

The Impact of Sacubitril/Valsartan on Ejection Fraction, K Level and NT Pro BNP: A Prospective Observational Study

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Abstract: Heart failure is a condition that occurs in the heart when it cannot pump enough blood to meet the body's demands. It can happen because the heart is unable to fill itself up with an adequate supply of blood.

Background:

Heart failure is a complex clinical syndrome characterized by the heart's inability to pump sufficient blood to meet the metabolic demands of the body. This impairment may result from structural or functional abnormalities that reduce the heart's capacity to fill or eject blood effectively. Heart failure with reduced ejection fraction (HFrEF) remains a major public health concern, contributing significantly to morbidity, mortality, and frequent hospitalizations worldwide. Biomarkers such as N-terminal pro-B-type natriuretic peptide (NT-proBNP), serum potassium levels, and echocardiographic parameters including ejection fraction (EF) play a crucial role in evaluating disease severity, guiding therapy, and monitoring treatment response. Sacubitril/valsartan, an angiotensin receptor–neprilysin inhibitor (ARNI), has emerged as an advanced therapeutic option for HFrEF, demonstrating superior benefits compared to conventional therapies. However, real-world evidence assessing its impact on key clinical markers such as EF, NT-proBNP, and serum potassium levels remains limited. Therefore, this study aims to evaluate the effect of sacubitril/valsartan therapy on these parameters in patients diagnosed with HFrEF.

Materials and Methods: The research is a 6-month single-centre, prospective observational in which 42 patients were enrolled at the centre. The patient's data was collected about the demographics etc. The lab parameters were collected, statistical test were performed.

Results: A total of 42 patients diagnosed with heart failure reduced ejection fraction was included in the study among 24(57%) patients were males and 18(43%) and 2(5%) patients were in the age group of years 21-30, 1(2%) were in the age group of 31-40 years, 10(24%) were in the age group of 41-50 years, 15(36%) were in the age group of 51-60 years, 5(12%) were in the age group of 61-70 years and 8(19%) were in the age group of 71-80 and 1(2%) were in the group of 81-90 years, majority of the patients were in the age group of 41 -60. Out of 42 people, the mean of the K level found during the 1st follow up was 4.33 were as in the last follow up was 4.52 which was shown K level maintenance. The mean of the NT pro BNP level found during the 1st follow up was 12382 were as in the last follow up was 1453. The NT-pro BNP levels were reduced by 88.21% from the first to the last follow-up. The mean of the EF level found during the 1st follow up was 33% were as in the last follow up was 38%. The EF levels were improved 5% from the first to the last follow-up.

Conclusion: This study concludes that the use of the sacubitril/valsartan in HF r EF patients shown significant improvement in the lab parameters such as NT pro BNP, K level and EF which leads to reduce the mortality related to cardiovascular death.

Key Word: ARNI ,Heart Failure preserved Ejection Fraction, NT-pro BNP

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I. Introduction

Heart failure is a dangerous illness in which the heart is unable to adequately pump blood to fulfil demands. It is the leading cause of death in India. Furthermore, it has impacted over 26 million individuals worldwide, which is why it is known as a global pandemic. Heart failure is linked to an extremely high death rate [1]. Heart failure with decreased ejection fraction is characterized by weakening of the left ventricle and a decrease in blood flow with a left ventricular ejection fraction of $\leq 40\%$. Enhancing quality of life, symptom relief,

function, and shortened hospital stays are the main objectives of HF r EF therapy [2]. From a hemodynamic point of view, the conventional pathophysiology of heart failure was understood, with the idea that intravascular volume was maintained in response to pump failure through a combination of peripheral vasoconstriction and sodium and water retention. Therefore, inotropes, vasodilators, and diuretics were the mainstays of treatment for individuals with HF.

The increasing deterioration in HF, however, was not entirely explained by the hemodynamic model. Packer (1992) first offered the idea that HF is a neurohormonal illness, a theory that has since gained support. As a means of compensating for pump failure in HF r EF, the sympathetic nervous system (SNS) and the renin-angiotensin-aldosterone system (RAAS) have been identified as the first and second neurohormonal axes, respectively [3].

Ejection fraction is a critical measure of cardiac function and improvement in EF is associated with better clinical outcomes in HF patients. Evaluating the effects of sacubitril/valsartan on these parameters in a real-world setting is crucial for optimizing treatment strategies and improving patient outcomes [4].

II. Materials and Methods

This study was designed as a 6-month, single-centre, prospective observational study conducted at a tertiary care hospital. A total of 42 patients diagnosed with heart failure with reduced ejection fraction (HFrEF) and initiated on sacubitril/valsartan therapy were enrolled after meeting the study's inclusion criteria.

Study Population

Patients aged above 18 years with a confirmed diagnosis of HFrEF (EF < 40%) and who were prescribed sacubitril/valsartan were included. Patients with incomplete medical records, severe comorbidities that could interfere with follow-up, or those not willing to participate were excluded.

Data Collection

Demographic and clinical details such as age, gender, comorbidities, and medication history were collected using a structured data collection form. Laboratory parameters including NT-proBNP, serum potassium (K⁺), and ejection fraction (EF) were recorded at baseline (first follow-up) and at the end of the study period (last follow-up). Echocardiographic measurements were performed by trained cardiology technicians using standard protocols.

Statistical Analysis

All collected data were entered into Microsoft Excel and analysed using appropriate statistical methods. Continuous variables were presented as means and standard deviations. Comparative analysis between baseline and final follow-up values was performed using paired statistical tests. A p-value of <0.05 was considered statistically significant.

Inclusion criteria:

- Patients aged more than 18 years of age [male or female]
- Patients diagnosed with heart failure reduced ejection fraction [less than 50%]
- Acceptable renal function (glomerular filtration rate >30ml/min/1.73m) and
- Potassium level ≤5.0mmol/l when initiation.
- Systolic blood pressure ≥100mm Hg when initiation

Exclusion criteria:

1. History of hypersensitivity or allergy as well as known or suspected
2. contraindications.
3. Acute coronary syndrome
4. Patients who have an history of angioedema or severe hepatic and renal impairment, history of severe pulmonary disease. Patients who are having a systolic blood pressure of less than 100 mm Hg at screening or 95 mm Hg at randomization

Procedure methodology

- The procedure of the study involves three main steps: collection of patients demographic details, obtaining the consent from the patient and finally assessment of patients through obtaining consent requires giving the patient full and accurate information about the benefits, risks and procedure of the study. If the patient consent to the study, then they are included in the study. And if the patient does not consent, then they are excluded from the study. The patient is followed up during the drug course. The information collected is then analyzed for the

initiation of ARNI as guidelines directed. Once analysis is over , the patients results are noted down and a final report is submitted.

Statistical analysis

All collected data were entered into Microsoft Excel and analysed using appropriate statistical methods. Continuous variables were presented as means and standard deviations. Comparative analysis between baseline and final follow-up values was performed using paired statistical tests. A p-value of <0.05 was considered statistically significant.

III. Result

Baseline characteristics		ARNI therapy N = 42		
Age in years with Mean and SD		N(%)		
a)	20-30	2(5%)		
b)	31-40	1(2%)		
c)	41-50	10(24%)		
d)	51-60	15(36%)		
e)	61-70	5(12%)		
f)	71-80	8(19%)		
g)	81-90	1(2%)		
Gender		N(%)		
a)	Male	24(57%)		
b)	Female	18(43%)		
COMORBIDITIES				
		N(%)		
a)	HTN	25(59%)		
b)	T2DM	26(62%)		
c)	AKI	5(12%)		
d)	CKD	5(12%)		
e)	RHD	6(4%)		
f)	Others	9(21%)		
DOSAGE AT THE TIME OF INITIATION				
Sacubitril/valsartan 50 mg		14(33%)		
Sacubitril/valsartan 50 mg		28(67%)		
DESCRIPTIVE STATISTICS OF VITALS		Mean ± SD	Mean difference	P value
1 st follow up k level (mEq/L)		4.33±0.64	+ 0.19	=0.19
Last follow up k level(mEq/L)		4.52±0.70		
1 st follow up NT pro BNP (pg/ml)		12382±3567	- 10929	<0.0001
Last follow up NT pro BNP (pg/ml)		1453±3396		
1 st follow up EF (%)		33±7.24	+ 5	<0.0035
Last follow up EF (%)		38±7.99		
outcome (%)		N (%)		
Cardiovascular health improvement		36(86%)		
Cardiovascular health decline(death)		6(14%)		

A total number of 42 patients' data were collected who were diagnosed with HFrEF with comorbidities as per inclusion criteria.

Table no1.

Sl. No.	Gender	Number of patients (%)
1.	Male	24(57%)
2.	Female	18(43%)

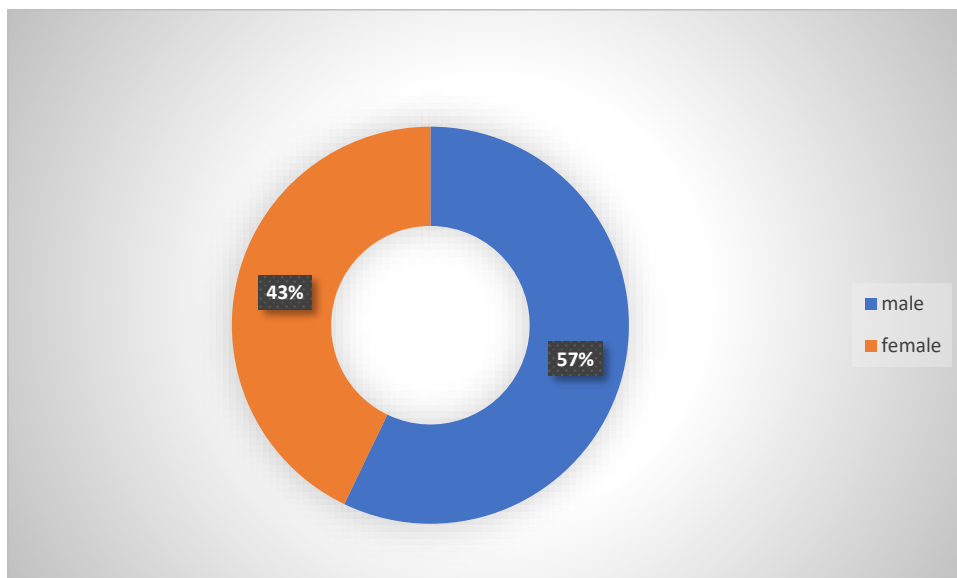


Table no2.

Sl. No.	Age in groups (in years)	Number of patients (%) N= 42
1.	20-30	2(5%)
2.	31-40	1(2%)
3.	41-50	10(24%)
4.	51-60	15(36%)
5.	61-70	5(12%)
6.	71-80	8(19%)
7.	81-90	1(2%)

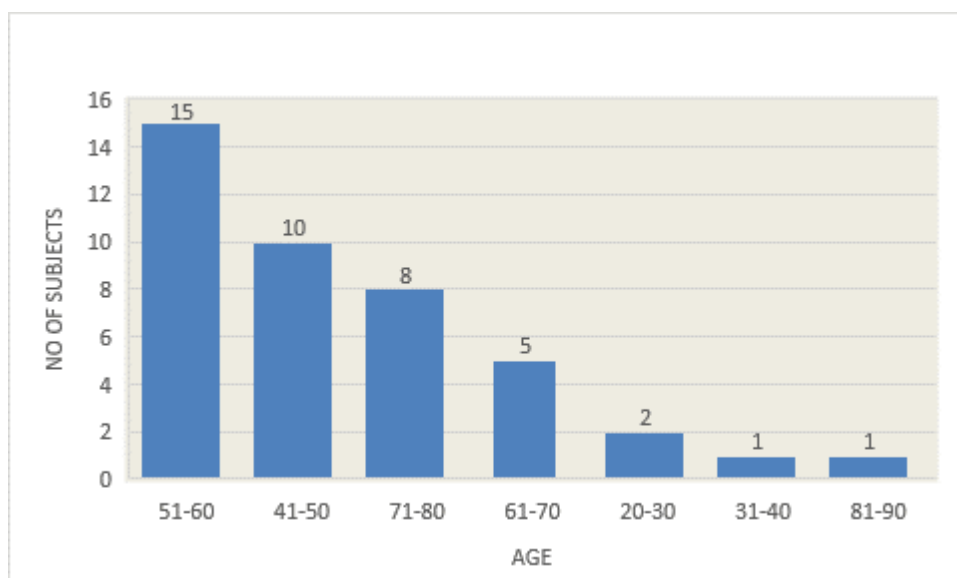


Table no. 3: - Department of admission distribution:

Sl. No.	Department of admission	Number of patients (%)
1.	General Medicine	12(28%)
2.	Cardiology	22(52%)

3.	Private care ward	4(10%)
4.	Intensive care unit	4(10%)

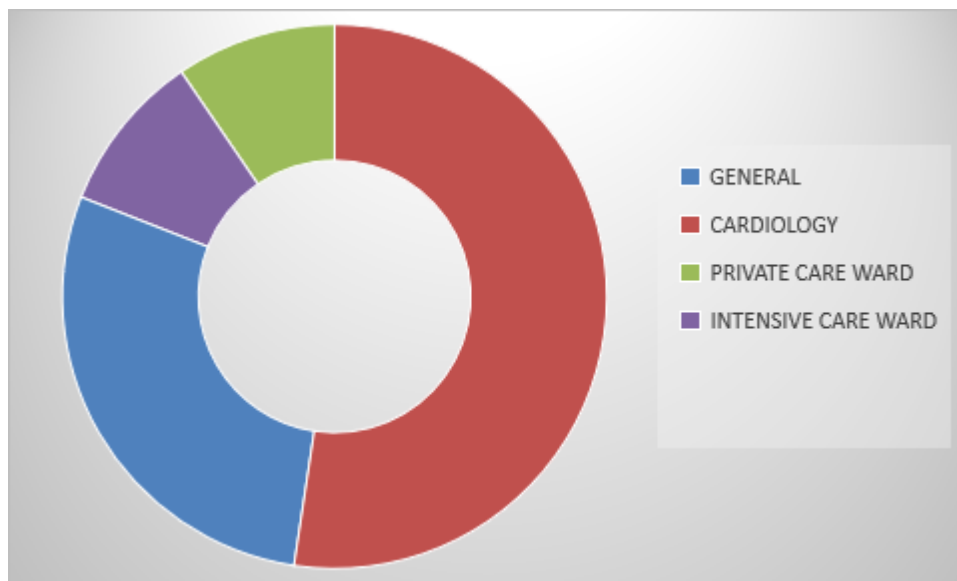


Fig: 8 shows department of admission distribution

Table no. 4: -Dose at the time of initiation:

Sl. No.	Dose at the time of initiation	Number of patients (%)
1.	Sacubitril/valsartan 50mg	14(33%)
2.	Sacubitril/valsartan 100mg	28(67%)

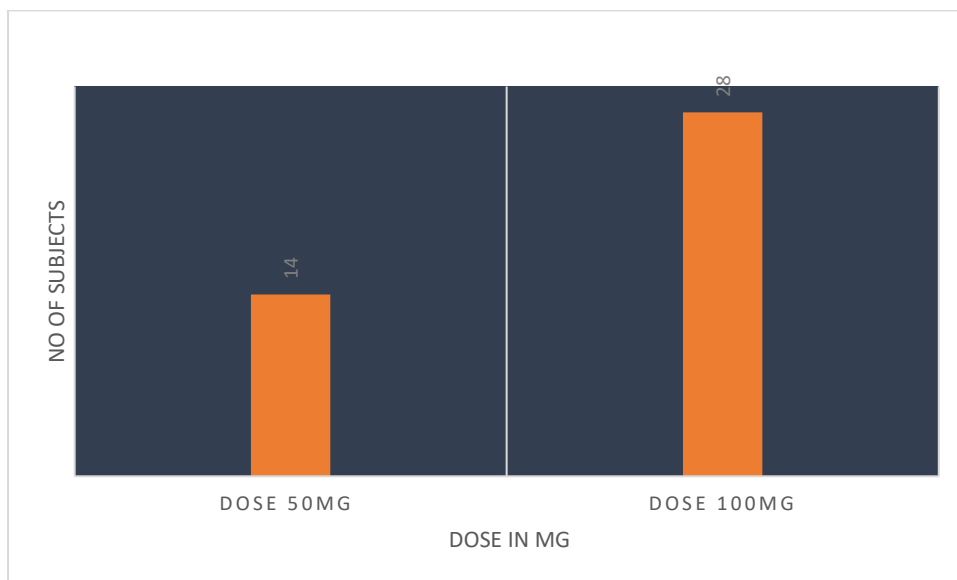


Table no 5: Improvement in K level

Sl. No	1 st Follow up	Last Follow up
01)	4.33	4.52

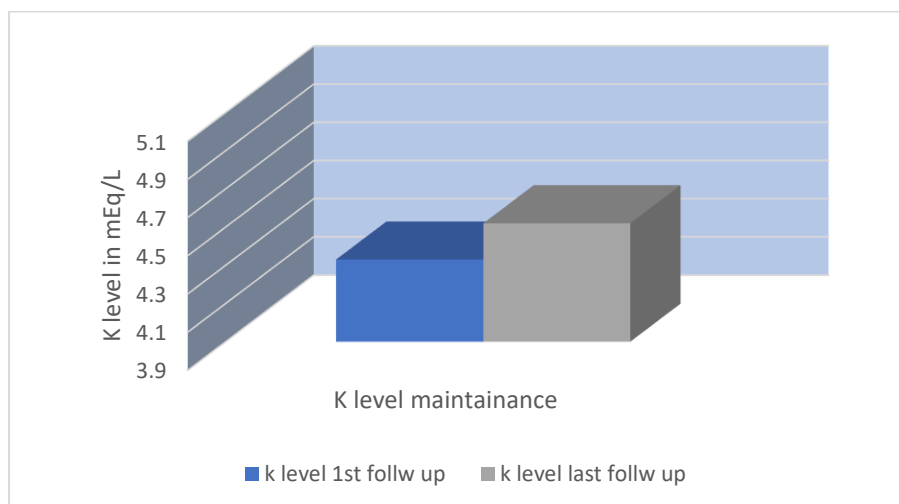


Table no 6: NT pro BNP level reduction

Sl. No	1 st Follow up	last Follow up
01)	12382	1453

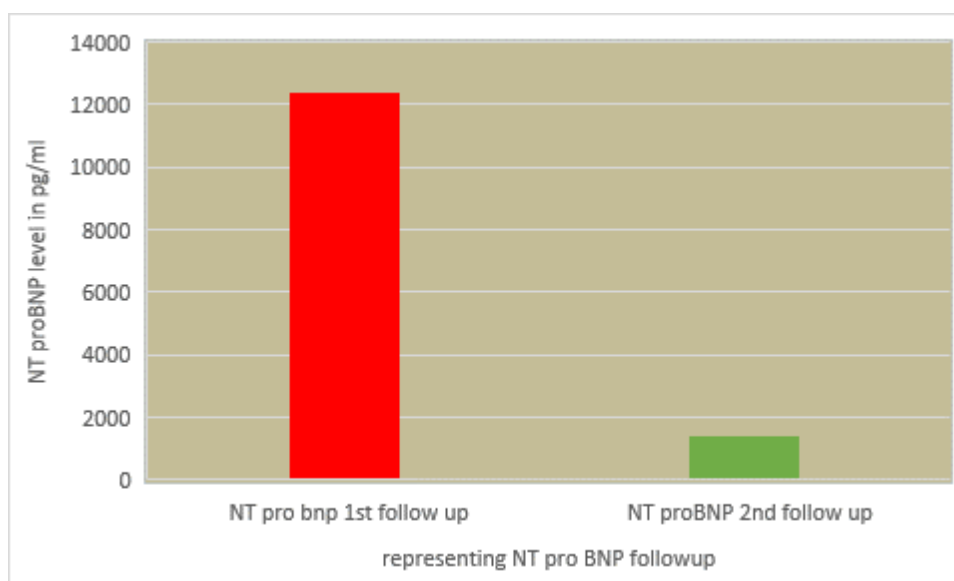


Table no 7: Improvement in EF level

Sl. No	1 st Follow up	Last Follow up
01)	33%	38%

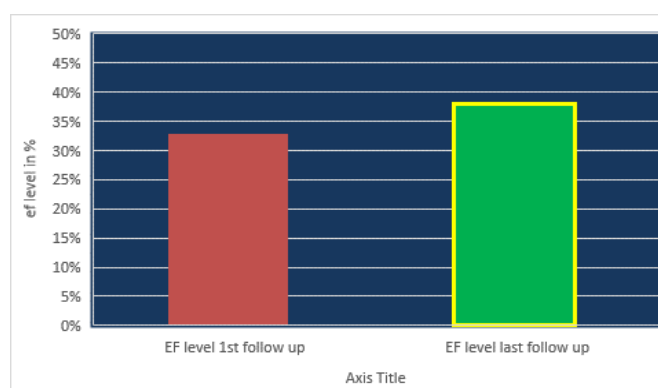


Table no 8: Adverse drug reactions and drug -drug interactions

Sl. No.	Problem with therapy	Number of patients(%)
1.	ADRs	9(21%)
2.	drug- drug interactions	8(19%)
3.	No problems with therapy	25(60%)

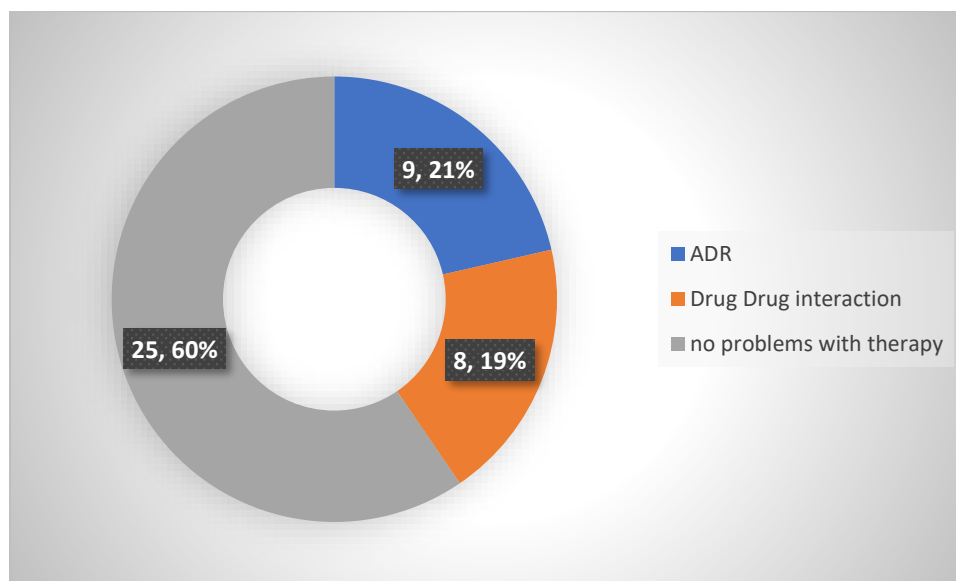
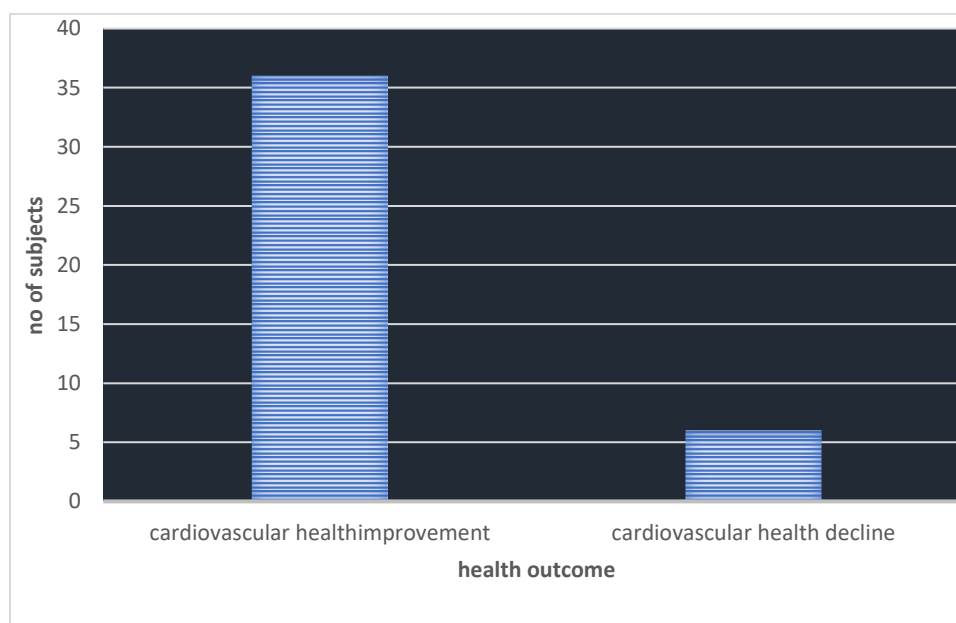


Table no 9: Outcome of ARNI therapy on cardiovascular health

Sl. No.	Outcome	Number of patients (%)
1.	Cardiovascular health improvement	36(86%)
2.	Cardiovascular health decline (death)	6(14%)



IV. Discussion

The present prospective observational study was conducted in the tertiary care hospital in Bangalore. The goal of the study was to find out the improvement of the lab parameters such as NT pro BNP, k level and EF level after initiation of the ARNI in 6-month course.

GENERAL DEMOGRAPHIC

In total of 42 patients, analysis of age, gender, diagnosis and vitals NT pro BNP, K LEVEL and EF were performed.

Age

The total mean age of the adult was 50 years ± 7 (67%) and mean age of elderly was 73 years (33%). The total mean age of study population is 57 years ± 13 . This study was consistent with the previous study with mean age of 57 years.

Gender

Total 42 patients were HFrEF patients, 24 (57%) patients were males and 18 (43%) patients were female in the present study.

Vitals:

K level:

Out of 42 people, the mean of the K level found during the 1st follow up was 4.33 were as in the last follow up was 4.52 compared with Ferreira JP research where it was shown slightly decrease in the potassium level which was consistent.

NT pro BNP:

Out of 42 people, the mean of the NT pro BNP level found during the 1st follow up was 12382 were as in the last follow up was 1453. The NT-pro BNP levels were reduced by 88.21% from the first to the last follow-up in this group of 42 people result of NT pro BNP (12382 $\pm$ 3567 Vs 1453 $\pm$ 3396 with CI 95%, P value <0.0001) compared with decreased NT-pro BNP by 17% (95% CI: 11% to 22%; p < 0.001) which was not consistent.

EF:

Out of 42 people, the mean of the EF level found during the 1st follow up was 33% were as in the last follow up was 38% (33 $\pm$ 7.24 to 38 $\pm$ 7.99). The EF levels were improved 5% from the first to the last follow-up in this group of 42 patients which was compared with Geoffrey Bayard LVEF from 32.6 $\pm$ 5 to 36 $\pm$ 6% which was improved 3.6% was consistent.

Problems associated with drug therapy:

Out of 42 people, the mean of the adverse drug reaction was found in 9 (21%), drug drug interaction was 8 (19%) and no problems with therapy found was 25 (60%). Thus, current study consistent with previous studies.

These findings, in conjunction with the results from larger clinical trials, support the use of sacubitril/valsartan in patients with HFrEF. The drug has been shown to improve clinical outcomes, reduce hospitalizations, and reverse cardiac remodelling in this population. However, individual patient factors and tolerability should be considered when initiating the ARNI therapy.

V. Conclusion

The following important biomarkers and clinical parameters may significantly improve with sacubitril/valsartan medication, according to the findings of this research of 42 patients with heart failure with reduced ejection fraction (HFrEF):

There was a statistically significant (p<0.001) rise in mean serum potassium levels from 4.33 mEq/L at the first follow-up to 4.52 mEq/L at the last follow-up.

- With ARNI medication, a little rise in potassium is normal and usually well-tolerated.
- There was a significant decline in the mean NT-pro BNP level, which dropped by 88.21% (p<0.001) from 12,382 pg/mL at the first follow-up to 1,453 pg/mL at the last follow-up.
- This significant reduction in NT-proBNP, a myocardial wall stress marker and outcome predictor, points to a positive reaction to sacubitril/valsartan.
- There was a 5% absolute increase (p<0.001) in the mean ejection fraction from 33% at the first follow-up to 38% at the last follow-up.
- Two key objectives of HF r EF treatment are improvement in EF and reversal of left ventricular remodelling.
- The majority (60%) of patients had no issues with sacubitril/valsartan treatment, despite 21% experiencing adverse medication responses and 19% experiencing drug-drug interactions.

The combo ARNI's tolerance can be maximized with careful titration. These results in a real-world patient population are in line with the findings of the historic PARADIGM-HF study, which showed that sacubitril/valsartan was superior to enalapril in lowering the risk of hospitalization for heart failure and cardiovascular mortality in individuals with HFrEF. The significant increases in EF and NT-proBNP reduction seen in this study offer mechanistic evidence for the therapeutic advantages of use of ARNI.

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