

# A Study on Assessment of Pharmacotherapy, Etiology, and Risk Factors in Heart Failure Patients in Tertiary Care Hospital

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## ABSTRACT

**Background:** Heart failure is described by the ACC Foundation and AHA as “a complex clinical syndrome resulting from any anatomical or functional impairment of ventricular filling or blood ejection. The main aim was to assess the pharmacotherapy, drug utilization pattern, precipitating factors, and aetiological factors of heart failure. **Materials and Methods:** The study is a single-centred prospective observational study that was conducted for 6 months. Patients were selected based on study criteria. **Results:** Out of 155 heart failure, the patient’s most prevalent age group was between 61 and 70 years (33.5%) with a mean of 61.96(± 13.72). Out of 155 patients, 86 (55.4%) had a decreased ejection fraction, and the majority of patients were men (53.45%). The most prevalent precipitating variables were found to be anaemia 51(18.68%), hypertension 82(30.03%), and diabetes mellitus 70(25.64%). Cardiomyopathy 70(43.48%) and ischemic heart disease 83(40.88%) were the most often discovered underlying causes in patients with heart failure. The most frequent comorbidities were renal disorders 42(21.53%), hypertension 46(23.58%), and diabetes mellitus 42(23.58%). Around 139(90.25%) prescriptions contained diuretic drugs. Furosemide (69.63%) was the most commonly prescribed diuretic. Followed by antihypertensives 132(85.71%) and digoxin was prescribed to 32 (20.64%) patients. About 36.90% of patients received aspirin and atorvastatin combination drugs. **Conclusion:** Our study concluded that ischemic heart disease and dilated cardiomyopathy are the core underlying causes of heart failure. Hypertension and diabetes mellitus is considered to be the most common predisposing factors. The most frequent monotherapy prescribed for heart failure includes diuretics, antihypertensives, antiplatelets, and lipid-lowering agents while aspirin and atorvastatin were the most commonly prescribed combination therapy.

**Keywords:** HF patients, Ejection fraction, Hypertension, Hypernatremia, Diuretics.

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## INTRODUCTION

Patients with heart failure are typically classified as having heart failure with reduced (HfrEF; LVEF40%), medium (HfmEF; LVEF 40-49%), or preserved (HfpEF; LVEF>50%) ejection fraction. Worldwide, an estimated 64.3 million people suffer from heart failure. The prevalence of documented heart failure is typically estimated to be between 1% and 2% of the overall adult population

in affluent nations. It is well known that heart failure increases with age. Aging can weaken and stiffen cardiac muscle to elevate the risk of heart failure. Hypertension is considered to be the most important risk factor involved in HfpEF pathophysiology. Men have a high probability of getting HfrEF than women. Type 2 diabetes mellitus causes heart failure by two-fold increases in men and a three-fold increase in women.<sup>1</sup> Elevations in both diastolic and systolic BP are strongly correlated with congestive heart



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disease mortality, use of drugs, lack of physical exercise, unhealthy diet, alcohol intake, and smoking. Smoking is considered to be a strong factor conferring a two-fold increase in total congestive heart disease and myocardial infarction.<sup>2</sup> Other medical conditions such as obesity, stress, infections, inflammations, sleep apnoea, anemia, thyroid, atrial fibrillation, arrhythmia, use of anti-diabetic drugs (thiazolidinediones), antipsychotics (risperidone) raise the risk of heart failure.<sup>3</sup>

Heart structural and functional defects, as well as additional initiating factors, are the causes of heart failure. In the past, myocardial infarction and coronary artery disease accounted for the vast majority of cases. The two main risk factors for HF have evolved over time to be coronary artery disease and diabetes mellitus. Hypertension, valvular heart disease, uncontrolled arrhythmia, myocarditis, and congenital heart disease are other structural causes of congestive heart failure. Restrictive cardiomyopathies and constrictive pericarditis can both result in diastolic HF with impaired ventricular filling. Decreased physical activity, sodium restriction, and improper medication therapy are the three main causes of decompensated chronic heart failure. The second most frequent factor contributing to decompensated HF is uncontrolled hypertension. Exacerbations of chronic heart failure can occur suddenly in patients with uncontrolled tachyarrhythmias in addition to congestive HF as an underlying pathology. High-output cardiac failure is caused by a different category of medical conditions related to congestive heart failure. By definition, this is not a cardiac function defect but rather the heart's inability to cope with the enhanced systemic demands driven on by extra cardiac illnesses. Severe anemia, thyrotoxicosis, obesity, nutritional deficiency (thiamine), and pregnancy are common possible causes of high-output type of heart failure. A condition referred to as cardiac failure with preserved ejection fraction is characterised by impaired and insufficient myocardial relaxation and filling. The ventricle is unable to maintain appropriate stroke volume, does not fill at low pressure, or accept an adequate volume of blood from the venous system. Age, diabetes mellitus, and hypertension are risk factors for HfpEF. When the left ventricular ejection fraction is 40% or less, heart failure with reduced ejection fraction develops. This condition is marked by increasing left ventricular enlargement and severe cardiac remodelling.<sup>4</sup> Arrhythmias are among the most common complications of HF; end-stage HF patients frequently experience ventricular arrhythmias, and roughly one-third of individuals with chronic heart disease experience atrial fibrillation. Stroke and thromboembolism are predisposed by chronic heart disease.<sup>5</sup>

The purpose of the study was to study the prescription pattern, precipitating factors, underlying causes, and comorbidities in the case of heart failure patients.

## MATERIALS AND METHODS

The study was a prospective observational study carried out over a period of 6 months (April 2022-September 2022) in the inpatient department of general medicine and intensive care unit of a tertiary care hospital. The patients above the age of 18 years diagnosed with heart failure and on treatment were included in the study irrespective of gender and comorbidities, Patients with a history of CAD, ECG abnormalities, HTN, DM rheumatic heart disease with echocardiographic evidence of valvular abnormalities, a history of degenerative heart disease and arrhythmia. Exclusion criteria for the study include patients below 18 years, OPD patients, cancer and immunocompromised patients, pregnancy, and lactating women. Required clinical data and demographic details were collected using a specially designed data collection form. The collected data were analyzed using appropriate statistical methods to evaluate the study outcome.

### Method of collection

The patients with Heart failure along with or without complications were identified. Demographic details such as age, gender, social habits, and comorbidities were noted in the patient record. Name, category, and combination of drugs prescribed for heart failure and relevant laboratory investigations were collected and recorded in the pre-designed data entry form.

### Ethical clearance

Ethical clearance for the study was obtained from the Institutional Ethics Committee (Ref No: FMIEC/CCM/232/2022), Father Mullers Medical College Hospital Mangalore.

### Statistical analysis

Categorical variables are analyzed using descriptive statistics- frequency and percentages. Mean  $\pm$  standard deviations were used for the analysis of continuous variables to outline the baseline characteristics of patients with heart failure.

## RESULTS

### Socio-demographic characteristics

A total of 155 patients with heart failure were enrolled in

this study. The age of patients ranged from 21 to 87 with an average of 61.96 ( $\pm 13.72$ ). A majority of the patients in the study were aged between 61-70 years 40(33.5%) and male to female ratio was 1.15:1. Among 155 patients majority of the patients were males, with duration of hospital stay of about 26 (16.77%).

### Basic clinical characteristics

Out of the 155 heart failure patients, 155 had documented echocardiographic measurements with the result of 40 (25.8%) having preserved ejection fraction and 86 (55.4%) patients have reduced ejection fraction.

Based on the findings the mean  $\pm$  SD of systolic blood pressure was observed as 134.87 $\pm$ 27.37 and diastolic blood pressure was 82.4 $\pm$ 14.04. Heart rate was measured in 155 patients which were observed as 86.28 $\pm$ 19.76 (mean  $\pm$  SD). Serum potassium was determined in 144 patients with a mean $\pm$ (SD) value of 4.36 $\pm$ 2.53 mEq/L; of these 31 (21.52%) had serum potassium concentration 5.55 mEq/L. The mean $\pm$ (SD) value of serum sodium for 150 patients was 132 $\pm$ 7.25 mEq/L, among those 70 (46.66%) had serum sodium concentration less than 135 mEq/L and 80 (53.33%) had serum sodium concentration  $\geq$  135 mEq/L.

The mean  $\pm$  (SD) value of hemoglobin for 155 patients at admission was 11.26 $\pm$ 2.08 g/dL, among those 35 (22.58%) had clinically significant anemia (Hb<10g/dL). Serum creatinine measurement was found for 140 patients among those elevated serum creatinine value (>1.2mg/dL) was found in 71(50.71%) of the patients at admission. AST and ALT measurement was done for 108 patients among those elevated AST and ALT value (AST>33U/L and ALT>55U/L) was found in 46 (42.59%) and 39 (36.11%) respectively. The results of the laboratory parameters are summarised in Table 1.

### Precipitating factors, underlying causes of heart failure patients

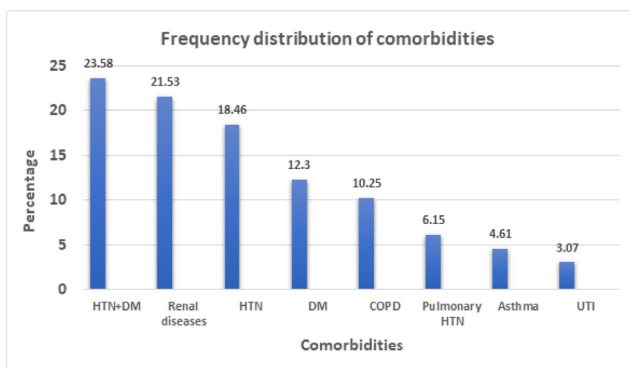
Factors that precipitate heart failure at admission were found for 155 patients and a total of 273 precipitating factors were identified. Among these the top-four precipitating factors were hypertension 82 (30.03%), diabetes mellitus 70 (25.64%), anaemia 51 (18.68%) and atrial fibrillation 19 (6.95%). A total of 203 underlying causes were identified in 155 patients. The two most underlying causes found in heart failure patients were ischemic heart disease 83 (40.88%), and cardiomyopathy 70 (34.48%). Frequency distribution of Precipitating factors, underlying causes were summarised in Table 2.

**Table 1: Baseline laboratory parameters.**

Variables	N	Frequency (%)	Mean	SD	Median
Systolic blood pressure(mm/Hg)	155		134.87	27.37	130
Diastolic blood pressure(mm/Hg)	155		82.4	14.04	80
Pulse rate(bpm)	155		86.28	19.76	84
Serum potassium(mEq/L)	144		4.36	2.53	4.21
Normal		105(72%)			
Hypokalaemia (<3.55 mEq/L)		31(21.52%)			
Hyperkalaemia (>5.55 mEq/L)		8(5.55%)			
Serum sodium(mEq/L)	150		133.26	7.25	135
Serum sodium $\geq$ 135mEq/L		80(53.33%)			
Serum sodium<135mEq/L		70(46.66%)			
Serum creatinine(mg/dL)	140		1.51	2.08	11.4
Normal serum creatinine $\leq$ 1.2mg/dL		69(49.28%)			
Elevated serum creatinine>1.2mg/dL		71(50.71%)			
Haemoglobin (g/dL)	155		11.26	2.08	11.4
Haemoglobin $\geq$ 12g/dL		56(36.12%)			
Haemoglobin<12g/dL		99(63.87%)			
Haemoglobin<10g/dL		35(22.58%)			
AST (Less than 33IU/L)	108		128.80	399.73	38.5
Greater than (33 IU/L)		46(42.59%)			
ALT (Less than 55 IU/L)	108		138.56	419.75	31.5
Greater than 55(IU/L)		39(36.11)			

**Table 2: Precipitating factors, underlying causes of heart failure patients.**

Factors/diseases	Frequency (%)
Precipitating factors (n=155)	
Hypertension	82(30.03%)
Diabetes Mellitus	70(25.64%)
Anemia	51(18.68%)
Atrial fibrillation	19(6.95%)
Thyroid disorders	18(6.59%)
Pneumonia	17(6.22%)
Acute coronary syndrome	11(4.02%)
Infective endocarditis	5(1.83%)
Underlying causes (n=155)	
Ischemic heart disease	83(40.88%)
Cardiomyopathy	70(34.48%)
Coronary artery diseases	25(12.31%)
Cor pulmonale	16(7.88%)
Rheumatic heart disease	6(2.95%)
Degenerative heart disease	3(1.47%)



**Chart 1: Frequency distribution of comorbidities.**

**Distribution of comorbidities in heart failure patients**

Co-morbid diseases were found in 155 patients with heart failure. The major co-morbidities in heart failure patients were observed to be both hypertension and diabetes mellitus 46(23.58%). 42 patients had renal diseases (21.53%), 36 patients had hypertension (18.46%) and 24 had diabetes mellitus. Frequency distribution of comorbidities were described in chart given below. (Chart 1).

**The prescription pattern in case of heart failure patients**

The prescribing pattern in heart failure patients was analyzed. A total of 687 drugs were prescribed for 154 patients. Out of these the most commonly prescribed drug classes were diuretics 139 (90.25%), antihypertensives 132 (85.71%), proton pump inhibitors

**Table 3: Prescribing pattern of drugs in heart failure patients.**

Category of drugs	No of prescription(n=154)	Percentage (%)
Diuretics	139	90.25
Antihypertensives	132	85.71
Proton pump inhibitors	100	64.93
Antiplatelet agents	68	44.15
Lipid-lowering agents	62	40.25
Antidiabetic agents	60	38.96
Inotropes	40	25.97
Anticoagulants	28	18.18
Corticosteroids	10	6.49
HCN-blockers	10	6.49
Antiarrhythmics	6	3.89
Anxiolytics	4	2.59
Antifibrinolytics	2	1.29
Vasodilators	30	19.48
Antianginals	2	1.29
Alpha-blockers	2	1.29
ARNI	2	1.29
Fibrinolytics	1	0.64

100 (64.93%), antiplatelets 68 (44.15%) and lipid-lowering agents 62 (40.25%). The results are summarised in the Table 3.

**Combination of drugs used in patients**

The cardiovascular drugs were given in combinations as shown in the table given below. Where, 26.19% (22) of patients received Aspirin, Clopidogrel, and Atorvastatin, 36.90% of patients were given Aspirin and Atorvastatin combination.

**DISCUSSION**

A total of 155 case records of patients were analyzed and the results indicated that the most prevalent age group was between 61 and 70 years with a mean of 61.96 ( $\pm 13.72$ ).

Gender-wise distribution of patients showed that males (53.45%) had a higher frequency of heart failure compared to females with a male-to-female ratio of 1.15:1. This was in concordance with the study conducted by Cowie M.R *et al.*<sup>6</sup>

Our study also documented patients' echocardiographic measurements and we found that 86 (55.4%) of them had reduced ejection fraction and 40 (25.8%) patients had preserved ejection fraction. Reporting of comorbidities

was more common in HF<sub>r</sub>EF trials as compared with HF<sub>p</sub>EF, this was similar to the study conducted by Muhammad SK *et al.*<sup>7</sup>

Electrolyte levels were monitored during the hospital stays where hyperkalemia was observed in 8 (5.55%) patients and hypokalemia was found in 31 (21.52%) patients. Hyponatremia was also found in 70 (46.66%) patients which was comparable to the study conducted by Eaterina U *et al* which suggested hyponatremia as the most common electrolyte abnormality observed in hospitalized subjects.<sup>8</sup>

The main factor precipitating heart failure were hypertension 82 (30.03%), diabetes mellitus 70 (25.64%), anemia 51 (18.68%) and atrial fibrillation 19 (6.95%). This is comparable to the study by H Risimiate and Hae Young Lee in which hypertension was present in 40% of patients.<sup>9</sup>

The two most underlying causes of heart failure were ischemic heart disease 83 (40.88%) and cardiomyopathy 70 (34.48%). This study is similar to the study conducted by Lloyd Jones DM *et al.* In their study nearly 70% of all heart failure syndromes were attributed to underlying ischemic heart disease.<sup>10</sup>

Both Diabetes and Hypertension 46 (23.58%) were the common comorbidities reported in our study. Patients with comorbidities of Ischemic etiology along with hypertension are most likely to develop heart failure. The prevalence of comorbidities was high in our study, which is comparable to the study conducted by Braunstein JA and Anderson GF *et al.*<sup>11</sup>

A total of 687 drugs were prescribed for 159 patients. Around 139 (90.25%) prescriptions contained diuretic drugs. The diuretic which was most frequently prescribed was furosemide. Furosemide, torsemide, and spironolactone were given to 107 patients (or 69.63%), 52 patients (or 33%), and 29 patients (or 18.70%), respectively. This was comparable to the research done by R Abhijith and colleagues. Diuretics continue to be the first line agent against volume overload edema, especially in CHF patients. Diuretics decrease pulmonary edema and venous congestion, and they might even be the essential medication required to treat mild heart failure in some cases.

Antiplatelet agent Aspirin was prescribed in 52 (33.54%) of patients and clopidogrel was given to 38 (24.57%) of patients. Most of the patients who received these two medications had either recently or in the past experienced a MI event and were taking antiplatelet medication. In

contrast to our analysis, the Clopidogrel vs Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial demonstrated that 75 mg of clopidogrel taken daily for three years after a MI is superior than 325 mg of aspirin in terms of lowering the rate of recurrent atherothrombotic events.<sup>12</sup>

The prescribing pattern of the anti-hypertensive drug was categorized. It was found that 132 (85.71%) patients received anti-hypertensive therapy. Beta-blockers were the most commonly prescribed drugs. About 21 (13.54%) patients received metoprolol and 21 (13.54%) patients received carvedilol. It is commonly acknowledged that -blockers have a positive impact on the management of HF. Studies like the Carvedilol Prospective Randomized Cumulative Survival (COPERNICUS) trial, the Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF), and the Carvedilol or Metoprolol European Trial (COMET) trials have demonstrated that they can lower mortality and morbidity.<sup>13</sup>

ARBs were prescribed, out of which Telmisartan was prescribed to 17(10.96%) of patients followed by Losartan, which was prescribed to 7(4.5%) of the patients.<sup>13</sup> Atorvastatin 62(40%) was the commonly prescribed lipid-lowering agent followed by rosuvastatin. Statin treatment has shown a reduction in heart failure in patients with coronary artery disease.<sup>14</sup>

Inotropes were prescribed in 40 (25.97%) patients. Digoxin was prescribed to a total of 32 (20.64%) patients.<sup>15</sup> The randomized trials Rationale and Design of the DIGIT-HF Trial (RADIANCE) and the DIG trial showed a significant reduction in hospitalizations for worsening heart failure but no reduction in mortality.<sup>16</sup> Although inotropic agents temporarily stabilize the hemodynamic status, their long-term use is associated with increased mortality.

A total of 31 patients (or 36.90%) received aspirin and atorvastatin combo medications. A total of 7 (8.33%) patients received atorvastatin and clopidogrel together. The pharmacodynamic effects of 150 mg of clopidogrel were enhanced by high-dose statin therapy, according to the ACHIDO (Atorvastatin and Clopidogrel High Dose in Stable Patients with Residual High Platelet Activity) research results.

Sacubitril/Valsartan was given to 4 (4.76%) of patients. It is the first novel family of medications to combine angiotensin II receptor antagonist with neprilysin inhibition. This combination increases endogenous natriuretic peptides while blocking the

renin-angiotensin-aldosterone system.<sup>17</sup> Sacubitril/Valsartan treatment decreased cardiovascular mortality or HF hospitalization by 20% and all-cause mortality by 16% in the PARADIGM-HF (Prospective Comparison of Angiotensin Receptor Blocker Nephilysin Inhibitor with Angiotensin Converting Enzyme Inhibitor) trial compared to standard treatment with an ACEI.<sup>18</sup>

## CONCLUSION

The results of the current study showed that heart failure is more common in individuals between the ages of 61 and 70 years, is slightly more common in men than in women, and increases with age. Ischemic heart disease, dilated cardiomyopathy, coronary artery disease, and rheumatic heart disease are the most prevalent underlying illnesses that lead to heart failure. Particularly for the aging, the incidence of risk factors and comorbidities is considerable and increasing. Hypertension, diabetes mellitus, and renal diseases were the highest identified predisposing factors for heart failure while thyroid disorders and lower respiratory tract infections were less prominent. Hypertension, diabetes mellitus, and renal diseases were identified as the most prominent comorbid conditions, while asthma and COPD were playing less prominent roles in heart failure.

The present study has important public health implications and suggests that targeting the prevention of hypertension and diabetes mellitus may have the greatest impact on reducing the number of heart failure cases in the population. The prescribing pattern in heart failure was also analyzed in our study. The most frequently used drugs in the management of heart failure are Diuretics, antihypertensives, antiplatelets, and lipid-lowering agents, while inotropes, anticoagulants, and vasodilators were prescribed less frequently. A combination of drugs was also given in which aspirin + atorvastatin was the most common combination drug prescribed. Combination therapy is proven to be more effective than monotherapy. Most of the drugs were prescribed rationally.

However, additional research with a bigger sample size is required to understand the state of drug use in hospital settings, including data from various centres with statistics on patient prognosis and future follow-up.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**HfrEF:** Heart Failure with reduced Ejection Fraction; **HfpEF:** Heart Failure with Preserved Ejection Fraction; **ACEIs:** Angiotensin Converting Enzyme Inhibitors; **AST:** Aspartate Aminotransferase; **ALT:** Alanine Aminotransferase; **HF:** Heart Failure; **ARNi:** Angiotensin Receptor-Nephilysin inhibitors.

## SUMMARY

Heart failure continues to be a highly significant and socio-economic issue. This study focuses on the most prevalent aetiologies and risk factors for heart failure. Throughout the past ten years, research on heart failure medication has helped us better grasp the many heart failure therapeutic options. The current pharmacotherapy used to treat heart failure in the regional area is also included in this study. The considerable mortality and morbidity among people 65 and older is so demonstrated by this study. Therefore, further research is needed to enhance our comprehension of different mechanisms, uncommon causes, and current treatment management of heart failure.

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