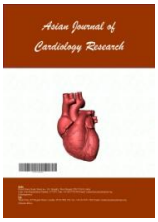

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Heart Failure Outcomes in Patients with and without Renal Impairment

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Authors' contributions

This work was carried out in collaboration among all authors. Author GRR helped in the research design, approval of final manuscript supervision of conduct and findings of the study and was also the treating physician of all the heart failure patients. Authors FK, TY, SH and HA managed the literature searches, writing of protocol, data collection, data compilation, data analysis, statistical analysis and drafting of manuscript. Authors AG and AUB helped in conceptualization and representation of work for approval from IRB. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To evaluate the differences in clinical characteristics, management patterns and outcomes in acute heart failure patients with and without renal impairment.
Study Design: Prospective observational study.
Place and Duration of the Study: Department of Cardiology, Princess Esra Hospital, Telangana, Hyderabad, from August 2019 to January 2021.
Methods: We included 127 acute heart failure patients who were divided into two groups based on their renal function: group I having GFR >60ml/min (normal renal function) and group II having GFR ≤60ml/min (renal impairment). Subjective data, objective parameters and management

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patterns of patients were recorded during the hospital stay and the outcomes (improvement in NYHA class, readmissions and mortality) were assessed at follow up.

Results: Among a total of 127 patients; 62 patients had a LVEF <40% (HFrEF), 38 patients had a LVEF 40-49% (HFmEF) and 27 patients had a LVEF ≥50% (HFpEF).The prevalence of renal impairment was found to be more in acute heart failure patients with preserved EF (77.7%). Patients in group II were less likely to receive ACEIs/ARBs (*P*=0.0010) and digoxin (*P*=0.001) and more likely to receive H+ISDN (*P*=0.0001).The mortality in group II patients was significantly more when compared to group I patients at the end of 1 year follow up (41.46% vs 13.33%; *P*=0.001). Group ll also showed less clinical improvement in NYHA class (32.92% vs 46.66%; *P*=0.12) at the end of 1 year follow up.

Conclusion: AHF patients with renal impairment had higher mortality at one year. In this study glomerular filtration rate was a stronger predictor of mortality than left ventricular ejection fraction. There was significant underutilization of important heart failure therapies in patients with renal impairment. Future clinical trials are suggested to validate benefits of disease modifying therapies (H+ISDN) and newer drugs (ARNIs, SGLT2 inhibitors) in patients with renal impairment.

Keywords: Acute heart failure; renal impairment; management; outcomes.

1. INTRODUCTION

Heart failure (HF) is a complex clinical syndrome caused by gradual decline of cardiac pump function due to structural and functional (systolic or diastolic) alterations leading to inability of heart to supply the peripheral tissues with required amount of blood and oxygen to meet their metabolic needs or demands.[1,2,3] It results in functional limitations, reduced quality of life, high risk of readmission and is the leading cause of morbidity and mortality worldwide. It is also the terminal stage of most cardiovascular diseases.[4,5] On admission, approximately 50% of patients hospitalized for HF will have renal impairment and even mild renal impairment is associated with elevated cardiovascular (CV) risk.[6,7,8] There is an underutilization of disease-modifying therapies in heart failure patients with renal impairment, because most of the medications used may lead to worsening renal function.[9,10] Treatment combined with active correction is essential to optimize both renal and cardiac function for patients with concomitant heart failure and renal impairment to improve the outcomes of heart failure in them.[11,12] In this study, we aim to evaluate the differences in clinical characteristics, management patterns and outcomes in acute heart failure patients with and without renal impairment.

2. MATERIALS AND METHODS

2.1 Objectives

The primary objective of the study was to assess the variation or differences in the management and their outcomes in AHF (Acute Heart Failure) patients with and without renal impairment. The secondary objectives were to assess and compare the clinical characteristics, laboratory parameters and mortality risk in acute heart failure patients with and without renal impairment and to estimate the prevalence rate of renal impairment in different types of heart failure: HFrEF (heart failure with reduced ejection fraction), HFmEF (heart failure with mid ejection fraction), HFpEF (heart failure with preserved ejection fraction).

2.2 Study Design and Participants

This is a prospective observational study in which a total of 127 acute heart failure patients who were admitted in the department of cardiology of a tertiary hospital were included for analysis. Patient enrolment was done from August 2019 to January 2020. The subjects were distributed into two groups on the basis of GFR (Glomerular Filtration Rate) - Group I: GFR >60ml/min i.e. normal renal function (n=45); Group II: GFR ≤60ml/min i.e. renal impairment (n=82).(Fig. 1) We reviewed the case sheets/ medical charts, which included a complete record of medications administered, laboratory measurements and daily progress notes of the patients.

2.3 Inclusion & Exclusion Criteria

Patients who were: >18 years age, NYHA(New York Heart Association) classification II-IV, diagnosed with de-novo or pre-existing heart failure were included in this study.

Exclusion criteria included: patients with acute STEMI (ST-segment elevation myocardial infarction), primary valvular heart disease, age less than 18 years, patients with incomplete data, patients lost to follow up, patients who did not comply to participate in the study, pregnant and lactating mothers, patients diagnosed with malignancies, congenital heart disease and rheumatic heart disease.

2.4 Covariates

The glomerular filtration rate was estimated on the basis of serum creatinine levels at admission and was calculated using MDRD (Modification of Diet in Renal Disease) study equation: eGFR=186 x (Sr. creatinine)-1.154 x (age)-0.203 (for females the value obtained was multiplied by 0.742).[13]

2.5 Assessment of Mortality Risk

The assessment of 1 year and 3 year mortality risk of HF patients was done using Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) risk calculator. The variables included in the risk score are as follows: age, gender, body mass index (BMI), New York Heart Association (NYHA) class, systolic BP, smoking, DM, left ventricular ejection fraction (LVEF), serum creatinine, use of RAAS blockers, beta-blocker use, chronic obstructive pulmonary disorder (COPD), and HF diagnosed >18 months ago.[14]

2.6 Evaluation Criteria of Medications Used

Medications were identified by therapeutic class. The data regarding the medications administered during hospitalization and prescribed at discharge in both the groups along with their variabilities was recorded.

2.7 Follow up

The follow up of all the patients was done at 1 month (hospital follow up), 3 months (hospital follow up) and 1 year (telephonic follow up) respectively and the outcomes of improvement in NYHA class, re-hospitalization and mortality were recorded at each follow-up.

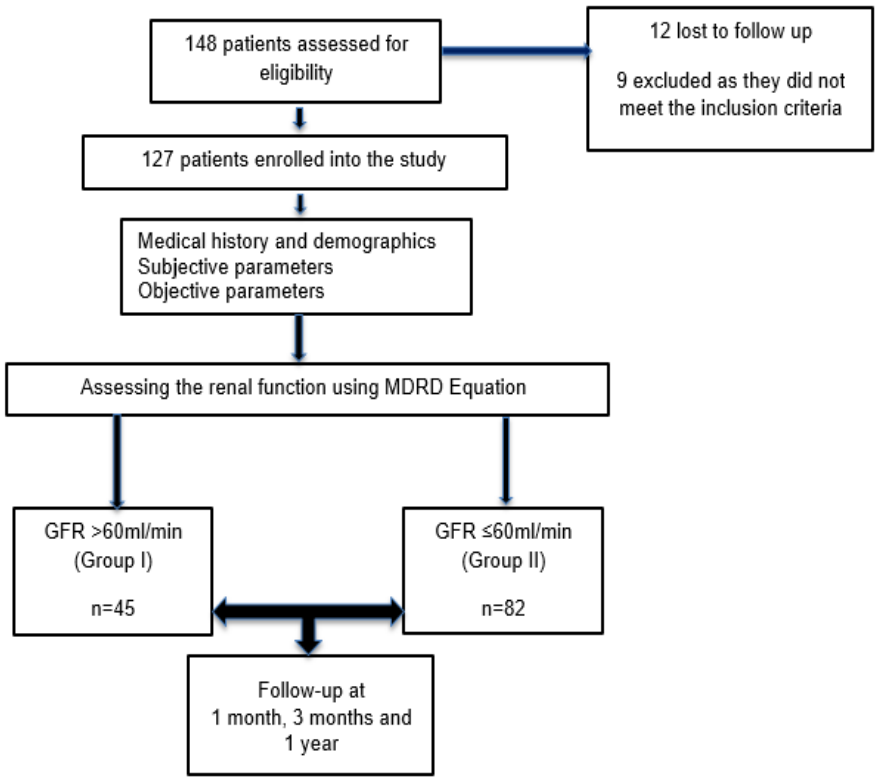

Fig. 1. Overview of patient distribution

n-no of patients, GFR – Glomerular filtration rate, MDRD-Modification of diet in renal disease

2.8 Outcomes

The primary end point of this study was mortality and the secondary end points were recurrent hospitalizations (for acute heart failure) and improvement in symptoms according to NYHA classification which was compared between both the groups.

2.9 Statistical Analysis

Mean and standard deviation were calculated for continuous variables whereas numbers and percentages for qualitative variables. The results on continuous variables were calculated by using independent t-test. Comparative analysis were performed using chi-square test and fisher's exact test for categorical variables, wherever suitable. A 5% level was used to identify differences in between groups that were of statistical significance (*P* value <0.05), since the CI(confidence interval) is 95%. Statistical evaluations were performed using SPSS version 20.0.

3. RESULTS

3.1 Group Wise Distribution

Patients in group I (n=45) had normal renal function and patients in group II had renal impairment (n=82). A significantly higher number of patients were found to have acute heart failure with renal impairment accounting for 65%. An overview of study distribution and plan of work is shown in Fig. 1. The comparison of demographics, clinical characteristics and other parameters is shown in Table 1.

3.2 Comparison of Age and Gender Distribution

The mean age among group I patients was found to be 55.91 ±13.35 whereas in group II patients, it was 63.05±11.24. Patients with renal impairment were observed to be of older age (*P* value =.001). The data collected on gender distribution revealed that there were more number of female subjects (65.55% females vs 44.44% males) in group I but that did not reach statistical significant difference.

3.3 Comparison of NYHA Classification

The NYHA class of all the patients was assessed and recorded upon admission. There was no significant statistical difference in the NYHA class between the two groups (*P* value= .97) but it was observed that AHF patients were found to be more in NYHA class III (53.33% in Group I & 51.21% in Group II) irrespective of renal function.

3.4 Comparison of Presence of Comorbidities and Variables at Admission

On comparing both the groups for the presence of comorbidities, we observed that there were significantly more number of patients with HTN (84.1%vs66.6%; *P*=.0230),IHD(85.36%vs55.5%; *P*=.0002) and Anemia (14.63% vs 2.22%;*P*=.027) in group II. On doing physical examination, pedal edema was found in more number of group I patients when compared to group II patients (60% vs 45.1%;*P* =.10) but this did not reach statistical significance. Patients in group II showed a higher diastolic blood pressure at admission (106.7±37.39 vs 81.33±20.29; *P*<0.0001).

3.5 Comparison of Mortality Risk Using MAGGIC Risk Score

At the time of admission, we calculated the mortality risk using the MAGGIC risk score and the results were obtained. On comparing both the groups, no significant difference in mortality risk was found at 1 year (*P*=.079) while a significant difference was observed in mortality risk in group II patients at 3 years (*P*=.003).

3.6 Comparison of Length of Stay and Revascularization Therapies

The mean length of stay in group II was found to be longer than group I (6.48±3.44 vs 5.55±2.41). CABG (Coronary Artery and Bypass Grafting surgery) and PTCA (Percutaneous Transluminal Coronary Angioplasty) were performed in more number of group I patients than group II patients (CABG: 13.3% vs 6.09%; PTCA: 20% vs 7.31%).

3.7 Prevalence of Different Types of Heart Failure

LVEF was obtained by 2-D Echo Doppler study at the time of admission: 62(48.81%) patients had HFrEF, 38(29.92%) patients had HFmEF and 27(21.25%) patients had HFpEF.

3.8 Onset of Renal Impairment and Prevalence of Renal Impairment in Different Types of Heart Failure

With regard to onset of renal impairment, it was found that, in-hospital identification of renal impairment was more commonly observed when compared to pre-existing renal impairment prior to being admitted in the hospital in group II patients (75.60% vs 24.39%). The order of prevalence of renal impairment in different types of acute heart failure was found to be as follows: HFpEF (77.7%) >HFmEF (73.68%) >HFrEF (53.22%). The prevalence of renal impairment was found to be more in acute heart failure patients with preserved EF. (Table 2) (Fig. 2)

3.9 Comparison Based on In-hospital and Discharge Management

Patients in group II were less likely to receive ACE/ARBs (57.7% vs 28.04%; *P*=.001) and Digoxin (44.4% vs 18.29%;*P*=.001) whereas they were more likely to receive CCBs (34.14% vs 15.5%,;*P*=.024), statins (97.5% vs 84.4%;*P*=.005),H+ISDN (52.43% vs 17.77%;*P*=.0001) and renal protective drugs (46.34% vs 0.02%;*P*>0.0001) when compared to group I patients during their hospital stay.

ACE/ARBs (42.22% vs 26.82%), Diuretics (93.33% vs 90.24%), MRAs (86.66% vs 71.95%), Anti-platelets (77.77% vs 76.82%), Digoxin (33.33% vs 13.41%), Ivabradine (60% vs 52.43%) and VRAs (2.22% vs 0%) were the medications that were prescribed in more number of group I patients at the time of discharge. CCBs (20.73% vs 2.22%), Statins (74.39% vs 64.44%), Anticoagulants (6.09% vs 4.44%), Antianginals (10.97% vs 8.88%), Anti-arrhythmics (9.75% vs 6.66%), H+ISDN (43.90% vs 0%), Renal protectives (35.36% vs 0%) and Calcium sensitizers (1.21% vs 0%) were the medications that were prescribed in more number of group II patients at the time of discharge. (Table 3) (Fig. 3)

3.10 Final Outcomes at 1 Month, 3 Months and 1 Year

The final outcomes (improvement in NYHA class, re-hospitalization & mortality) were assessed and compared in both groups at the end of 1 month, 3 months and 1 year respectively. Patients who were readmitted for acute heart failure was considered as re-hospitalization. An improvement in NYHA class (60% vs 57.31%) and reduced mortality rate (4.44% vs 13.41%) was observed in group I whereas the outcomes were quite similar with respect to re-hospitalization (6.66% vs 7.31%) when follow up of patients of both the groups was done at one month.

A significant difference was observed with respect to improvement in NYHA class and mortality at 3 months follow up. One year follow-up revealed an improvement in NYHA class (46.66% vs 32.92%), decreased re-hospitalization (15.55% vs 18.29%) in group I patients while a higher mortality rate was seen in group II patients(*P*=.001). (Table 4) (Fig. 4).There was one COVID-19 related death. Only 5 patients (12.5%) had in-hospital mortality whereas most of the deaths were out of hospital (87.5%).

4. DISCUSSION

Heart failure is the terminal stage of most cardiovascular diseases which results in functional limitations and reduced quality of life.[13,14,15] Population with multiple comorbidities is mainly affected by heart failure.[16] Renal impairment in comparison to impaired cardiac function has been shown to be a stronger predictor of mortality.[15,17,18] The true estimates to track the incidence, prevalence, etiology and outcomes of heart failure in Indian population are lacking.[19,20] In our study, we evaluated the differences in clinical characteristics, management patterns and outcomes in AHF patients with and without renal impairment.

In this study, a total of 148 AHF patients admitted in the cardiology department of the hospital from August 2019 to January 2020 were assessed. Out of which 9 patients did not meet inclusion criteria and 12 patients were lost to follow up. Hence 127 patients who met the inclusion criteria were included in the study and all these patients were followed up for 1 year. A small sample size will not allow analysis of five CKD subcategories hence renal impairment which is commonly defined using the CrCl threshold of 60 mL/min was considered to be acceptable.[8] In the present analysis, patients in group I had GFR >60ml/min and were categorized as those with normal renal function (n=45) while patients in Group II had GFR ≤60ml/min and were categorized as those with renal impairment (n=82). The incidence of renal impairment at admission was higher in our study which accounts for 65% compared to another study in which it was found to be 50% wherein a similar cutoff of GFR (60 ml/min) was used.[8]

Table 1. Demographic profile and other variables of patients of both groups

Variable	Group I n=45	Group II N=82	*P*-value
Age distribution	55.91±13.35	63.05±11.24	.001
Gender			
Male	20 (44.44%)	41 (50%)	.54
Female	25 (65.55%)	41 (50%)	
NYHA class			
II	3 (6.66%)	6 (7.31%)	.97
III	24 (53.33%)	42 (51.21%)	
IV	18 (40%)	34 (41.46%)	
Comorbidities			
HTN	30 (66.6%)	69 (84.14%)	.023
DM	25 (55.5%)	59 (71.95%)	.06
IHD	25(55.5%)	70 (85.36%)	.0002
AF	6 (13.33%)	6 (7.31%)	.26
COPD	3(6.66%)	8 (9.75%)	.59
Anemia	1 (2.22%)	12 (14.63%)	.027
OSA	2 (4.44%)	7 (8.53%)	.39
At admission			
Heart rate	94.84±19.47	100.7±22.25	.14
Systolic BP	129.3±24.99	132.5±27.51	.52
Diastolic BP	81.33±20.29	106.7±37.39	<0.0001
Pedal edema	27 (60%)	37 (45.12%)	.10
Laboratory parameters at admission			
Sodium	138.2±5.041	137.6±5.44	.51
Potassium	3.90±1.00	4.02±0.58	.40
Chloride	97.96±4.95	98.10±4.84	.87
Creatinine	0.93±0.21	1.81±0.64	<0.0001
Blood Urea	24.61±16.94	51.42±34.51	<0.0001
Laboratory parameters at discharge			
Sodium	139.1±4.38	137.8±5.29	.15
Potassium	3.96±0.51	4.00±0.53	.64
Chloride	98.13±3.92	98.13±4.78	.99
Creatinine	1.00±0.28	2.00±1.03	<0.0001
Blood Urea	36.62±12.91	65.77±34.59	<0.0001
Biomarkers			
Troponin	0.36±0.72	1.87±5.56	.16
NT-proBNP	10786±9042	11311±8215	.84
CAG	(Performed n=24)	(Performed n=26)	
SVD	12(50%)	5(19.23%)	<0.001
DVD	4(16.66%)	7(26.92%)	.020
TVD	8(33.33%)	14(53.84%)	<0.001
Revascularization therapies	(Performed n=11)	(Performed n=15)	
CABG	6(54.54%)	9(60%)	
PTCA	5(45.45%)	6(40%)	.47
Length of stay	5.552±2.41	6.48±3.44	.10

Data are number (%) of patients, mean, standard deviation
P value is calculated by independent t-test, chi square test
Group I: patients without renal impairment; Group II: patients with renal impairment
HTN-hypertension; DM-diabetes mellitus; IHD-Ischemic heart disease; AF-Atrial fibrillation; COPD-Chronic obstructive pulmonary disease; OSA-obstructive sleep apnea; BP-blood pressure; NT- proBNP-N-terminal pro b-type natriuretic peptide; CAG-Coronary artery angiography; SVD-Single vessel disease; DVD-Double vessel disease; TVD-Triple vessel disease; CABG-Coronary artery and bypass grafting; PTCA-Percutaneous Transluminal Coronary Angioplasty.

Table 2. Renal impairment related parameters

Parameters	Group II (n=82)	Percentage (%)
Onset of Renal Impairment:	62	75.60%
In-hospital	20	24.39%
Pre – existing		
Prevalence of Renal Impairment:		
HFrEF(n=62)	33	53.22%
HFmEF(n=38)	28	73.68%
HFpEF(n=27)	21	77.73%

Data are number (%) of patients
Group I: patients without renal impairment; Group II: patients with renal impairment
n-total number of patients with respective type of heart failure; HFrEF-heart failure with reduced ejection fraction; HFmEF-heart failure with mid ejection fraction; HFpEF-heart failure with preserved ejection fraction.

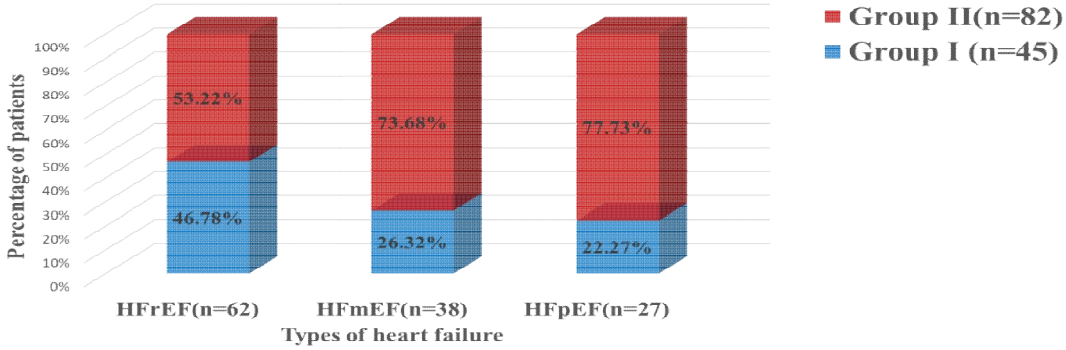

Fig. 2. Prevalence of renal impairment

Group I: patients without renal impairment; Group II: patients with renal impairment
HFrEF-heart failure with reduced ejection fraction, HFmEF-Heart failure with mid ejection fraction, HFpEF-heart failure with preserved ejection fraction.

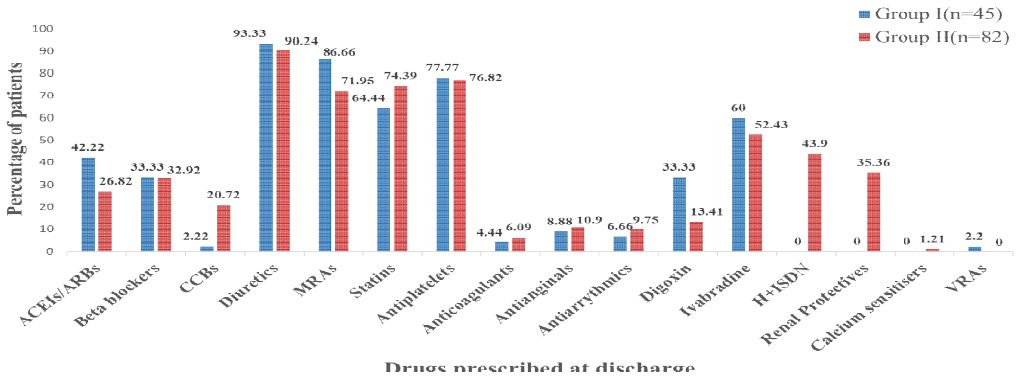

Fig. 3. Drugs prescribed in both groups at discharge

Group I: patients without renal impairment; Group II: patients with renal impairment
ACEIs/ARBs-Ace Inhibitors/Angiotensin Receptor Blockers; CCBs-Calcium Channel Blockers; MRAs-Mineralocorticoid receptor antagonists; H+ISDN-hydralazine+isosorbide dinitrate; VRAs-vasopressin receptor antagonists

Table 3.Differences in drugs prescribed during hospital stay and at discharge in both groups

Therapeutic drugs	Group I n=45	Group II n=82	*P*-value
In-hospital management			
ACEIs/ARBs	26(57.77%)	23(28.04%)	.001
Beta blockers	13(28.88%)	28(34.14%)	.54
CCBs	7(15.55%)	28(34.14%)	.024
Diuretics	45(100%)	80(97.56%)	.29
MRAs	41(91.11%)	68(82.92%)	.20
Statins	38(84.44%)	80(97.56%)	.005
Antiplatelets	37(82.22%)	75(91.46%)	.012
Anticoagulants	34(75.55%)	67(81.70%)	.41
Antianginals	9(20%)	22(26.82%)	.39
Antiarrhythmics	4(8.8%)	6(7.31%)	.75
Digoxin	20(44.44%)	6(7.31%)	.001
Ivabradine	31(68.88%)	61(74.39%)	.50
H+ISDN	8(17.77%)	43(52.43%)	0.0001
Renal Protectives	1(2.22%)	38(46.34%)	<0.0001
Calcium sensitisers	12(26.66%)	13(15.85%)	.14
VRAs	3(6.66%)	4(4.87%)	.67
Discharge management			
ACEIs/ARBs	19(42.22%)	22(26.82%)	.076
Beta blockers	15(33.33%)	27(32.92%)	.96
CCBs	1(2.22%)	17(20.73%)	.004
Diuretics	42(93.33%)	74(90.24%)	.74
MRAs	39(86.66%)	59(71.95%)	.059
Statins	29(64.44%)	61(74.39%)	.23
Antiplatelets	35(77.77%)	63(76.82%)	.90
Anticoagulants	2(4.44%)	5(6.09%)	1.000
Antianginals	4(8.88%)	9(10.9%)	1.000
Antiarrhythmics	3(6.66%)	8(9.75%)	.74
Digoxin	15(33.33%)	11(13.41%)	.008
Ivabradine	27(60%)	43(52.43%)	.41
H+ISDN	0(0%)	36(43.90%)	.035
Renal Protectives	0(0%)	29(35.36%)	<0.001
Calcium sensitisers	0(0%)	1(1.21%)	<0.001
VRAs	1(2.2%)	0(0%)	1.000

Data are number (%) of patients, mean, standard deviation
P value is calculated by chi square test, fisher's exact test
Group I: patients without renal impairment; Group II: patients with renal impairment
ACEIs/ARBs-Ace Inhibitors/Angiotensin Receptor Blockers; CCBs-Calcium Channel Blockers; MRAs-Mineralocorticoid receptor antagonists; H+ISDN-hydralazine+isosorbide dinitrate; VRAs-vasopressin receptor antagonists

Heart failure has been found to become the main reason of hospital admission in people older than 65 years of age.[21,22] The mean age of patients in our study was 55.91 ±13.35 compared to 63.05±11.24 in ESCAPE trial.[23] Like ischemic heart disease, heart failure also occurs at younger age in the Indian population compared to the western population.

Renal impairment leads to further advancement of heart failure and poor HF control which leads to a rapid decline of creatinine clearance rate at one mL/minute per month, causing an endless loop.[13,24] From the data obtained it was found

Table 4. Final Outcomes in both groups at each follow-up

Outcomes	Group I n=45	Group II n=82	*P*-value
1 month			
Improvement in NYHA class	27(60%)	47(57.31%)	.76
Rehospitalisation			
Mortality	3(6.6%)	6(7.31%)	.89
	2(4.44%)	11(13.41%)	.11
3 months			
Improvement in NYHA class			
Rehospitalisation	29(64.44%)	38(46.34%)	.051
Mortality			
	3(6.66%)	6(7.31%)	.89
1 year	396.66%)	20(24.39%)	.013
Improvement in NYHA class			
Rehospitalisation			
Mortality	21(46.66%)	27(32.92%)	.12
	7(15.55%)	15(18.29%)	.69
	6(13.33%)	34(41.46%)	.001

Data are number (%) of patients,
P value is calculated by chi square test, fisher's exact test
Group I: patients without renal impairment; Group II: patients with renal impairment
NYHA-New York heart association

Table 5. Cause of death in the patients

Cause of death	Group I(n=6)	Group II(n=34)
Cardiac (SCD)	3 (0)	22 (9)
Non cardiac (R)	2 (0)	9 (5)
Unknown	1	3

SCD-Sudden cardiac death; R-Renal cause

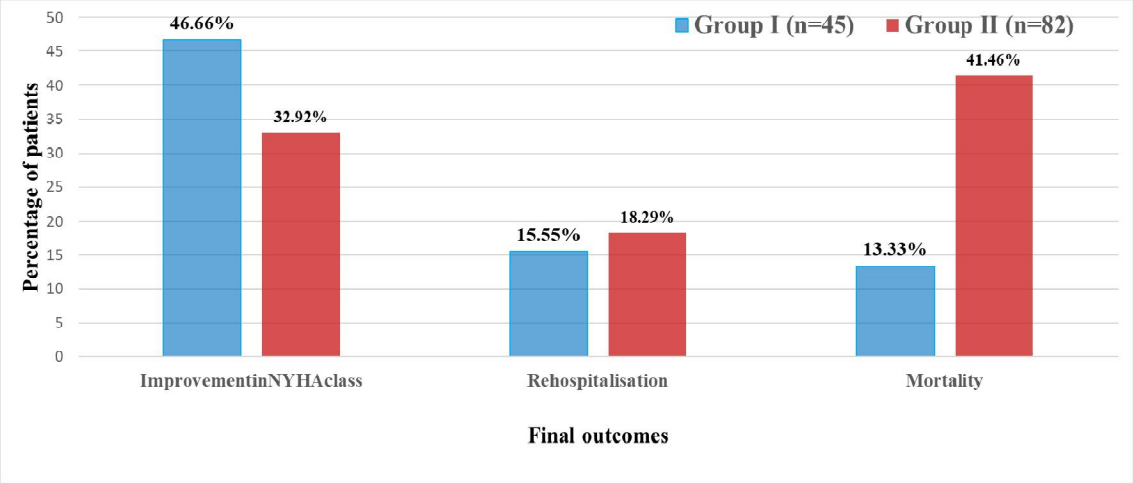

Fig. 4.Final Outcomes at one year in both groups

Group I: patients without renal impairment; Group II: patients with renal impairment
NYHA-New York heart association

that, in-hospital (75.60%) identification of renal impairment was more commonly observed when compared to pre-existing (24.39%) renal impairment in acute heart failure patients. Patients with renal impairment had more severe disease i.e. double & triple vessel disease compared to patients with normal renal function who had more prevalence of single vessel disease.

The European Society of Cardiology (ESC) has introduced a new category i.e. mid-range EF (HFmrEF) in which patients with an LVEF of 40–49% are included.[25] There is paucity of data regarding the association of LVEF and renal impairment.[26] HFpEF constituted one third of patients with renal impairment (Group II) but only one fifth of the total study population. The increased prevalence of renal impairment in HFpEF shows that heart failure in them is probably due to increase in preload and afterload that occurs with falling GFR (renal impairment), whereas in HFrEF, the principal reason is cardiac i.e. reduced myocardial contractility. The reduced GFR in these patients with HFrEF is probably a reflection of the global reduction in end organ perfusion resulting in poorer outcomes in this subset of patients.

In our study, GFR <60ml/min was a stronger predictor of mortality than ejection fraction. The mortality in patients with renal impairment irrespective of the type of heart failure (HFrEF, HFmEF, HFpEF) was similar.

The management of impaired renal function is crucial in the prognosis of patients with heart failure.[27] In case of hospital management, in acute heart failure patients with renal impairment there was underutilization of ACEIs/ARBs and Digoxin whereas they were more likely to receive H+ISDN which was slightly different from that reported in previous studies.[28] A similar prescription trend was also seen at the time of discharge. There is no proven efficacy of ACEIs/ARBs, MRAs & Beta blockers in HFpEF.[29] Since the patients with HFpEF were disproportionately high in Group II compared to Group I , the use of these drugs was significantly lower in Group II. The risk of initial renal function deterioration and hyperkalemia were the other reasons for their underutilization in those with renal impairment which is comparable to another study.[30]

Heart failure is the foremost cause of mortality worldwide and furthermore renal impairment is associated with higher one month re-hospitalization rate and poor prognosis.[7,31] Prediction of outcomes can guide the interventions made for better prognosis of heart failure patients which can be calculated using a risk score. Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) Risk Calculator is recommended which calculates 1 year and 3-year mortality risk. [32,33]

Although the MAGGIC risk calculator in our study projected mortality difference between the groups only at 3 years, there was significant difference in mortality at 1 year itself in our study. This may probably be due to poorer outcomes in Indian population especially those in lower socioeconomic strata like our study population.

The study period also coincided with the outbreak of first wave of COVID-19 pandemic in India which probably contributed to the poorer outcomes.

The difference in hospitalization was not statistically significant between the two groups despite significant mortality difference. This can also be attributed to the pandemic. Despite deteriorating health, probably many patients were reluctant to seek medical care due to fear of contracting COVID-19 infection as well as due to financial constraints during this difficult period. This is supported by the fact that most of the patients died at home (>80%).

In future, longer duration studies are suggested in order to determine the accuracy and beneficial aspects of using the risk score.

This analysis highlights the need for better evidence for treatment of the acute heart failure in Indian patients with renal impairment to improve morbidity and mortality in them.

5. LIMITATIONS

The design of our study is a prospective observational study. Since it is a single centre study, the management of AHF in our institution may not be representative of other hospitals, hence the findings may be less generalizable across all populations. Only two groups were analyzed (i.e., patients with or without renal impairment), because of smaller sample size the subgroup analysis on the basis of different stages of CKD wasn't feasible. The duration of the study was limited, hence the follow up of the patients could not be done for a longer period of time which otherwise would have helped us in determining better outcomes. The use of newer heart failure drugs like ARNIs and SGLT2 inhibitors was not in vogue during the study period and hence underutilized. COVID-19 pandemic could have also influenced the outcomes.

6. CONCLUSION AND FUTURE INSIGHTS

This study provides important insights into the demographics, treatment patterns and outcomes of AHF patients with and without renal impairment in an Indian setup. The prevalence of renal impairment is high in AHF patients with preserved LVEF (77.7%). On evaluating the treatment patterns, there was underutilization of ACEIs/ARBs and Digoxin in AHF with renal impairment. Heart failure occurs at an earlier age in Indian population with renal impairment and had poorer outcomes when compared to the western population. In this study, eGFR was a stronger predictor of mortality than the ejection fraction. The findings of our study also suggest a need for randomized controlled trials of acute heart failure patients with renal impairment to ascertain the benefits and risks of potentially disease modifying therapies like H+ISDN and newer drugs like ARNIs and SGLT2 inhibitors.

Renal impairment in different types of heart failure is a poor prognostic indicator. Renal impairment is the effect of decreased cardiac output in HFrEF whereas it is one of the causes for elevated cardiac filling pressures in HFpEF.It is of no wonder that drugs targeted on the RAAS system (ACEIs/ARBs/MRAs/ARNIs) and sympathetic system (β blockers) have been shown to work in HFrEF where these compensatory mechanisms become overactivated to compensate for the reduced cardiac output. On the other hand, these drugs have not shown benefits in HFpEF as they do not target its primary abnormality of increased cardiac filling pressures (rather than decreased cardiac output). For the same reason, diuretics which target it are the only drugs proven to be beneficial in HFpEF. By measuring the plasma renin activity, catecholamines in different types of compensated heart failure, future studies should investigate this hypothesis so that treatment can be tailored and targeted accordingly. Newer drugs like SGLT2 inhibitors are also likely to be useful in HFpEF. Future studies should explore this possibility.

CONSENT AND ETHICAL APPROVAL

This study has been approved by institutional review board (IRB) of the hospital. A written informed consent form was obtained from all the subjects enrolled in the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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