and heart failure with preserved ejection fraction was the predominant type of heart failure. With a short length of stay and low in-hospital mortality, the short-term outcome was good.

Keywords: Clinical profile, Heart failure, Hospitalization.

INTRODUCTION:

State of the art heart failure (HF) diagnostics and therapeutics have increased both the prevalence and longevity in HF, making frequent HF hospitalization a universal health concern [1,2,3] and it is expected to rise in

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coming days.[4,5] Erewhile in low- and middle income countries, valvular heart diseases were frequent. However, in prevailing time due to shift of paradigm in epidemiology, ischemic heart disease takes humongous share.[6,7] Few publications only mention sparsely the commonest cause, different risk factors, outcome of those heart failure hospitalizations in our setting.[6,7,8,9,10,11,12,13] Hence this study was conducted to evaluate the epidemio-clinical profile of heart failure patients and their short-term outcome in our setting.

METHODS:

This descriptive cross-sectional study was carried out at Pokhara Academy of Health Sciences (PoAHS) from 1st October 2021 to 31st January 2022 after approval from the Institutional Review Committee, PoAHS (Ref. No. 68/078). All hospitalized patients aged 18 years or above with the diagnosis of heart failure were enrolled. The patients who could not undergo cardiac evaluation including necessary investigations and post operative patients ($\leq$ 3 months of surgery) were excluded.

The sample size was calculated using the formula:

Minimum sample size (n) = Z^2pq/ e^2. Taking prevalence (p) as 7.5% from the study of Sharma et al.[8], Z=1.96 at 95% confidence interval and e=5%, the minimum sample size was calculated to be 107.

Recent European Society of Cardiology guidelines for diagnosis and treatment of acute and chronic heart failure (2021) were adopted for defining, classifying and diagnosing heart failure.[1] Patients data were collected from medical history sheets acquired during admission, stay and discharge from the hospital. A comprehensive history, essential physical examination and obligatory laboratory investigations were noted in a working proforma which was formulated after discussion with all the team members and after careful review of various literatures. Quantitative N-Terminal Pro Brain Natriuretic Peptide (NT-Pro BNP) estimation was processed using the Chemiluminescence Immunoassay (CLIA) approach. A focused systemic cardiovascular assessment along with Chest X-Ray (CXR), Electrocardiogram (ECG) and echocardiogram were carried out. Antero-posterior view CXR was repeated to postero-anterior view whenever feasible and cardiomegaly was labeled only when cardiothoracic ratio was > 50% in postero-anterior view. Updated guideline on standardization and interpretation of ECG laid by respective heart rhythm society was exercised for calibration and other technicalities of ECG.[14] Recent European Association of Cardio-Thoracic Surgery protocol (2020) was followed for identifying atrial fibrillation.[15] American College of Cardiology and American Heart Association diagnostic criteria were adopted for detecting bundle branch block pattern and translating other ECG abnormalities.[16] Likewise, recent instructions of American Society of Echocardiography and the European Association of Cardiovascular Imaging were preferred for summarizing echocardiographic results.[17] European Society of Cardiology working group classification of the cardiomyopathies (2008) guideline was used for defining cardiomyopathies.[18]

All these data were noted in Statistical Package for Social Sciences (SPSS) for further analysis. Quantitative data were expressed in terms of number, percentage, mean ± standard deviation. Pre- and post hospitalization data were compared using paired t-test. A p value < 0.05 was designated significant.

RESULTS:

There were a total of 116 patients with female

Table 1: Baseline Characteristics, Clinical Presentations and Risk Factors (n=116)

Characteristics		**Frequency (%)**
Sex	Female	76 (65.5%)
	Male	40 (34.5%)
Symptoms	SOB:	
	NYHA 3	51 (44%)
	NYHA 4	62 (53.4%)
	PND/Orthopnoea	84 (72.4%)
	Chest Pain	54 (46.6%)
	Palpitation	54 (46.6%)
	Sweating	38 (32.8%)
	Epigastric Pain	32 (27.6%)
	Pre-Syncope	16 (13.8%)
Clinical Signs	Edema (pedal/sacral)	95 (81.9%)
	B/l basal crepitations	81 (69.8%)
	Distended neck veins	56 (48.3%)
	Raised JVP	35 (30.2%)
	S3	30 (25.9%)
	Hepatomegaly	14 (12.1%)
Risk Factors	Tobacco (Smoking/Chewing)	83 (71.6%)
	HTN	44 (37.9%)
	COPD	42 (36.2%)
	DM-II	22 (19.0%)
	Anemia	17 (14.7%)
	Past history of heart failure	15 (12.9%)
	Obesity	13 (11.2%)
	Arrhythmia (excluding sinus arrhythmia)	12 (10.3%)
	Renal disease	06 (5.2%)
	CAD/PCI/CABG	03 (2.6%)

Note: Bilateral (B/L), Chronic Obstructive Pulmonary Disease (COPD), Coronary Artery Bypass Graft (CABG), Coronary Artery Disease (CAD), Diabetes Mellitus-type II (DM-II), Hypertension (HTN), Jugular Venous Pressure (JVP), New York Heart Association (NYHA) grading for dyspnoea, Paroxysmal Nocturnal Dyspnoea (PND), Percutaneous Coronary Intervention (PCI), Shortness of Breath (SOB), Third Heart Sound (S3).

predominance of 65.5% and mean age of 64.20 ± 16.35 years. Most of them presented with shortness of breath (SOB). Tobacco consumption (71.6%) either in the form of smoking or chewing was the most common risk factor. These baseline findings are depicted in more detail in Table 1.

Table 2: Investigations findings in the study population (n=116)

Laboratory Parameters	**Mean ± Standard Deviation**
Haemoglobin (g/dl)	12.72 ± 2.22
Urea (mg/dl)	36.68 ± 26.69
Creatinine (mg/dl)	1.31 ± 1.26
Sodium (meq/L)	136.84 ± 4.57
Potassium (meq/L)	4.11 ± 0.66
Random Blood Sugar (mg/dl)	134.66 ± 63.48
NT Pro-BNP* (pg/ml)	4946.47 ± 454.21
NT Pro-BNP in HFpEF** (pg/ml)	4235.72 ± 388.90
NT Pro-BNP in HFrEF*** (pg/ml)	7171.54 ± 549.74

*N-Terminal Pro Brain Natriuretic Peptide, **Heart Failure with preserved Ejection Fraction ***Heart Failure with reduced Ejection Fraction

The mean values of hemoglobin, creatinine and random blood sugar are shown in Table 2. The mean serum N-terminal pro brain natriuretic peptide (NT-Pro BNP) level was 4946.47 ± 454.21 pg/ml. Chest x-ray (CXR) showed pleural effusion in 65.5% and cardiomegaly in 36.2% of the patients. The most common ECG abnormalities were sinus tachycardia (91.38%) followed by ST/T changes (62.06%). Echocardiography demonstrated distinctive left ventricular diastolic dysfunction (LVDD) in 87.9%, followed by tricuspid regurgitation (78.4%). Table 3 highlights various investigation findings of those patients.

Almost all heart failure hospitalizations were from the emergency department (96.6%). The most common cause of heart failure was dilated cardiomyopathy (27.6%). Table 4 illustrates all these heart failure hospitalization parameters in detail.

Clinical variables like Heart Rate (HR), Respiratory Rate (RR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and body weight mean values were significantly reduced when compared between pre- and post hospitalization (Table 5).

Table 3: Investigations findings in the study population (n=116)

Laboratory Parameters	**Number (%)**
Chest X-Ray Findings:	
Pleural Effusion	
U/L	23 (19.8%)
B/L	53 (45.7%)
Cardiomegaly	42 (36.2%)
Electrocardiographic Findings:	
Sinus Tachycardia	106 (91.38%)
ST/T changes	72 (62.06%)
LBBB	35 (30.17%)
A. Fib.	15 (12.93%)
RBBB	12 (10.34%)
LAFB	05 (4.31%)
Echocardiographic Findings:	
LVDD	102 (87.9%)
TR	91 (78.4%)
MR (excluding trace MR)	71 (61.2%)
AR	48 (41.4%)
LVSD	45 (38.8%)
PR	31 (26.7%)
Pericardial Effusion	17 (14.7%)

Note: Aortic Regurgitation (AR), Atrial Fibrillation (A. Fib.), Bilateral (B/L), Left Anterior Fascicular Block (LAFB), Left Bundle Branch Block (LBBB), Left Ventricular Diastolic Dysfunction (LVDD), Left Ventricular Systolic Dysfunction (LVSD), Mitral Regurgitation (MR), Pulmonary Regurgitation (PR), Right Bundle Branch Block (RBBB), Tricuspid Regurgitation (TR), Unilateral (U/L).

Table 4: Heart failure hospitalization parameters (n=116)

Parameters		**Frequency (%)**
Admission	ED	112 (96.6%)
	OPD	4 (3.4%)
Diagnosis	HFpEF (LVEF ≥ 50%)	71 (61.2%)
	HFmEF (LVEF: 41-49%)	11 (9.5%)
	HFrEF (LVEF ≤ 40%)	34 (29.3%)
Etiology	DCM (including PPCM)	32 (27.6%)
	Cor Pulmonale with RHF	27 (23.3%)
	HTN	21 (18.1%)
	VHD (including RHD, IE)	19 (16.4%)
	CAD	13 (11.2%)
	Structural Heart Disease (ASD)	02 (1.7%)
	Arrhythmia	02 (1.7%)
Median length of stay (days)	Ward	4.0
	ICU (n=15)	3.0
Status of patient	Discharged	111 (95.7%)
	Death	03 (2.6%)
	Referred	02 (1.7%)
Medications	Loop Diuretics	76 (65.5%)
	ACEI/ ARB	55 (47.4%)
	β-Blocker	44 (37.9%)
	Bronchodilator	39 (33.6%)
	Aspirin	35 (30.2%)
	MRA	23 (19.8%)
	Statin	19 (16.4%)
	CCB	16 (13.8%)
	ADA (including Insulin)	08 (6.9%)
	Digoxin	07 (6.0%)
	Penicillin	04 (3.5%)
	Antibiotics (Other than Penicillin)	03 (2.6%)

Note: Angiotensin Converting Enzyme Inhibitor (ACEI), Angiotensin Receptor Blocker (ARB), Anti-Diabetic Agents (ADA), Atrial Septal Defect (ASD), Beta Blocker (β-Blocker), Calcium Channel Blocker (CCB), Coronary Artery Disease (CAD), Dilated Cardiomyopathy (DCM), Emergency (ED), Heart Failure with mildly reduced Ejection fraction (HFmEF), Heart Failure with preserved Ejection fraction (HFpEF), Heart Failure with reduced Ejection fraction (HFrEF), Hypertension (HTN), Infective

Endocarditis (IE), Intensive Care Unit (ICU), Mineralocorticoid Receptor Antagonist (MRA), Outpatient department (OPD), Peripartum Cardiomyopathy (PPCM), Rheumatic Heart Disease (RHD), Right Heart Failure (RHF), Valvular Heart Disease (VHD)

Table 5: Pre- and Post- hospitalization clinical parameters

Parameters	Pre-Hospitalization (Mean ± SD)	Post-Hospitalization (Mean ± SD)	p value*
Systolic blood pressure (mm Hg)	121.03 ± 20.19	113.53 ± 21.15	0.001
Diastolic blood pressure (mm Hg)	78.28 ± 13.66	72.84 ± 13.50	<0.001
Body weight (Kg)	58.00 ± 9.59	54.97 ± 9.67	<0.001

**Paired t test*

DISCUSSION:

Heart failure is a hyperonym for any deterioration of ventricular filling and ejection fraction of the heart and consists of a myriad of symptoms and signs with diverse clinical presentations and ranges of laboratory and radiological changes. Multitude criteria and algorithms have been formulated for diagnosis and management. However, paucity of resources compels rigorous integrated algorithm- based management of heart failure inapplicable especially in low- and middle income countries. Moreover, keeping abreast with recent heart failure guidelines, gross pragmatic evaluation and management is practiced universally. This study tried to highlight some of these issues.

The mean age of the patients in this study was 64.20 ± 16.35 years which was similar to recent national studies done by Shrestha et al.[9] (63.7 years) and Adhikari et al.[10] (62.8 years). However, compared to preceding studies done in Nepal, this was slightly an elder age which illustrated accelerated epidemiological transition towards longevity. [4,6,7,9,13] When these data were compared to international database studies, Kyoto congestive heart failure registry [19] had mean age of 80 years, Japanese diagnosis procedure combination database [20] had mean age of 79 years, China PEACE retrospective heart failure study [21] had mean of 73 years and BIOSTAT- CHF study [2] had mean of 68 years. The mean age of our study was comparatively less which is consistent with low national life expectancy. Female to male ratio in this study was 1.9, suggesting possibility of higher prevalence of heart failure in female which was also consistent with previous national publications.[4,6,9,11,12.13]

The patients presented with the gamut of complaints of which shortness of breath (SOB) was present in almost all of the cases

(97.4%). Patients with decompensated heart failure presented with either New York Heart Association (NYHA) Class III or IV symptoms possibly suggesting higher threshold for inpatient admission of high-acuity patients and a trend of seeking medical attention at late stage because of lack of medical awareness or limited access to health facility or health insurance policy. Orthopnoea and paroxysmal nocturnal dyspnoea (PND) were also in substantial frequency in this study. Antecedent studies showed various severity of SOB including orthopnea and PND.[7,9,10,12]

Congestion is regarded as one of the cardinal features of heart failure. Edema (pedal and/or sacral) was present in four-fifths of the patients compared to bilateral basilar crepitations which was present in about two-third of the patients. Both the signs of systemic as well as pulmonary venous congestion were profound in this study. Contrary to this, frequent pulmonary congestion was observed in other studies.[7,21] Raised JVP, third heart sound (S3) and tender hepatomegaly were also present in conspicuous extent in this study.

Tobacco consumed in any form; either smoking or chewing, was the most common associated risk factor in this study. Tobacco is considered one of the major health burdens of developing nations. Tobacco is a traditional cardiovascular risk factor and shares fellowship with other conventional risk factors like hypertension, diabetes, coronary artery disease and atrial fibrillation, all of which have equal potential of decompensating heart failure. Nicotine, a noxious compound found in tobacco, thereby activating the sympathetic nervous system, increases the heart rate and blood pressure and by virtue of increasing myocardial demand results into heart failure. Generation of reactive oxygen species, accumulation of unhealthy lifestyle and unhealthy feeding habits in tobacco consumers lead to structural changes in the heart ensuing heart failure.[22] Available national literatures also have suggested that tobacco, anemia and chronic obstructive pulmonary disease (COPD) are predominant risk factors associated with heart failure.[4,10,12,13] This inculpable finding needs a large sample randomized control trial study for validation.

Hypertension (HTN) and diabetes mellitus type-II (DM-II) were present in 37.9% and 19% of the patients respectively in this study. There was a striking difference in prevalence of HTN and DM-II in international studies where HTN was the most common associated comorbidity. In a Japanese database cohort study,[20] the prevalence of HTN and DM-II was 76.7% and 38.3% respectively. The China PEACE study [21] showed a prevalence of 53.8% for HTN and comparable prevalence of 19.9% for DM-II. This shift in trend in risk factors from developing to developed nations is the root cause for emergence of cardiovascular disease epidemics.

Heart failure and COPD can coexist together and is thought to be a dangerous liaison. Resemblance in clinical presentations, sharing same risk factors and association with similar comorbidities make the picture complicated. More than one-third (36.2%) of the patients in this study had COPD. Similar reports were narrated in previous studies. Similarly, heart failure is more common in patients with atrial fibrillation (A. Fib) and is related with unfavorable outcomes including mortality and longer stay in hospital. The prevalence of A. Fib in this study was 12.93% which was much less compared to Japanese database cohort study [20] (41.8%), Kyoto registry [19] (41%), and the China PEACE study [21] (35.9%). This difference was postulated to occur due to difference in age group and other associated risk factors between our patients and those registries.

There were only 12.9 % of patients having past history of heart failure which was much lower compared to around 60% reported in the China, Europe and the United States.[21,23,24] As many of our patients were from rural community with limited access to health services, there is a possibility that many of them remained undiagnosed or there may be incomplete documentation regarding previous admission or outpatient department visits. Additionally, as our patients were younger, they have less chance of having heart failure in the past compared to international registries.

The strength of this study was inclusion of biomarker N terminal pro-brain natriuretic peptide (NT Pro-BNP) in the diagnostic algorithm of heart failure. These high levels of NT Pro-BNP observed in this study definitely vowed for worsening/severe heart failure and ruled out confounding errors resulting from elderly age, anemia, renal failure, infection or arrhythmia. The level of NT Pro-BNP noted in this study was similar to other studies. [2,19,21,24,25]

Incorporation and interpretation of all investigatory modality in heart failure is novelty of this study. Pleural effusion was visible in almost two-third of the chest x-ray (CXR) in this study. Pleural effusion is the result of pulmonary venous congestion. Similarly, cardiomegaly was noticed only in one-third of the patients. The study done by Shrestha et al.[9] had illustrated a higher percentage for cardiomegaly compared to pleural effusion. This flip flop in percentages may be due to inclusion of severely symptomatic patient in this study and large number of patients with echocardiography proven dilated left ventricle on Shrestha et al.[9]

The most common electrocardiographic (ECG) findings observed was sinus tachycardia (91.38%) followed by ST segment and T wave (ST/T) changes, which was observed in almost two-thirds of the patients. Atrial fibrillation and bundle branch block (BBB) were present in varying proportions in this study. Various arrhythmia and blocks are characteristics of heart failure. These ECG changes are a consequence of counter-regulatory neuro-endocrine and maladaptive sympathetic over activation of the heart. Risk factors like HTN, COPD, anemia and various other etiology of heart failure including myocardial ischemia, associated features like electrolyte disturbances or structural changes in the heart can contribute to ECG changes. Similar ECG findings were noted in antecedent researches.[4,12]

Echocardiography remains one of the cornerstones in diagnosis and management of heart failure. In this study, left ventricular diastolic dysfunction (LVDD) was the most common (87.8%) echocardiographic finding which was then followed by valvular regurgitation. Similar echocardiographic profiling was documented in previous studies.[12,25,26] Contrary to that, left ventricular systolic dysfunction (LVSD) was present only in about one-third of the patients in this study. These findings later explain the predominant prevalence of heart failure with preserved versus reduced ejection fraction in this study. Pericardial effusion is recognized as a yardstick for presence of heart failure. Pericardial effusion was noted in a considerable number of patients in this study.

As most of the patients in this study were hospitalized with severe symptoms, almost all (96.6%) patients landed up in ED while only a few showed up in OPD. Categorically, about two-third of the patients were diagnosed as heart failure with preserved ejection fraction (HFpEF) while remaining one-third were classified as heart failure with reduced ejection fraction (HFrEF). This study found that dilated cardiomyopathy (DCM) was the

most common cause of heart failure similar to few previous studies.[4,10] Cor pulmonale with right heart failure was placed in second position elaborating the fact that COPD and its consequences are still the predominant deciding factor in heart failure. Valvular heart disease (VHD) including rheumatic heart disease (RHD) was also a contributing cause for heart failure in some percentage of patients but not as much in that frequency as explained in literatures.[6,11,13] Coronary artery disease (CAD) accounted for only a small percentage (11.2%) of heart failure in this study which is in contrast to few national[7,9,12] and other international studies where CAD was the dominant etiology. The diverse etiology of heart failure observed in those previous national studies corresponds to different time frames of those studies and different medical services those hospitals provide including comprehensive cardiac services.

The median length of hospital stay was 5 days with a stay of 3 days in intensive care unit (ICU) for a few patients. International registries had documented longer duration of stay for heart failure hospitalization.[25,26,28] This could be due to financial constraints, high bed occupancy rate indicating crisis of bed in government hospitals, lower age of the patient, low prevalence of comorbidities. Compared to the available data and other disease admission rates, the length of stay documented in this study denotes that guideline directed medical therapy for heart failure has prompt response resulting in shorter stay in hospital.

The in-hospital mortality of 2.6% documented in this study was lower compared to international data and registries.[21, 27] Most of the patients (95.7%) were discharged out from the hospital in this study. Reason for this could be many but less number of worsening or advanced failure in this study compared to those registries.

Loop diuretics were the most common medications used. Diuretics by relieving congestion produce symptomatic relief as well as maintain hemodynamic harmony. This balanced hemodynamics makes way for other heart failure medications to act effectively. Use of angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), beta-blocker and mineralocorticoid receptor antagonist (MRA) were in increasing trend compared to previous study but suboptimal compared to international registries suggesting that there is still a long way to go.[2, 10,11,13, 19-21, 28] There is still a huge potential regarding application of novel therapy like angiotensin receptor neprilysin inhibitor (ARNI) and sodium glucose cotransporter-2 (SGLT2) inhibitor.

Several limitations ought to be considered. Because of the design of the study, its data could not be generalized; neither can it be extrapolated to find causal relationship of heart failure with any other entities. As patients included in this study were symptomatic, the other half of heart failure, i.e., asymptomatic and compensated heart failure patients was not taken into consideration. Limited sample size and inability to look for other parameters of short term outcome were also its limitations.

CONCLUSION:

Dilated cardiomyopathy was the most common etiology and heart failure with preserved ejection fraction dominated heart failure hospitalization. This shift of paradigm in epidemics of heart failure resulted due to accumulation of risk factors like tobacco consumption, hypertension and diabetes. Moreover, the length of stay was short and the short term outcome of hospitalized heart failure patients was good, representing the favorable response of anti-heart failure medications. However, to achieve optimal

response, use of novel as well as adequate anti-heart failure medications is desired.

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