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Rate of Rehospitalization in 60 Days of Discharge and It's Determinants in Patients with Heart Failure with Reduced Ejection Fraction in a Tertiary Care Centre in India

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The authors have no financial conflicts of interest.

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ABSTRACT

Background and Objectives: Identifying the patients with acute heart failure (HF) at high risk for rehospitalization after hospital discharge will enable proper optimization of treatment. This study is aimed to evaluate the rehospitalization rate at 60 days of discharge and their predictors in patients of chronic heart failure with reduced ejection fraction (HFrEF).
Methods: This prospective observational study enrolled patients with left ventricle ejection fraction (LVEF) <40%, who were admitted because of acute decompensation. Patients were followed for 60 days to analyze rehospitalization rate and its predictors.
Results: Of 103 HFrEF patients (74% male; mean age 55.8 years) enrolled, 7 patients died during index admission and 3 patients lost to follow up. The 60-day rehospitalization rate was 37% (34/93). We studied 23 clinical and 9 biochemical predictors of rehospitalization. Out of 34 events of rehospitalization, 79.41% (n=28) was due to cardiac cause followed by respiratory 5.8% (n=2), renal 5.8% (n=2) and others 5.8% (n=2). Among all the parameters, on logistic regression analysis having longer length of index hospital stay (>7 days) (52.8% vs. 28.8%; odds ratio [OR], 1.79; confidence interval [CI], 1.2–7.25; p=0.040) and chronic kidney disease (CKD) (26.5% vs. 8.5%; OR, 3.06; CI, 1.1–57.04; p=0.050) independently increased the risk of rehospitalization at 60 days of discharge. Further higher haemoglobin level (11.3 vs. 9.9 gm/dL; OR, 0.71; CI, 0.48–0.97; p=0.050) and higher LVEF at index admission (30.4% vs. 26.5%; OR, 0.87; CI, 0.75–0.99; p=0.049) were associated with decreased the risk of rehospitalization.
Conclusions: Our study reveals that patients with HFrEF have significantly higher rehospitalization rate (37%) and in-hospital mortality rates (6.78%) of any chronic cardiac disease conditions. Correction of low hemoglobin and special care in those who are having very low LVEF, CKD and longer length of stay, including tailored therapy and frequent visits may play an important role in preventing future rehospitalization in these patients.

Keywords: Heart failure; Anemia; Chronic kidney disease

INTRODUCTION

Cardiovascular disease (CVD) is currently the leading cause of death worldwide and its prevalence is projected to rise. Improvement in care and decreasing mortality of heart diseases has left us with more patients with heart failures (HFs). Although less than USA in total burden, HF in India was about 5.4 million (approximately 0.5%) in 2016.[1] This may be because of less number of patients taking healthcare attention and also inadequate notification of disease. An increasing trend in proportionate CVD mortality has been reported in Indian medical registry from 19% in 1990 to 34% in 2017.[2] International studies evaluating the economic burden of HF among several countries reveal estimated HF costs about 1–2% of total healthcare expenditures, with the majority of costs attributable to hospitalization.[3] The rehospitalization rate of patients with HF following discharge is high, with over 20–30% of patients requiring rehospitalization within 30–60 days.[4]

HF is becoming a major burden to the health system of India and is likely to increase in the coming decades. Although many prognostic markers of death and/or HF hospitalization have been identified in patients with HF their clinical applicability is limited and precise risk stratification in HF remains challenging. Identifying patients with acute HF at high risk for rehospitalization or death after hospital discharge will enable the optimization of treatment and tailoring management. This study aimed to evaluate the rehospitalization rate at 60 days of discharge and their predictors in patients of heart failure with reduced ejection fraction (HFrEF).

METHODS

Study population

This prospective observational study enrolled patients who were admitted because of acute decompensation of HF in the Department of Cardiology, from February 2018 to June 2019. Acute decompensated heart failure (ADHF) is defined as the rapid change in HF signs and symptoms resulting in a need for urgent therapy, usually resulting in unplanned hospital visits, emergency room visits, or hospitalization.[5] Inclusion criteria included patients with age >18 years, 2D Echocardiogram showing systolic dysfunction (left ventricle ejection fraction [LVEF] <40% as per European Society of Cardiology 2016 guidelines[6]) within 6 months of admission, brain natriuretic peptide (BNP) level >100 pg/mL level at admission, having at least one of the following findings on chest X-ray (CXR): pulmonary edema, pulmonary congestion, cardiomegaly, and/or pleural effusion and at least two of the following: dyspnea, peripheral edema, clinical signs of volume overload, jugular venous distention, left ventricle S_3 gallop, heart rate >100 beats per minute. Patients with acute myocardial infarction were excluded from this study. Patients with in-hospital mortality or lost to follow-up of 60 days were excluded from the analysis. The remaining patients were then grouped into the rehospitalization and the non-rehospitalization group (**Figure 1**). Rehospitalization was defined as any rehospitalization or emergency department visit longer than 24 hours. Rehospitalization could be because of cardiac or non-cardiac reasons. All Patients received guideline-directed medical therapy (GDMT). Informed consent was obtained from the subjects and/or parents and the protocol was cleared by the Institutional Ethical Committee.

Data collection

Patients' baseline characteristics were recorded in a standard case report form. The clinical variables included age, gender, diabetes mellitus (DM), hypertension (HTN), coronary artery

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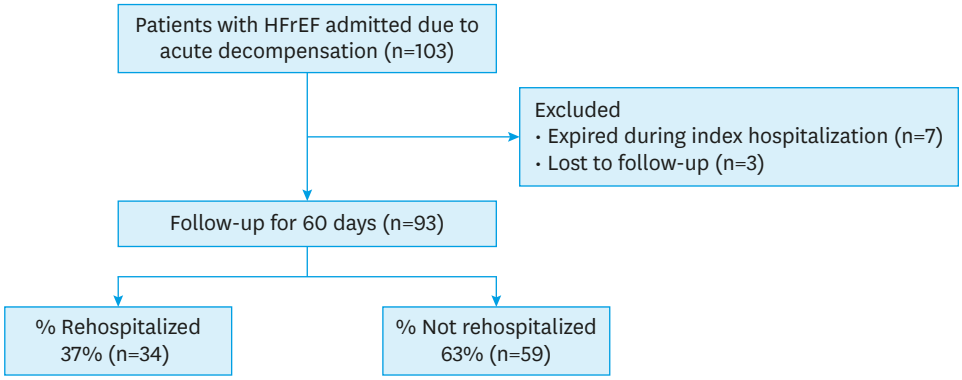

Figure 1. Patient enrolment.
HFrEF = heart failure with reduced ejection fraction.

disease (CAD), cerebrovascular accident (CVA), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), New York Heart Association (NYHA) functional class at admission and discharge, length of hospital stay (LOS) (short ≤7 days or long >7 days), blood pressure (BP) and heart rate (HR). Treatment on discharge was also noted. Laboratory data included hemoglobin (Hb) level, complete blood count, urea level, creatinine level, serum sodium and serum potassium levels at admission. BNP and troponin I levels were measured both at admission and discharge. BNP and troponin I levels were done by a rapid quantitative test using Alere Triage Cardio3 Panel (Alere, San Diego, CA, USA). Additionally, 12-lead electrocardiography, CXR, and 2D-echocardiography were performed according to the protocol. We used pulmonary venous hypertension (PVH) grading as given by Larry Elliot on CXR.[7] Grading of mitral regurgitation on Doppler echocardiography was done according to the American Society of Echocardiography 2017 guidelines.[8] Two-dimensional echocardiography was done using Philips Model Sonos 5500 machine (Phillips Medical Systems, Andover, MA, USA).

Follow-up evaluation

Enrolled patients were followed up in the HF clinic as per departmental protocol. The first follow-up clinic visit was scheduled within the first 2 weeks post-discharge in the HF clinic followed by at 30 and 60 days. Rehospitalization information was obtained mainly from telephone contact with the patients or their relatives if patients are not admitted to our hospital or missing the outpatient department visits. The causes of rehospitalization were noted.

Statistical analysis

Categorical variables were expressed as percentages, and continuous variables were expressed as mean±standard deviation. The χ^2 test with Fisher's exact test was used to compare categorical variables between the 2 groups. Continuous variables were compared utilizing the student's t-test. Multiple logistic regression analysis with a stepwise variable selection method (using a significant level of entry of 0.2 and a stay of 0.05) was used to explore predictors of rehospitalization. All predictors of frequent rehospitalization used in the univariate level were included in a multivariate logistic regression analysis. Data were analyzed with SPSS version 23.0 (SPSS, Chicago, IL, USA).

RESULTS

Demographic, clinical and biochemical baseline characteristics of the study population

A total of 103 patients were enrolled in this study. In-hospital mortality during index hospitalization was 6.78% (7/103). Three patients were excluded from the analysis because of lost to follow-up. The cohort of all patients had an average age of 55.8±13.5 years) with 74% males. Most of the patients were in the age group of 50–60 years (34%). The duration of hospital stay was >7 days in 27% of patients. In our study 53% of individuals had history of CAD, 46% were diabetic, 38% HTN, 19% CKD, 7% COPD and 3% had old CVA. The mean systolic BP at admission was 110.9±11.6 mmHg and mean diastolic BP at admission was 63.5±15.8 mmHg. Twenty-nine percent of patients had wide QRS complex (>120 msec) and 47% had grade 3 PVH in CXR on admission. Mean ejection fraction (EF) of the left ventricle at admission was 28.2±6.6% and 23% hade grade 3 mitral regurgitation on echocardiography. In our study, 42% of individuals had Hb of <10 gm/dL. The mean urea level at admission was 68.9±41.7 mg/dL and the mean serum creatinine level at admission was 1.8±1.3 mg/dL. The mean sodium level at admission was 135±6.3 mEq/L and the mean potassium level at admission was 4.4±0.7 mEq/L. The mean BNP level at admission was 1,646.1±1,251.8 pg/mL and at discharge was 409.6±261.3 pg/mL. The mean troponin I level at admission was 0.5±1.0 ng/mL and at discharge was 0.01±0.01 ng/mL. In our study 95% of patients were discharged on beta-blocker, 65% on angiotensin converting enzyme (ACE) inhibitor, 81% on aldosterone antagonist, 31% on digoxin, 100% on diuretics and 23% on angiotensin receptor-neprilysin inhibitor (ARNI). There were 7% patients who had implantable cardioverter-defibrillator (ICD), 15% cardiac resynchronization therapy-defibrillator (CRT-D), and 4% cardiac resynchronization therapy-pacemaker (CRT-P) implanted. The most common cause of acute decompensation during index hospitalization was infection (35%) (respiratory tract infection most common) followed by non-compliance to treatment (31%), anemia (16%) and arrhythmia (3%).

The rehospitalization rate at 60 days of discharge was 37% (34/93). Thirty days rehospitalization rate was 27.95% (26/93). Median duration of hospital stay was 6 days. 24 patients were rehospitalized once, 8 patients twice and 2 patients thrice in 60 days of discharge. Out of the 34 rehospitalization, 27 (79.41%) was due to cardiac cause (progression of HF, arrhythmia, ischemia) followed by respiratory (infection, exacerbation of COPD) (5.8%), renal (5.8%) and others (5.8%). For patients discharged alive, 60-day all-cause mortality was 5.3% (5/93).

Baseline characteristic distribution in 2 study groups

The average age of patients in the rehospitalization group was 56.3 years compared to 55.8 years in the non-rehospitalization group and the difference was non-significant (p=0.651). There were 23.53% (8/34) females in the rehospitalization group compared to 27.12% (16/59) in the non-rehospitalization group (p=0.703).

The rehospitalization group had significantly more patients with NYHA class III at discharge (85.3% vs. 59.3%; p=0.009), longer index LOS >7 days (52.9% vs. 28.8%; p=0.021) (**Figure 2**), more patients with CKD (26.5% vs. 8.5%; p=0.019), higher PVH grade 3 (61.8% vs. 33.9%; p=0.03), lower LVEF (26.5% vs. 30.4%; p=0.003) (**Figure 3**), higher mitral regurgitation (MR) grade3 (32.4% vs. 6.8%; p=0.013), higher use of digoxin (55.9% vs. 8.5%; p=0.001), higher use of ICD (14.7% vs. 3.4%; p=0.046), lower use of spironolactone (73.5% vs. 94.9%;

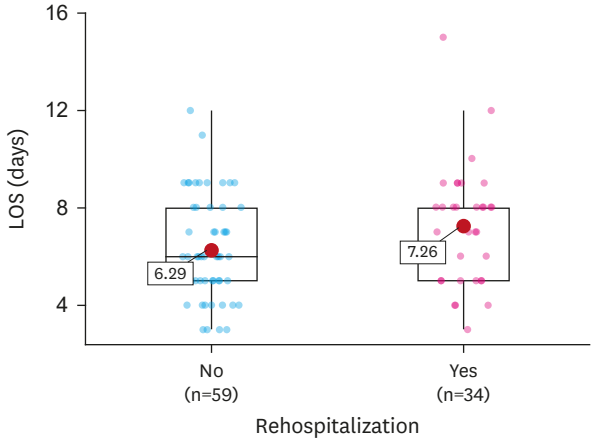

Figure 2. Boxplot of distribution of length of index hospital stay in 2 groups.
The figure below we see boxplot of length of index hospital stay in 2 sub-groups. The individual jittered data points of LOS are overlaid over transparent Boxplot for better visualisation. We see distribution of data in individual sub-groups of readmission based on these boxplots. The lower edge of box plot represents first quartile (Q1), horizontal bar represents the median, upper edge represents third quartile (Q3), two black lines (whiskers) emanating from boxplots signify range of non-outlier data for the particular sub-group. Lower whisker represents minimum (Q1– 1.5 interquartile range) non-outlier limit of LOS and upper whisker represents maximum (Q1+ 1.5 interquartile range) of LOS. Any data beyond whiskers of boxplots represents outliers in the sub-groups. The big brown point in the boxplots represents mean LOS of 2 groups and it has been annotated in the figure itself.
LOS = length of hospital stay.

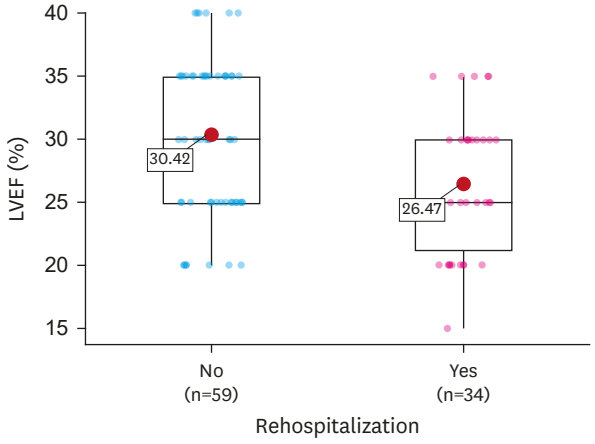

Figure 3. Boxplot of distribution of LVEF (%) in 2 groups.
The figure below we see boxplot of LVEF in 2 sub-groups. The individual jittered data points of LVEF are overlaid over transparent boxplot for better visualisation. We see distribution of data in individual sub-groups of readmission based on these boxplots. The lower edge of boxplot represents first quartile (Q1), horizontal bar represents the median, upper edge represents third quartile (Q3), two black lines (whiskers) emanating from boxplots signify range of non-outlier data for the particular sub-group. Lower whisker represents minimum (Q1– 1.5 interquartile range) non-outlier limit of LVEF and upper whisker represents maximum (Q1+ 1.5 interquartile range) of LVEF. Any data beyond whiskers of boxplots represents outliers in the sub-groups. The big brown point in the boxplots represents mean LVEF at admission of 2 groups and it has been annotated in the figure itself.
LVEF = left ventricle ejection fraction.

p=0.003), and lower use of ARNI (11.8% vs. 32.2%; p=0.028). There was no significant difference between the 2 study groups in terms of comorbidities such as HTN, DM, CAD, COPD, CVA and clinical parameters such as BP, HR, wide QRS complex (>120 msec), use of beta-blockers, ACE inhibitors and CRT devices. Regarding the laboratory data, the rehospitalized patients had significantly lower Hb at admission (10.2 vs. 11.3 gm/dL; p=0.032) (**Figure 4**), higher levels of blood urea at admission (83.1 vs. 51.9 mg/dL; p<0.001), higher

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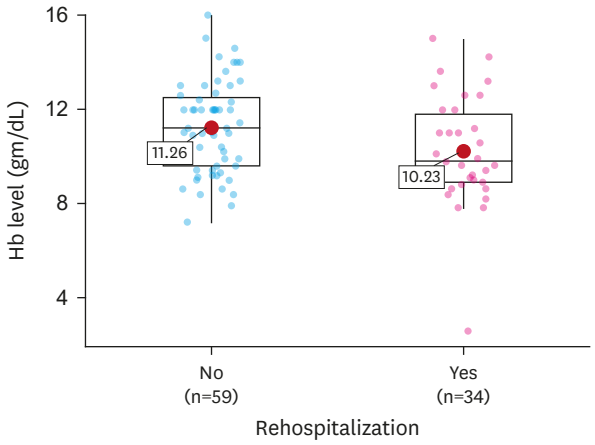

Figure 4. Boxplot of distribution of Hb level (gm/dL) in 2 groups.
The figure below we see boxplot of Hb level in 2 sub-groups. The individual jittered data points of Hb level are overlaid over transparent boxplot for better visualisation. We see distribution of data in individual sub-groups of readmission based on these boxplots. The lower edge of box plot represents first quartile (Q1), horizontal bar represents the median, upper edge represents third quartile (Q3), two black lines (whiskers) emanating from boxplots signify range of non-outlier data for the particular sub-group. Lower whisker represents minimum (Q1− 1.5 interquartile range) non-outlier limit of Hb and upper whisker represents maximum (Q1+ 1.5 interquartile range) of Hb. Any data beyond whiskers of boxplots represents outliers in the sub-groups. The big brown point in the boxplots represents mean Hb at admission of 2 groups and it has been annotated in the figure itself.
Hb = hemoglobin.

creatinine at admission (2.2 vs. 1.3 mg/dL; p=0.001), higher BNP level at admission (1,856.5 vs. 1,111.7 pg/mL; p<0.001), higher BNP level at discharge (586.1 vs. 307.8 pg/mL; p<0.001), higher troponin I level at admission (0.6 vs. 0.2 ng/mL; p<0.001) and higher troponin I level at discharge (0.10 vs. 0.01 ng/mL; p<0.001). There was no significant difference between the 2 study groups in terms of serum sodium and serum potassium levels at admission (**Table 1**).

Predictors of rehospitalization

Logistic regression analysis was carried out to look for significant predictors of rehospitalization. We selected variables based upon pre-specified clinical importance. Among all the parameters, on univariate analysis, patients being discharged with NYHA class III (odds ratio [OR], 3.98; CI, 1.44–12.99; p=0.012), longer LOS (>7 days) (OR, 2.78; CI, 1.16–6.80; p=0.022), having CKD (OR, 0.26; CI, 0.07–0.82; p=0.026), high urea level (OR, 1.03; CI, 1.01–1.05; p=0.001), high serum creatinine level (OR, 2.79; CI, 1.57–6.04; p=0.003), higher BNP level at admission (OR, 1.00; CI, 1.00–1.00; p<0.001) and at discharge (OR, 1.01; CI, 1.00–1.01; p<0.001), higher Troponin I level at admission (OR, 3.06; CI, 1.36–7.78; p=0.012) and having grade 3 MR (OR, 9.17; CI, 1.81–60.55; p=0.012) were significant predictors of rehospitalization at 60 days of discharge. Further on univariate analysis, higher Hb level (11.3 vs. 9.9 gm/dL; OR, 0.76; CI, 0.60–0.93; p=0.012) and higher LVEF at admission (30.4% vs. 26.5%; OR, 0.89; CI, 0.82–0.96; p=0.004) were associated with lesser risk of rehospitalization (**Table 2**).

On multivariate analysis of all the parameters which were included in univariate analysis, having longer length of index hospital stay (>7 days) (52.8% vs. 28.8%; OR, 1.79; CI, 1.2–7.25; p=0.040) and CKD (26.5% vs. 8.5%; OR, 3.06; CI, 1.1–57.04; p=0.050) independently increased the risk of rehospitalization at 60 days of discharge. Further, higher haemoglobin level (11.3 vs. 9.9 gm/dL; OR, 0.71; CI, 0.48–0.97; p=0.050) and higher LVEF at index admission (30.4% vs. 26.5%; OR, 0.87; CI, 0.75–0.99; p=0.049) were associated with

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Table 1. Baseline characteristic distribution between the 2 study groups

Variable	Rehospitalization		p value
	No	Yes	
No. of patients	59 (63.4)	34 (36.6)	
Age (years)	55.8±13.5	56.3±12.4	0.651
Sex			0.703
Male	43 (72.9)	26 (76.5)	
Female	16 (27.1)	8 (23.5)	
NYHA class at admission			0.357
II	1 (1.7)	0 (0.0)	
III	28 (47.5)	12 (35.3)	
IV	30 (50.8)	22 (64.7)	
NYHA alass at discharge			0.009
II	24 (40.7)	5 (14.7)	
III	35 (59.3)	29 (85.3)	
Length of stay			0.021
Long (>7 days)	17 (28.8)	18 (52.9)	
Short (≤7 days)	42 (71.2)	16 (47.1)	
DM			0.756
Yes	28 (47.5)	15 (44.1)	
No	31 (52.5)	19 (55.9)	
HTN			0.251
Yes	19 (32.2)	15 (44.1)	
No	40 (67.8)	19 (55.9)	
CAD			0.813
Yes	31 (52.5)	17 (50.0)	
No	28 (47.5)	17 (50.0)	
CVA			0.445
Yes	1 (1.7)	0 (0.0)	
No	58 (98.3)	34 (100.0)	
CKD			0.019
Yes	5 (8.5)	9 (26.5)	
No	54 (91.5)	25 (73.5)	
COPD			0.719
Yes	4 (6.8)	3 (8.8)	
No	55 (93.2)	31 (91.2)	
HR at admission	109.0±9.8	110.9±12.3	0.622
Systolic BP at admission (mmHg)	103.6±16.5	113.1±29.4	0.538
Diastolic BP at admission (mmHg)	62.6±14.0	69.0±17.0	0.159
Hb at admission (gm/dL)	11.3±1.9	10.2±2.3	0.032
Serum urea at admission (mg/dL)	51.9±24.0	83.1±45.5	<0.001
Serum creatinine at admission (mg/dL)	1.3±0.6	2.2±1.5	0.001
Serum sodium level at admission (mEq/L)	135.8±6.8	133.5±5.4	0.093
Serum potassium level at admission (mEq/L)	4.3±0.5	4.3±0.8	0.336
BNP at admission (pg/mL)	1,111.7±575.9	1,856.5±975.1	<0.001
BNP at discharge (pg/mL)	307.8±163.2	586.1±304.8	<0.001
Troponin at admission (ng/mL)	0.2±0.5	0.6±0.7	<0.001
Troponin at discharge (ng/mL)	0.01±0.1	0.1±0.1	<0.001
ECG			0.720
Wide QRS complex	42 (71.2)	23 (67.6)	
Narrow QRS complex	17 (28.8)	11 (32.4)	
CXR PA view			0.030
Grade 1	4 (6.8)	2 (5.9)	
Grade 2	35 (59.3)	11 (32.4)	
Grade 3	20 (33.9)	21 (61.8)	
LVEF (%)	30.4±6.1	26.5±5.4	0.003
MR grade			0.013
0	10 (16.9)	3 (8.8)	
1	28 (47.5)	12 (35.3)	
2	17 (28.8)	8 (23.5)	
3	4 (6.8)	11 (32.4)	

(continued to the next page)

Table 1. (Continued) Baseline characteristic distribution between the 2 study groups

Variable	Rehospitalization		p value
	No	Yes	
Beta-blocker			NA
Yes	59 (100.0)	34 (100.0)	
No	0 (0.0)	0 (0.0)	
ACE inhibitors			0.294
Yes	39 (66.1)	26 (76.5)	
No	20 (33.9)	8 (23.5)	
Aldosterone antagonists			0.003
Yes	56 (94.9)	25 (73.5)	
No	3 (5.1)	9 (26.5)	
Digoxin			<0.001
Yes	5 (8.5)	19 (55.9)	
No	54 (91.5)	15 (44.1)	
ARNI			0.028
Yes	19 (32.2)	4 (11.8)	
No	40 (67.8)	30 (88.2)	
ICD			0.046
Yes	2 (3.4)	5 (14.7)	
No	57 (96.6)	29 (85.3)	
CRT-D			0.257
Yes	7 (11.9)	7 (20.6)	
No	52 (88.1)	27 (79.4)	
CRT-P			0.121
Yes	4 (6.8)	0 (0.0)	
No	55 (93.2)	34 (100.0)	

Values are expressed as number (%) or mean±standard deviation.
ACE = angiotensin converting enzyme; ARNI = angiotensin receptor-neprilysin inhibitor; BNP = brain natriuretic peptide; BP = blood pressure; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CRT-D = cardiac resynchronization therapy-defibrillator; CRT-P = cardiac resynchronization therapy-pacemaker; CVA = cerebrovascular accident; CXR = chest X-ray; DM = diabetes mellitus; ECG = electrocardiogram; Hb = hemoglobin; HR = heart rate; HTN = hypertension; ICD = implantable cardioverter-defibrillator; LVEF = left ventricle ejection fraction; MR = mitral regurgitation; NA = not applicable; NYHA = New York Heart Association; PA = posterioranterior.

decreased the risk of rehospitalization (**Table 2**). In forest plot we can see NYHA class III at discharge has highest Odds of being rehospitalized followed by having CKD, higher creatinine levels, longer LOS, Troponin I level at admission, being male, higher BNP level at admission and discharge (**Figure 5**).

DISCUSSION

In this prospective study, we analyzed rehospitalization rate and predictors of rehospitalization in patients with LVEF <40% who were admitted for acute decompensation. Our study population was younger (55.8 years) as compared to western registries of acute HF like Acute Decompensated Heart Failure Syndromes (ATTEND)[9] (73 years), Acute Decompensated HEart Failure National REgistry (ADHERE)[10] (74 years), Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF)[11] (73 years), EuroHeart Failure Survey II (EHFSII)[12] (70 years), ADHERE International[13] (66 years), and Korean Acute Heart Failure (KorAHF)[14] (68.5 years) (**Table 3**). In our study, most common etiology of HF was CAD (53%) which is higher compared to Indian study by Vakil[15] (31%) and western registries like ATTEND[9] (33%) and KorAHF[14] (42.9%). The incidence of ischemic cause for HF was nearly similar to study by Docherla et al.[16] (55%) and other western registries like ADHERE[10] (58%), OPTIMIZE-HF[11] (46%), and EHFSII[12] (54%).

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Table 2. Univariate and multivariate analysis of predictors of rehospitalization

Variable	Rehospitalization		Univariate analysis		Multivariate analysis	
	No	Yes	OR (95% CI)	p value	OR (95% CI)	p value
No. of patients	59 (63.4)	34 (36.6)				
Age (years)	55.8±13.5	56.3±12.4	1.00 (0.97–1.04)	0.868	0.98 (0.92–1.04)	0.572
Sex			0.83 (0.30–2.16)	0.703	1.28 (0.29–5.80)	0.740
Male	43 (72.9)	26 (76.5)				
Female	16 (27.1)	8 (23.5)				
NYHA class at discharge			**3.98 (1.44–12.99)**	**0.012**	3.13 (0.70–18.02)	0.158
II	24 (40.7)	5 (14.7)				
III	35 (59.3)	29 (85.3)				
Length of hospital stay			**2.78 (1.16–6.80)**	**0.022**	**1.79 (1.2–7.25)**	**0.040**
Short (≤7 day)	42 (71.2)	16 (47.1)				
Long (>7 day)	17 (28.8)	18 (52.9)				
CKD			**0.26 (0.07–0.82)**	**0.026**	**3.06 (1.1–57.04)**	**0.050**
Yes	5 (8.5)	9 (26.5)				
No	54 (91.5)	25 (73.5)				
Hb level at admission (gm/dL)	11.3±1.9	9.9±2.6	**0.76 (0.60–0.93)**	**0.012**	**0.71 (0.48–0.97)**	**0.050**
Serum urea level at admission (mg/dL)	51.9±24.0	83.1±45.5	**1.03 (1.01–1.05)**	**0.001**	1.01 (0.98–1.05)	0.465
Serum creatinine at admission (mg/dL)	1.3±0.6	2.2±1.5	**2.79 (1.57–6.04)**	**0.003**	2.34 (0.44–14.01)	0.325
Serum sodium at admission (mEq/L)	135.8±6.8	133.5±5.4	0.94 (0.88–1.01)	0.097	0.98 (0.87–1.10)	0.738
BNP at admission (pg/mL)	1,111.7±575.9	1,856.5±975.1	**1.00 (1.00–1.00)**	**<0.001**	1.00 (1.00–1.00)	0.263
BNP at discharge (pg/mL)	307.8±163.2	586.1±304.8	**1.01 (1.00–1.01)**	**<0.001**	1.00 (1.00–1.01)	0.458
Troponin at admission (ng/mL)	0.2±0.5	0.6±0.7	**3.06 (1.36–7.78)**	**0.012**	1.30 (0.16–8.92)	0.796
Troponin at discharge (ng/mL)	0.0±0.1	0.1±0.1	180.11 (1.21–5,146.65)	0.096	10.87 (0.00–27,712.89)	0.636
CXR (PVH grade)						
1	4 (6.8)	2 (5.9)	-	-	-	-
2	35 (59.3)	11 (32.4)	0.63 (0.11–4.97)	0.619	0.23 (0.02–3.13)	0.235
3	20 (33.9)	21 (61.8)	2.10 (0.37–16.37)	0.420	0.19 (0.01–2.98)	0.225
LVEF (%)	30.4±6.1	26.5±5.4	**0.89 (0.82–0.96)**	**0.004**	**0.87 (0.75–0.99)**	**0.049**
MR grade						
0	10 (16.9)	3 (8.8)	-	-	-	-
1	28 (47.5)	12 (35.3)	1.43 (0.36–7.21)	0.631	0.39 (0.04–3.90)	0.393
2	17 (28.8)	8 (23.5)	1.57 (0.36–8.43)	0.567	0.11 (0.00–2.10)	0.151
3	4 (6.8)	11 (32.4)	**9.17 (1.81–60.55)**	**0.012**	0.53 (0.02–11.01)	0.678

Values are expressed as number (%) or mean±standard deviation.
BNP = brain natriuretic peptide; CI = confidence interval; CKD = chronic kidney disease; CXR = chest X-ray; Hb = hemoglobin; LVEF = left ventricle ejection fraction; MR = mitral regurgitation; NYHA = New York Heart Association; OR = odds ratio; PVH = pulmonary venous hypertension.

In contrast, some studies from India found Rheumatic heart disease as the most common etiology of HF (52%) followed by CAD.[17][18] To be consistent with previously published studies of HF rehospitalization, we found infection as the most common cause of precipitation of HF on index admission.[19] We had higher (6.78%) in-hospital mortality during the index hospital stay as compared to some western studies, which may be because of more sick patients admitted in our study.[10][11][13] We had lesser number of patients with hypertension (38%), compared to ATTEND[9] (59%), ADHERE[10] (74%), OPTIMIZE-HF[11] (71%), EHFSII[12] (63%) and KorAHF[14] (62%) survey. In our study diabetics were more (46%) and patients with COPD were less (7%) as compared to the western registries.[9][12] In contrast to western registries mean systolic BP in our study was lower i.e. 110 vs. 135–145mmHg.[9][12] These differences maybe because we included only chronic HF patients with low EF (<40%) who are likely to have lesser BP. Almost every patient was prescribed diuretic on discharge. The use of ACE inhibitor (65%) was almost similar to ADHERE International[13] and KorAHF[14] registry but lesser compared with ADHERE[10] (83%) and EHFSII[12] survey (80%). Beta-blocker and aldosterone antagonist prescription on discharge were higher compared to other registries.[10][12][14] The use of all these drugs was higher in our study mainly because they were all with reduced EF patients and admitted in the more decompensated state of HF.

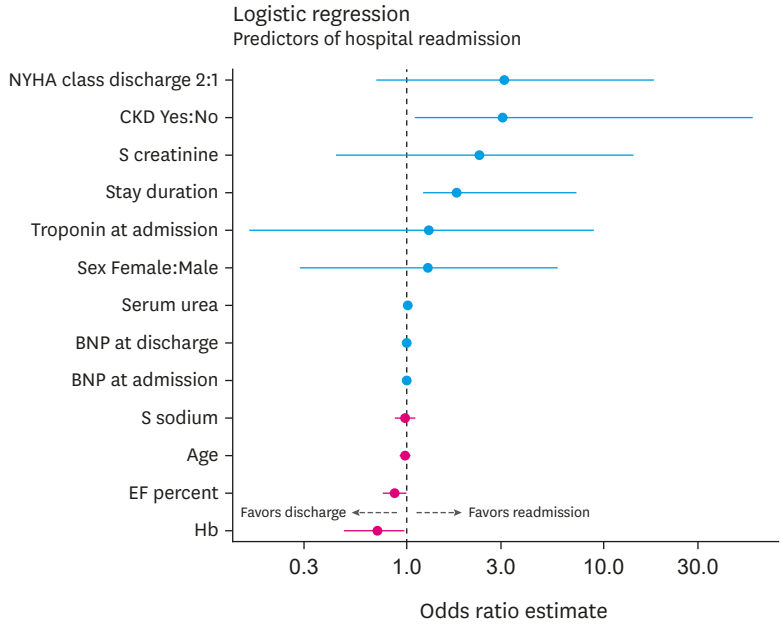

Figure 5. Forest plot of predictors of rehospitalization.
BNP = brain natriuretic peptide; CKD = chronic kidney disease; EF = ejection fraction; Hb = hemoglobin; NYHA = New York Heart Association.

The 60-day rehospitalization rate was 37% which was higher compared to western studies, most of which were readmitted in 30 days of discharge (80%).[20][21] We have similar 60-day mortality (5.3%) as O'Connor et al.[22] and lower than AFAR study by Seth et al.[17] (15.8%) (North India). The most common cause of rehospitalization was the cardiac cause (progression of the disease) similar to study by Arora et al.[23]

Identifying predictors among HF patients will help to improve risk stratification and to determine the optimal post-discharge plan for preventing readmission. Out of 23 clinical and

Table 3. Comparison of clinical characteristics of patients hospitalized with acute heart failure syndromes in our study with other registries

Characteristics	Our study	KorAHF[14]	ATTEND[9]	ADHERE[10]	OPTIMIZE-HF[11]	EHFSII[12]	ADHERE Internatinal[13]
Region	India	Korea	Japan	USA	USA	Europe	Asia-pacific countries
Sample size	103	5,625	1,110	15,968	48,612	3,580	10,171
Average age (years)	55.8±13.5	68.5±14.5	73±14	72±14	73±14	70±13	66±11
Male (%)	74	53.2	59	48	48	61	57
HTN (%)	38	62.2	71	74	71	63	64
Diabetes (%)	46	40	34	44	42	33	45
COPD (%)	7	11.3	9	31	31	39	24
CAD (%)	53	42.9	33	58	46	54	50
HR at admission (beats/min)	109 (9.8)	92.6 (26)	99 (30)	NA	87 (22)	Median, 95	NA
Systolic BP (mmHg)	110±11.6	131±30.3	147±38	144±33	143±33	135	NA
Creatinine at admission (mg/dL)	1.8±1.3	1.5±1.5	1.4±1.5	1.8±1.6	1.8±1.6	NA	NA
Length of stay (days)	6	9	21	4.3	4	9	6
Diuretics at discharge (%)	100	74.9	80	87	NA	84	85
ACE inhibitor at discharge (%)	65	65.9	NA	83	NA	80	63
Beta-blockers at discharge (%)	95	49.9	NA	80	NA	61	41
Aldosterone antagonist at discharge (%)	81	44.9	NA	33	NA	48	31
In hospital mortality (%)	6.78	4.8	7.7	3.8	3.8	6.7	4.8

Values are presented as mean±standard deviation not otherwise specified.
ACE = angiotensin converting enzyme; BP = blood pressure; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; HR = heart rate; HTN = hypertension; NA = not applicable; SD = standard deviation.

9 biochemical predictors of rehospitalization, those who were readmitted had a significantly higher proportion of patients with NYHA class III at discharge, longer LOS, CKD, low Hb, high Urea and Creatinine levels, high BNP and Troponin I level at admission and discharge, higher PVH grade, lower EF, higher MR grade, lower use of ARNI and aldosterone antagonist and higher use of digoxin and ICD. On multivariate analysis, longer LOS (>7 days) and having CKD were associated with increased risk, whereas low haemoglobin level and low LVEF at admission was associated with decreased risk of rehospitalization at 60 days of discharge.

The longer LOS (>7 days) (OR, 1.79) was found to be a significant independent predictor of rehospitalization similar to some of western studies, which may be due to more decompensated status at admission which took more time to recover.[24)25)] This suggests that patients who required longer LOS at index admission were more likely to get rehospitalized. Hence, such patients should be counselled for regular and frequent hospital visits, tailored treatment and lifestyle modifications.

As similar to some previous studies, we also found renal failure (OR, 3.09) to be an independent predictor of rehospitalization.[23)26)] One explanation for worse outcomes in CKD could be lack of effective therapeutic options available or possible underutilization of current therapies due to apprehensions surrounding side effects. Moreover, various factors like volume and pressure overload, anaemia and uremic toxins may be contributing to disease process in these patients. This may be also because of interdependent pathophysiology of HF and CKD (Cardio-Renal syndrome). Hence, patients with CKD should be counselled to avoid excess salt and fluid intake and to consult nephrologist frequently, in order to reduce frequent readmission. Incorporating nephrologist's care in such patient's management may become quite helpful. Studies addressing the optimal up-titration of HF drugs in case of concomitant CKD are required because such patients have been excluded from most HF trials. There are nearly one fourth of AHF patients in our study who were readmitted within 60 days of discharge, these results suggest that patients may benefit if therapies that preserve renal function were available.

We only enrolled patients with LVEF <40%. Similar to previous studies, patients with higher EF (30.4% vs. 26.5%; OR, 0.87) in our study had lesser risk of rehospitalization at 60 days of discharge.[27)] This suggests that patients with very low EF (<30%) should be optimized with better pharmacological treatment, frequent follow-up visits with tailored changes and measures to improve EF like the use of CRT.

Lower haemoglobin level at admission is likely related to haemodilution secondary to volume overload, malabsorption due to bowel congestion and the high number of associated chronic diseases. The mean Hb level at admission was 10.8 gm/dL. More than 50% of patients were having Hb <10 gm/dL, nearly similar to Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) study[28)] which has reported a 12% increase in the probability of death or rehospitalization within 60 days for every 1 g/dL decrease in admission Hb. Similar to some prior studies, we also found that higher Hb level at index admission (11.3 vs. 9.9 gm/dL; OR, 0.71) was associated with decreased risk rehospitalization.[26)29)] As one previous study has shown that correction of anemia, especially through intravenous route in HF patients reduced the risk of rehospitalisation, so by increasing level of Hb by intravenous infusion of iron we can reduce the rehospitalizations.[30)]

Other predictors like increased BNP levels, Troponin I levels, advanced age, female sex, wide QRS complex, grade 3 MR, increased blood urea level, altered serum sodium level, serum

potassium levels and higher pulmonary venous hypertension grading from CXR at admission were not found to be an independent predictor of rehospitalization. These findings maybe because of a lesser sample size and short duration of follow up.

It is suggested that all patients hospitalized for HF should be risk-stratified as high or low risk of rehospitalization according to the presence of the number of predictors. Those patients who are at the highest risk for rehospitalization should be given the highest intensity of multi-disciplinary support, education, follow-up, therapy, and access to resources, while those at lower risk should be followed less frequently in HF clinics. This customized approach is crucial when resources are sparse and finances limited and may lead to reduced rehospitalisation of HF patients.

Our study sample size was small. It was an observational study and thus prone to observer bias. These results could not be generalized to the whole spectrum of HF patients because of potential selection bias. All predictors were not included in the study. In our study maybe because of smaller sample size overall confidence interval values were broad, so further evaluation with larger study is warranted.

In conclusion, patients with HFrEF continue to have significantly higher rehospitalization rate (37%) and in-hospital mortality rates (6.78%) of any chronic disease. Predictors of worse outcomes after an initial HF hospitalization like low Hb, CKD, long LOS and very low EF can be used to identify patients, who require aggressive tailored therapy and follow-up. Further research is needed to identify the targets to improve survival among patients with HFrEF.

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