Section: Miscellaneous

Original Research Article

THE CLINICAL OUTCOME IN PATIENTS OF HEART FAILURE WITH REDUCED EJECTION FRACTION (HFREF) ON SACUBITRIL/VALSARTAN

Gaurav Sharma[1], Narinder Singh[2], Gaurav Mohan[3], Jaswinder Singh[2], Vikram Bhandari[2]

[1]3rd year JR, Department of Pharmacology, Sri Guru Ram Das University of Health and Sciences, Amritsar, Punjab, India
[2]Professor, Department of Pharmacology, Sri Guru Ram Das University of Health and Sciences, Amritsar, Punjab, India
[3]D.M. Cardiologist, Assistant Professor, Department of Medicine, Sri Guru Ram Das University of Health and Sciences, Amritsar, Punjab, India

Received *: 10/02/2026*
Received in revised form *: 20/03/2026*
Accepted *: 06/04/2026*

Corresponding Author:
Dr. Gaurav Sharma,
3rd year JR, Department of Pharmacology, Sri Guru Ram Das university of health and sciences, Amritsar, Punjab, India.
Email: dr.gauravsharma1985@gmail.com

DOI: 10.70034/ijmedph.2026.2.731

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (2); 4462-4469

ABSTRACT

Background: Heart failure (HF) is a global health crisis, impacting over 64 million individuals world-wide, with its prevalence steadily increasing due to aging populations and rising comorbidities. Sacubitril/valsartan represents a transformative therapy for HFrEF, offering significant reductions in mortality, hospitalization, and symptoms burden while improving left ventricular function and quality of life. The aim and objectiv was to evaluate the Clinical outcome in patients of heart failure with reduced ejection fraction (HFrEF) on Sacubitril/valsartan. Objective of it was to assess the quality of life using MLHFQ Questionnaire, to assess the temporal changes in BNP level at 2 weeks, 1 month, 3 month, and 6 months post treatment and to assess the tolerability of sacubitril/valsartan at 2weeks, 1 month, 3 months and 6 months.

Materials and Methods: An Interventional Study was conducted in the department of cardiology at Sri Guru Ram Das University of Health Sciences. The study subject (50) is fulfilling the inclusion criteria was selected for the study purpose. They were prescribed Tab Sacubitril/valsartan 50mg BD for 2 weeks. Study subjects were followed up at 2 weeks, 1 month, 3 months and 6 months of starting treatment. Quality of life was measured using the MLHFQ questionnaire. Data was compiled and statistically analyzed.

Results: Showed that sacubitril/valsartan provides substantial therapeutic benefits in patients with heart failure with reduced ejection fraction. The medication demonstrated sustained control of systolic and diastolic blood pressure, along with a marked and progressive reduction in BNP levels, indicating improved cardiac stress and neurohormonal balance.

Conclusion: Overall, patients experienced improvements in multiple domains including blood pressure control, cardiac function, neurohormonal balance, symptom relief, reduction in hospitalization needs, and maintenance of quality of life.

Keywords: Heart Failure, Sacubitril/valsartan, MLHFQ Questionnaire, control of systolic and diastolic blood pressure.

INTRODUCTION

The global prevalence of HF is estimated at 1–2% of the adult population, with higher rates in older age groups.[1] The Trivandrum Heart Failure Registry highlights that heart failure with reduced ejection fraction (HFrEF) constitutes 62% of cases, followed by heart failure with preserved ejection fraction (HFpEF) at 20%, with an in-hospital mortality rate of 8.4%.[2] Diagnosis of HF involves a comprehensive medical history, physical examination, elevated natriuretic peptide levels (above age- and context-specific thresholds), and confirmation of LNEF ≤40% via echocardiography.[3] Guideline-directed medical therapy (GDMT) for HFrEF emphasizes four key drug classes: beta-blockers, angiotensin receptor-neprilysin inhibitors (ARNIs), mineralocorticoid receptor antagonists (MRAs), and sodium-glucose

transport protein 2 (SGLT2) inhibitors.[4] These therapies, when used in combination, significantly improve clinical outcomes. Among these, sacubitril/valsartan, an ARNI, has emerged as a cornerstone therapy due to its robust evidence base.

Sacubitril/valsartan combines a neprilysin inhibitor (sacubitril) with an angiotensin receptor blocker (valsartan), targeting both the degradation of natriuretic peptides and the renin-angiotensin-aldosterone system (RAAS).[5] This dual mechanism promotes vasodilation, reduces ventricular remodeling, and mitigates neurohormonal activation, leading to improved cardiovascular outcomes.

The landmark PARADIGM-HF trial demonstrated that sacubitril/valsartan reduced the composite endpoint of cardiovascular death or HF hospitalization by 20% compared to enalapril in HFrEF patients (LNEF ≤40%, NYHA class II–IN).Current guidelines recommend sacubitril/valsartan as first-line therapy for HFrEF patients with NYHA class II–III symptoms who tolerate ACEIs or ARBs, and for de novo HFrEF treatment due to its benefits in improving health status, prognostic markers, and left ventricular remodeling.

Despite its efficacy, sacubitril/valsartan's use is limited by cost, access, and tolerability. In low-resource settings like India, high costs may restrict adoption, particularly among patients without insurance.[6] Sacubitril/valsartan represents a transformative therapy for HFrEF, offering significant reductions in mortality, hospitalization, and symptom burden while improving left ventricular function and quality of life. Its incorporation into GDMT, supported by robust evidence from trials like PARADIGM-HF and PRONE-HF, underscores its role as a first-line treatment.

Aim of the study is to evaluate the clinical outcome in patients of heart failure with reduced ejection fraction (HFrEF) on Sacubitril/valsartan whereas objective is to assess the quality of life using MLHFQ Questionnaire (Minnesota Living with Heart Failure Questionnaire- license issued on 8th Apr 2024), to assess the temporal changes in BNP level and toassess the tolerability of sacubitril/valsartan.

MATERIALS AND METHODS

An Interventional Study was conducted in the department of cardiology at Sri Guru Ram Das University of Health Sciences. A total of 50 patients were selected for the study based on the inclusion and exclusion criteria.

Inclusion Criteria

1. HFrEF patients aged 18 years and above.
2. New York heart association (NYHA) class 2-4

Exclusion Criteria

1. Heart failure primarily resulting from Right ventricular failure, pericardial disease, congenital heart disease.

A written and informed consent was obtained from all those who are enrolled in study. Confidentiality and privacy was ensured at all stages of the study period. Study was conducted from July 2024 to December 2025. A predesigned, pre tested and semi structured questionnaire was used for assessment. This was translated to Hindi, Punjabi and pretested and suitable modifications was done to get desired answer and retranslated back to English. The questionnaire was have the following information-sociodemographic details of the study subject, presenting complaints, follow up visits at 2 weeks, 1 month, 3 months and 6 months.

All of subjects were tested for blood pressure measurement (lying down, siting, standing) 2D Echo (machine name is NINID E 95) and BNP levels at baseline. They were prescribed Tab Sacubitril/valsartan 50mg BD for 2 weeks. Study subjects were followed up at 2 weeks, 1 month, 3 months and 6 months of starting treatment. 2D Echo was done at 6 months following treatment and number of days of hospitalization in previous 6 months were recorded. Quality of life was measured using the MLHFQ questionnaire.

MLHFQ Questionnaire (Minnesota Living with Heart Failure Questionnaire): The questionnaire is comprised of 21 questions around several physical, emotional and socioeconomic ways heart failure can adversely affect a patient's life. the patient marks a 0 (zero) to 5 (five) scale to indicate the extent to which each itemized adversity of heart failure has prevented the patient from living as they wanted to live during the past 4 weeks. The questionnaire is simply scored by summation of all 21 responses.7Data was collected and statistically analyzed.

RESULTS

The analysis focused on evaluating their clinical outcomes, including changes in functional status, symptom improvement, and cardiac performance parameters over the study period.

Table 1: Social background Distribution

Age wise distribution		
Age group	**No. of cases**	**%age**
21-40	4	8.0
41-60	23	46.0
61-80	21	42.0
81-90	2	4.0
Total	50	100.0
Gender wise distribution		
Gender		
Female	26	52%

Male	24	48%
Total	50	100.0
Area wise distribution		
Living area		
Rural	29	58.0
urban	21	42.0
Total	50	100.0
Occupation wise distribution		
Occupation		
Business man	4	8.0
Farmer	8	16.0
House wife	26	52.0
Labourer	7	14.0
Nad	2	4.0
Punjab police	1	2.0
Retired government officer	2	4.0
Total	50	100.0

[Table 1] demostrates that out of a total of 50 cases, the majority belonged to the age slab of 41–60 years, accounting for 23 cases (46%), making it the most affected group. This was followed closely by the 61–80 years age group with 21 cases (42%). Nery few cases were seen in the 21–40 years group (4 cases; 8%) and the 81–90 years group (2 cases; 4%). Overall, the data show that most cases (88%) occurred in individuals aged 41–80 years, indicating a higher prevalence in middle-aged and elderly populations.

In the present study on patients with heart failure with reduced ejection fraction (HFrEF) receiving sacubitril/valsartan, the gender distribution 24 males (48%) and 26 females (52%). In the present study on patients with heart failure with reduced ejection fraction (HFrEF) treated with sacubitril/valsartan, the majority of participants were from rural areas, accounting for 58% of the total cases, while 42% of patients resided in urban areas. This distribution indicates a higher representation of rural patients in the study population. On the basis of occupation, Farmers constituted 16% of the cases, followed by labourers at 14% and businessmen at 8%. A small proportion included retired government officers (4%), individuals with no active duty (NAD) (4%), and one member of the Punjab Police (2%). This distribution indicates that most patients belonged to non-working or physically active occupational backgrounds.

Table 2: Distribution of cases according to SBP and DBP

Systolic Blood pressure (mmHg)	**Mean±SD**
Sitting	116.01±12.68
Standing	112.94±11.31
Laying	111.72±9.98
Diastolic Blood pressure (mmHg)	**Mean±SD**
Sitting	67.56±12.08
Standing	66.66±9.21
Laying	66.00±8.31

In the present study patients with heart failure with reduced ejection fraction (HFrEF) treated with sacubitril/valsartan, the mean systolic blood pressure was found to be 116.01 ± 12.68 mmHg in the sitting position, 112.94 ± 11.31 mmHg in the standing position, and 111.72 ± 9.98 mmHg in the lying position. the mean diastolic blood pressure was 67.56 ± 12.08 mmHg in the sitting position, 66.66 ± 9.21 mmHg in the standing position, and 66.00 ± 8.31 mmHg in the lying position. These findings indicate a slight variation in both systolic and diastolic blood pressure upon changing posture from sitting to standing or lying, consistent with normal physiological variation.

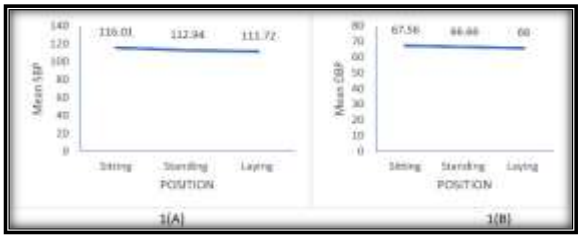


Figure 1: A and B depicts distribution of cases according to SBP and DBP

Table 3: distribution of cases according to followup of SBP and DBP

Follow up Systolic Blood pressure (mmHg)	**Mean±SD**
2 weeks	108.88±14.79
1 month	107.78±7.00
3 month	107.48±6.79
6 month	108.22±7.26
Follow up diastolic Blood pressure (mmHg)	**Mean±SD**
2 weeks	60.76±4.42
1 month	60.44±4.30

3 month	59.80±4.33
6 month	61.04±4.16

In the present study on patients with heart failure with reduced ejection fraction (HFrEF) receiving sacubitril/valsartan, the follow-up assessment of systolic blood pressure showed a gradual stabilization over time. The mean systolic blood pressure was 108.88 ± 14.79 mmHg at 2 weeks, 107.78 ± 7.00 mmHg at 1 month, 107.48 ± 6.79 mmHg at 3 months, and 108.22 ± 7.26 mmHg at 6 months. These findings indicate that systolic blood pressure remained well-controlled and stable throughout the follow-up period with minimal fluctuations. The mean diastolic blood pressure was 60.76 ± 4.42 mmHg at 2 weeks, 60.44 ± 4.30 mmHg at 1 month, 59.80 ± 4.33 mmHg at 3 months, and 61.04 ± 4.16 mmHg at 6 months. These findings suggest that diastolic blood pressure remained stable throughout the treatment period, reflecting effective hemodynamic management with sacubitril/valsartan therapy.

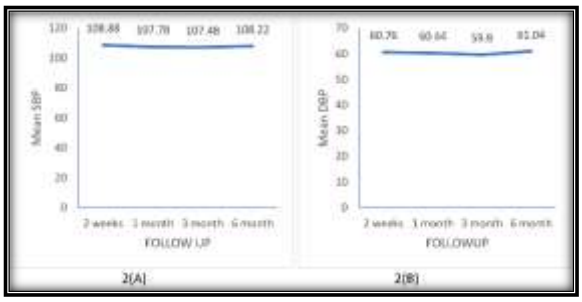


Figure 2: A and B distribution of cases according to followup of SBP and DBP.

Table 4: Mean difference in sitting BNP at follow-up intervals of 2 weeks, 1 month, 3 months, and 6 months.

BNP (pg/ml)	Mean±SD
Sitting	464.64±112.17
2 weeks	456.88±111.75
1 month	453.78±111.70
3 month	449.88±111.73
6 month	446.76±111.57

Repeated measures:

Source	SS	Df	MS	F	P	Ƞ2p
Between groups	9459.852	4	2364.963	1367.865	0.001	0.964
Within groups	352.705	196	1.729			

SS: Sum of square; df: degree of freedom; MS: mean square

BNP (pg/ml)	Post Hoc Tests (Tukey ANOVA)			Sig. (2-tailed)
	Mean±SD	95% Confidence Interval of the Difference		
		Lower	Upper	
Sitting/2 weeks	7.76±1.48	7.34	8.18	0.001
Sitting/1 month	10.86±1.67	10.39	11.33	0.001
Sitting/3 months	14.76±1.82	14.24	15.28	0.001
Sitting/6 months	17.88±2.02	17.31	18.45	0.001

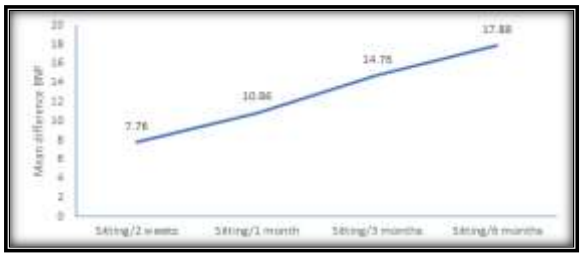


Figure 3: Mean difference in sitting BNP at follow-up intervals of 2 weeks, 1 month, 3 months, and 6 months

In the present study involving patients with heart failure with reduced ejection fraction (HFrEF) receiving sacubitril/valsartan therapy, a progressive and highly significant reduction in B-type natriuretic peptide (BNP) levels was observed across all follow-up intervals. The baseline mean BNP level of 464.64 ± 112.17 pg/mL decreased to 456.88 ± 111.75 pg/mL at 2 weeks, 453.78 ± 111.70 pg/mL at 1 month, 449.88 ± 111.73 pg/mL at 3 months, and further to 446.76 ± 111.57 pg/mL at 6 months. Repeated measures ANOVA demonstrated a highly significant difference over time ($F = 1367.865$, $p = 0.001$, partial $\eta^2 = 0.964$), indicating a very large effect size. Post hoc Tukey analysis revealed significant mean reductions in BNP compared to baseline, with differences of 7.76 pg/mL at 2 weeks, 10.86 pg/mL at 1 month, 14.76 pg/mL at 3 months, and 17.88 pg/mL at 6 months, all statistically highly significant ($p = 0.001$) with narrow confidence intervals. These findings suggest that sacubitril/valsartan therapy produces a consistent, progressive, and clinically meaningful decline in BNP levels over a 6-month period, reflecting sustained improvement in cardiac function and effective neurohormonal modulation in patients with HFrEF.

Table 5: 2D Echo comparison between baseline and after 6 months

2D echo	LVEF Mean±SD	p-value
Baseline	25.52±3.73	0.001
After 6 months	28.72±3.56	

In the present study on patients with heart failure with reduced ejection fraction (HFrEF) treated with sacubitril/valsartan, the 2D echocardiographic evaluation demonstrated a significant improvement in cardiac function over the study period. The mean baseline ejection fraction was 25.52 ± 3.73%, which improved to 28.72 ± 3.56% after six months of therapy. The change was statistically significant ($p = 0.001$), indicating that sacubitril/valsartan contributed to a meaningful enhancement in left ventricular performance and overall cardiac function in HFrEF patients.

Table 6: Distribution of Cases According to Hospital Stay (Days)

Number of hospitalization	No. of cases	%age
1	42	84.0
2	8	16.0
Total	50	100.0

In the present study on patients with heart failure with reduced ejection fraction (HFrEF) receiving sacubitril/valsartan, the majority of patients (84%) experienced only one time hospitalization during the study period, while 16% of patients required two time hospitalizations. This indicates that most patients had fewer hospital admissions after initiation of sacubitril/valsartan therapy, suggesting better clinical stability and improved disease control.

Table 7(a): Total MLHFQ at 2wk, 1 Month, 3 Month and 6 Months

Questions	2 week			1 mnth			3 mnth			6mnth		
	Score	No.	%age	Score	No.	%age	Score	No.	%age	Score	No.	%age
Causing swelling in your ankles or legs?	4	24	48.00	3	20	40.00	2	18	36.00	1	20	40.00
	2	26	52.00	2	30	60.00	1	32	64.00	0	30	60.00
Making you sit or lie down to rest during the day?	4	26	52.00	3	15	30.00	2	18	36.00	1	22	44.00
	2	24	48.00	2	35	70.00	1	32	64.00	0	28	56.00
Making your walking about or climbing stairs difficult	2	22	44.00	2	20	40.00	0	22	44.00	1	24	48.00
	2	28	56.00	2	30	60.00	1	28	56.00	0	26	52.00
Making your working around the house or yard difficult?	3	23	46.00	3	15	30.00	1	28	56.00	0	26	52.00
	3	27	54.00	3	35	70.00	2	22	44.00	1	24	48.00
Making your going places away from home difficult?	2	24	48.00	2	18	36.00	1	23	46.00	0	28	56.00
	2	26	52.00	2	32	64.00	0	27	54.00	0	22	44.00
Making your sleeping well at night difficult?	3	26	52.00	3	22	44.00	2	25	50.00	1	22	44.00
	2	24	48.00	2	28	56.00	1	25	50.00	0	28	56.00
Making your relating to or doing things with your friends or family difficult?	3	27	54.00	3	28	56.00	1	26	52.00	1	24	48.00
	2	23	46.00	2	22	44.00	1	24	48.00	0	26	52.00
Making your working to earn a living difficult?	2	28	56.00	2	22	44.00	2	24	48.00	1	28	56.00
	1	22	44.00	1	28	56.00	1	26	52.00	2	22	44.00
Making your recreational pastimes, sports or hobbies difficult?	2	26	52.00	2	28	56.00	1	28	56.00	1	22	44.00
	1	24	48.00	1	22	44.00	2	22	44.00	0	28	56.00
Making your sexual activities difficult?	2	30	60.00	2	32	64.00	1	34	68.00	0	28	56.00
	2	20	40.00	1	18	36.00	0	16	32.00	1	22	44.00
Making your eat less of the foods you like?	2	28	56.00	2	30	60.00	1	32	64.00	0	28	56.00
	1	22	44.00	1	20	40.00	0	18	36.00	1	22	44.00
Making you short of breath?	2	28	56.00	2	20	40.00	1	22	44.00	0	22	44.00
	1	22	44.00	1	30	60.00	0	28	56.00	1	28	56.00
Making you tired, fatigued, or low on energy?	2	23	46.00	2	25	50.00	1	28	56.00	0	24	48.00
	1	27	54.00	1	25	50.00	0	22	44.00	1	26	52.00
Making you stay in a hospital?	2	28	56.00	2	30	60.00	2	28	56.00	1	26	52.00
	1	22	44.00	1	20	40.00	0	22	44.00	0	24	48.00
Costing you money for medical care?	2	26	52.00	2	30	60.00	1	32	64.00	0	28	56.00
	2	24	48.00	1	20	40.00	0	18	36.00	1	22	44.00
Giving you side effects from treatments?	1	27	54.00	1	20	40.00	2	25	50.00	1	24	48.00
	0	23	46.00	0	30	60.00	1	25	50.00	0	26	52.00
Making you feel you are a burden to your family or friends?	3	26	52.00	2	30	60.00	1	25	50.00	0	26	52.00
	4	24	48.00	3	20	40.00	2	25	50.00	1	24	48.00
Making you feel a loss of self control in your life?	2	22	44.00	2	20	40.00	1	28	56.00	0	28	56.00
	1	28	56.00	1	30	60.00	2	22	44.00	1	22	44.00
Making you worry?	3	21	42.00	2	18	36.00	1	22	44.00	0	22	44.00
	2	29	58.00	1	32	64.00	0	28	56.00	1	28	56.00
Making it difficult for you to concentrate or remember things?	2	26	52.00	1	24	48.00	1	14	28.00	0	16	32.00
	1	24	48.00	0	26	52.00	0	36	72.00	1	34	68.00
Making you feel depressed	3	25	50.00	2	25	50.00	1	16	32.00	0	20	40.00
	2	25	50.00	1	25	50.00	0	34	68.00	1	30	60.00

Score 0= No effect, Score 1= Very little, Score 2= Little
Score 3= Moderate, Score 4= Much, Score 5= Very much

At 2 weeks, a substantial proportion of patients reported a moderate degree of limitation in daily activities and symptoms. Swelling of ankles or legs was reported with score 4 by 48% of patients and score 3 by 52%, indicating a considerable symptom burden in the early follow-up period. Similarly, 52% of patients reported that heart failure made them sit or lie down to rest during the day (score 4), while 48% experienced moderate difficulty (score 3). Limitations in walking or climbing stairs were present in the majority of patients, with 44% reporting moderate difficulty (score 3) and 56% reporting little difficulty (score 2). At 1 month, there was a noticeable improvement in most MLHFQ domains, with a shift from moderate scores (3–4) toward lower scores (1–2), indicating that the severity of symptoms and limitations in daily activities had decreased in many patients. Improvements were particularly observed in physical activities such as walking, household work, and traveling, as well as in sleep patterns and social interactions. By 3 months, further improvement was observed across most parameters, with a greater proportion of patients reporting minimal effect or little limitation, especially in domains related to mobility, fatigue, breathlessness, and emotional well-being.At 6 months of follow-up, many patients reported score 0 or score 1, indicating very little or no effect of heart failure symptoms on daily life.

Table 7(b): Total Mlhfq At Base Line, 2 Wks, 1 Months 3 Months And 6 Months Maximum score-105

MLHFQ	Mean±SD
Sitting	78.64±11.17
2 weeks	65.88±12.75
1 month	60.78±10.70
3 month	57.52±11.93
6 month	52.76±14.57

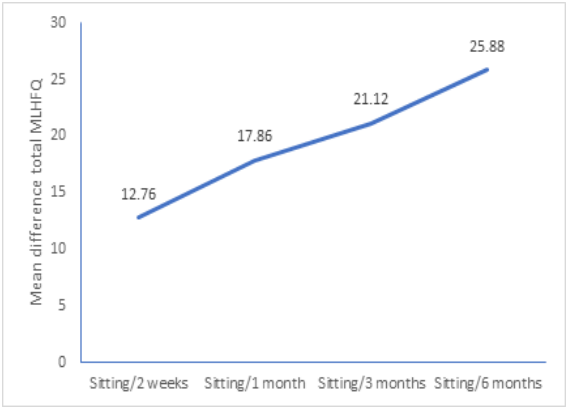
Repeated measures:

Source	SS	Df	MS	F	P	Ƞ2p
Between groups	4012.384	4	2038.096	33.84	<0.001	0.408
Within groups	444.200	196	8.75			

SS: Sum of square; df: degree of freedom; MS: mean square

MLHFQ	Post Hoc Tests (Tukey ANOVA)			Sig. (2-tailed)
	Mean±SD	95% Confidence Interval of the Difference		
		Lower	Upper	
Sitting/2 weeks	12.76±2.36	6.05	19.47	0.001
Sitting/1 month	17.86±4.55	11.15	24.57	0.001
Sitting/3 months	21.12±7.25	14.41	27.83	0.001
Sitting/6 months	25.88±6.22	19.17	32.59	0.001

[Table7(B)] a progressive and highly significant improvement in quality of life, as assessed by the Minnesota Living with Heart Failure Questionnaire (MLHFQ), was observed across all follow-up intervals. The baseline mean MLHFQ score of 78.64 ± 11.17 showed a steady decline to 65.88 ± 12.75 at 2 weeks, 60.78 ± 10.70 at 1 month, 57.52 ± 11.93 at 3 months, and further to 52.76 ± 14.57 at 6 months, indicating continuous symptomatic improvement. Repeated measures ANOVA demonstrated a statistically highly significant difference over time.



DISCUSSION

The burden of HF is substantial, with significant morbidity, mortality, and economic costs. Data from the Atherosclerosis Risk in Communities (ARIC) study indicate 30-day, 1-year, and 5-year case fatality rates post-hospitalization of 10.4%, 22%, and 42.3%, respectively.[8] A large-scale Lancet population study also revealed temporal shifts in HF incidence worldwide, highlighting growing prevalence in younger and middle-aged groups.[9] Over 70% of HF patients have comorbidities such as hypertension, diabetes, or chronic kidney disease, which exacerbate morbidity, diminish quality of life, and elevate mortality risk.[10,11]

With respect to age distribution, the highest number of cases was observed in the 41–60 years age group, which accounted for 46% (23 cases) of the total. This was closely followed by the 61–80 years age group, comprising 42% (21 cases). Together, these two groups represented 88% of all cases, indicating that the condition was predominantly seen in middle-aged and elderly individuals. The increased occurrence in these age groups may be attributed to age-related physiological changes, the presence of multiple

comorbidities, polypharmacy, and increased exposure to medications or risk factors. Overall, the study highlights that age is a significant factor, with the majority of cases occurring in individuals above 40 years of age, while gender does not appear to be a strong determining factor, given the nearly equal distribution between males and females.

Baseline mean systolic blood pressure (SBP) was 116.01 ± 12.68 mmHg (sitting), decreasing modestly to 112.94 ± 11.31 mmHg (standing) and 111.72 ± 9.98 mmHg (lying), with diastolic blood pressure (DBP) showing similar stability (67.56 ± 12.08 mmHg sitting; 66.66 ± 9.21 mmHg standing; 66.00 ± 8.31 mmHg lying). This postural variation (~3–5 mmHg SBP drop) falls within physiological norms and suggests absence of significant orthostatic hypotension at baseline, a common concern prior to initiating angiotensin receptor-neprilysin inhibitors (ARNIs) like sacubitril/valsartan.

The significant reduction in sitting systolic blood pressure (SBP) observed in patients with heart failure with reduced ejection fraction (HFrEF) on sacubitril/valsartan, with mean differences of 7.22 mmHg at 2 weeks, 8.32 mmHg at 1 month, 8.62 mmHg at 3 months, and 7.88 mmHg at 6 months compared to baseline (mean SBP 116.01 ± 12.68 mmHg), aligns with the vasodilatory and natriuretic effects of sacubitril/valsartan mediated through neprilysin inhibition and angiotensin receptor blockade, yielding sustained hemodynamic improvement over 6 months. This pattern is consistent with the PARADIGM-HF trial, which reported a mean SBP reduction of approximately 3–5 mmHg at 8 months with greater early drops in the sacubitril/valsartan arm versus enalapril (McMurray et al., 2014),[12] and the TITRATION study, which demonstrated safe SBP lowering to ~5–8 mmHg within 3–6 weeks using gradual up-titration in stable HFrEF patients (Senni et al., 2019).[13]

The progressive and statistically significant reduction in sitting B-type natriuretic peptide (BNP) levels in HFrEF patients treated with sacubitril/valsartan—mean differences of 7.76 pg/mL ($p<0.001$) at 2 weeks, 10.86 pg/mL ($p<0.001$) at 1 month, 14.76 pg/mL ($p<0.001$) at 3 months, and 17.88 pg/mL ($p<0.001$) at 6 months compared to baseline (464.64 ± 112.17 pg/mL)—demonstrates sustained neurohormonal deactivation and reduced myocardial wall stress, consistent with the drug's enhancement of natriuretic peptide bioactivity and suppression of the renin-angiotensin system. Although absolute BNP reductions appear modest, the consistent downward trajectory over 6 months aligns with biomarker substudies from the PARADIGM-HF trial, which reported a ~12–15% relative reduction in NT-proBNP (a more stable analyte) by 1 month and ~20–25% by 8–12 months with sacubitril/valsartan versus enalapril (Książczyk M et al), 2020; Zile et al, 2019).[14,15]

The statistically significant improvement in left ventricular ejection fraction (LNEF) from 25.52 ± 3.73% at baseline to 28.72 ± 3.56% after 6 months of sacubitril/valsartan therapy (mean increase 3.20%, $p=0.001$) in patients with HFrEF indicates favorable reverse cardiac remodeling and enhanced systolic function, driven by the drug's combined neprilysin inhibition and angiotensin receptor blockade, which reduce afterload, wall stress, and fibrotic signaling. This magnitude of LNEF gain is consistent with the PARADIGM-HF echocardiographic substudy, which reported a ~2.5–3.0% absolute increase in LNEF at 9 months with sacubitril/valsartan versus enalapril (Januzzi et al, 2019),[16] and the PRONE-HF trial, demonstrating a mean LNEF improvement of 5.2% at 6 months and 9.4% at 12 months, strongly correlated with reductions in NT-proBNP (Januzzi et al, 2019).[16] There were few limitations of the study which includes delimited to patients visiting a single health centre, Study duration was restricted, as it was an academic project with time-limit. Moreover, study had a small sample size.

CONCLUSION

The findings of this study suggests that the initiation of sacubitril/valsartan, systolic blood pressure demonstrated a gradual but consistent reduction at 2 weeks, 1 month, 3 months, and 6 months, with each decrease being statistically significant and clinically meaningful. Diastolic blood pressure also declined significantly across all follow-up intervals. BNP levels, which reflect cardiac wall stress and neurohormonal activation, showed a marked decline from a high baseline value. This decrease was progressive and statistically significant at every follow-up interval, indicating improved cardiac unloading and reduced ventricular strain.

Hospitalization analysis revealed that the majority of patients required only one time hospital admission during the study period, reflecting good treatment tolerance and reduced episodes of acute decompensation. Symptoms assessment across physical, emotional, and social dimensions showed that most patients reported very little or little difficulty, indicating good functional status and stable day-to-day activity levels. Fatigue, breathlessness on exertion, leg swelling, and exercise intolerance were generally mild, highlighting the improvement in symptomatic burden with ongoing therapy. Emotional well-being indicators such as anxiety, tension, and feelings of depression were also rated as minimal by most participants, suggesting that better clinical stability translates into improved mental health status. Hence, it was concluded that sacubitril/valsartan provides substantial therapeutic benefits in patients with heart failure with reduced ejection fraction. The medication demonstrated sustained control of systolic and diastolic blood pressure, along with a marked and progressive reduction in BNP levels, indicating improved cardiac stress and neurohormonal balance. The significant enhancement in ejection fraction after six months reflects positive cardiac remodelling and improved myocardial performance.

REFERENCES

1. Savarese G, Lund LH. Global public health burden of heart failure. Card Fail Rev. 2017;3(1):7.
2. Harikrishnan S, Sanjay G, Anees T, Niswanathan S, Nijayaraghavan G, Bahuleyan CG, et al. Clinical presentation, management, in-hospital and 90-day outcomes of heart failure patients in Trivandrum, Kerala, India: the Trivandrum Heart Failure Registry. Eur J Heart Fail. 2015;17(8):794-800.
3. Hunt SA. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult. J Am Coll Cardiol. 2005;46(6):e1-82.
4. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42(36):3599-726.
5. McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, et al. Angiotensin–neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014;371(11):993-1004.
6. Shanbhag D, Graham ID, Harlos K, Haynes RB, Gabizon I, Connolly SJ, et al. Effectiveness of implementation interventions in improving physician adherence to guideline recommendations in heart failure: a systematic review. BMJ Open. 2018;8(3):e017765.
7. Bilbao A, Escobar A, García-Perez L, Navarro G, Quirós R. The Minnesota living with heart failure questionnaire: comparison of different factor structures. Health and Quality of Life Outcomes. 2016;14:1-1.
8. Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart failure incidence and survival (from the Atherosclerosis Risk in Communities study). Am J Cardiol. 2008;101(7):1016-22.
9. Conrad N, Judge A, Tran J, Mohseni H, Hedgecott D, Crespillo AP, et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. Lancet. 2018;391(10120):572-80.
10. Paolillo S, Scardovi AB, Campodonico J. Role of comorbidities in heart failure prognosis. Part I: Anaemia, iron deficiency, diabetes, atrial fibrillation. Eur J Prev Cardiol. 2020;27(Suppl 2):27-34.
11. Chamberlain AM, St Sauver JL, Gerber Y. Multimorbidity in heart failure: a community perspective. Am J Med. 2015;128(1):38-45.
12. McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, et al. Angiotensin–neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014;371(11):993-1004.
13. Senni M, McMurray JJ, Wachter R, McIntyre HF, Anand IS, Duino N, Sarkar A, Shi N, Charney A. Impact of systolic blood pressure on the safety and tolerability of initiating and up-titrating sacubitril/valsartan in patients with heart failure and reduced ejection fraction: insights from the TITRATION study. European journal of heart failure. 2018 Mar;20(3):491-500.
14. Książczyk M, Lelonek M. Angiotensin receptor/neprilysin inhibitor—a breakthrough in chronic heart failure therapy: summary of subanalysis on PARADIGM-HF trial findings. Heart failure reviews. 2020 May;25(3):393-402.
15. Zile MR, Claggett BL, Prescott MF, McMurray JJ, Packer M, Rouleau JL, Swedberg K, Desai AS, Gong J, Shi NC, Solomon SD. Prognostic implications of changes in N-terminal pro-B-type natriuretic peptide in patients with heart failure. Journal of the American College of Cardiology. 2016 Dec 6;68(22):2425-36.
16. Januzzi JL, Prescott MF, Butler J, Felker GM, Maisel AS, McCague K, Camacho A, Piña IL, Rocha RA, Shah AM, Williamson KM. Association of change in N-terminal pro–B-type natriuretic peptide following initiation of sacubitril-valsartan treatment with cardiac structure and function in patients with heart failure with reduced ejection fraction. Jama. 2019 Sep 17;322(11):1085-95.