



ASSOCIATION OF AST – ALT RATIO WITH FUNCTIONAL SEVERITY IN HEART FAILURE WITH REDUCED EJECTION FRACTION: A CROSS-SECTIONAL OBSERVATIONAL STUDY

Dr. Vinoth Khanna Gunasekaran¹, Dr.K.Sunthari ², Dr. K.Ram Kumar ³. Dr. Nichal KM ⁴

¹Associate Professor, Department of General Medicine, Government Thiruvapur Medical College, Thiruvapur, India.

² Assistant Professor, Department of General Medicine, Government Thiruvapur Medical College, Thiruvapur, India

³ Assistant Professor. Department of General Medicine, Government Thiruvapur Medical College, Thiruvapur, India

⁴ Post Graduate, Department of General Medicine, Government Thiruvapur Medical College, Thiruvapur, India

***Corresponding Author:** Dr. J. B. Ashraf Ali

*Associate Professor, Department of Physiology, Government Thiruvapur Medical College, Thiruvapur, India. E-mail: jeabeeaa@hotmail.com Phone: +91 98416 40600

Abstract

Background: Heart failure with reduced ejection fraction (HFrEF) frequently results in hepatic dysfunction due to persistent venous congestion and a diminished cardiac output. The aspartate aminotransferase to alanine aminotransferase (AST/ALT) ratio has been proposed as a marker of disease severity in heart failure. However, its relationship with functional severity is unclear.

Objectives: To evaluate the association between the AST/ALT ratio and functional severity, assessed by the New York Heart Association (NYHA) class and left ventricular ejection fraction (LVEF), in patients with HFrEF.

Methods: In this hospital-based cross-sectional study, 75 consecutive patients with HFrEF (LVEF <40%) were enrolled over a year. Patients with primary liver disease, alcohol use, sepsis, malignancy, or hepatotoxic drug exposure were excluded from the study. AST and ALT levels were measured using standardized assays, and the AST-to-ALT ratio was calculated. The participants were stratified into two groups: AST/ALT <1 and AST/ALT ≥1. Functional severity was assessed using the NYHA classification and echocardiographic LVEF. Group comparisons and correlation analyses were conducted. **Results:** Patients with AST/ALT ≥1 were older and had a higher prevalence of ischemic heart disease. They exhibited higher AST levels, whereas ALT levels were comparable between the groups. Although patients with AST/ALT ≥1 tended to have a higher NYHA class and lower LVEF, the differences were not statistically significant. Correlation analysis demonstrated no significant association between the AST/ALT ratio and the NYHA class or LVEF. The AST/ALT ratio correlated positively with AST levels, suggesting that the ratio elevation was driven primarily by AST increases.

Conclusions: In patients with HFrEF, the AST/ALT ratio was not independently correlated with functional severity, as measured by the NYHA class or LVEF. This ratio appears to reflect hepatic enzyme alterations rather than cardiac functional impairment. These findings support the role of the AST/ALT ratio as an adjunctive marker of hepatic involvement in HFrEF but not as a surrogate of functional severity.

Keywords: Heart failure; Reduced ejection fraction; AST/ALT ratio; Liver function tests; Functional severity

Introduction

Heart failure with reduced ejection fraction (HFrEF) remains a major contributor to global morbidity and mortality, despite advances in pharmacological and device-based therapies. (1) Beyond its primary cardiac manifestations, HFrEF is increasingly recognized as a systemic disorder characterized by multiorgan involvement, including renal dysfunction, skeletal muscle abnormalities, and hepatic impairment. (2) Among these, hepatic dysfunction represents a common but often underappreciated complication of chronic heart failure. (3)

The liver is particularly vulnerable to the hemodynamic effects of heart failure. Elevated right-sided filling pressures result in passive hepatic congestion, whereas reduced cardiac output may contribute to hepatocellular hypoxia. (4) These mechanisms can lead to biochemical abnormalities in liver function tests, even in the absence of intrinsic liver disease. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are frequently measured enzymes in routine clinical practice, and their ratio has long been used in hepatology to differentiate patterns of liver injury. (5)

In recent years, interest has emerged in repurposing the AST/ALT ratio as a potential biomarker for cardiovascular diseases, including heart failure. Some studies have suggested that an elevated AST/ALT ratio may be associated with worse outcomes or greater disease severity in patients with heart failure. However, the evidence remains inconsistent, and the biological interpretation of this ratio in the context of heart failure has not been well established. (6)

Functional severity in HFrEF is commonly assessed using the New York Heart Association (NYHA) classification and left ventricular ejection fraction (LVEF). (7) Although these measures capture symptomatic burden and systolic dysfunction, respectively, they do not fully reflect the complexity of systemic congestion and end-organ involvement. Whether hepatic enzyme patterns, specifically the AST/ALT ratio, correlate with these measures of functional severity remains unclear. (1)

The present study aimed to evaluate the association between the AST/ALT ratio and functional severity in patients with HFrEF. We hypothesized that if the AST/ALT ratio reflects cardiac functional impairment, it would correlate with the NYHA class and LVEF. Alternatively, the absence of such an association would suggest that the ratio primarily reflects hepatic involvement rather than cardiac dysfunction.

Methods

Study Design and Population

This hospital-based cross-sectional observational study was conducted at the Department of Medicine, Government Thiruvavur Medical College over a one-year period. Consecutive adult patients diagnosed with HFrEF were screened for eligibility criteria.

HFrEF was defined according to standard criteria, including clinical features of heart failure and echocardiographic evidence of left ventricular ejection fraction (LVEF) <40%. Diagnosis was established using the Framingham criteria and confirmed by transthoracic echocardiography.

Exclusion Criteria

To minimize confounding from non-cardiac causes of liver enzyme abnormalities, patients were excluded if they had any of the following:

- Known chronic liver disease
- History of significant alcohol consumption
- Acute or chronic viral hepatitis
- Sepsis or shock
- Malignancy
- Pregnancy
- Recent exposure to hepatotoxic medications

Data Collection

After obtaining written informed consent, demographic and clinical data were collected, including age, sex, comorbidities, etiology of heart failure, and the use of medications. Functional status was assessed using the NYHA classification by the treating physicians at the time of enrollment.

Laboratory Measurements

Venous blood samples were obtained at admission or during a stable outpatient evaluation. AST and ALT levels were measured using standardized enzymatic assays in an institutional laboratory. The AST/ALT ratio was calculated by dividing the AST level by the ALT level for each patient.

Participants were stratified into two groups:

- AST/ALT <1
- AST/ALT ≥1

This cutoff was chosen based on the prior literature and conventional interpretation of aminotransferase ratios, acknowledging that it is not specifically validated for heart failure populations.

Echocardiographic Assessment

Transthoracic echocardiography was performed by experienced cardiologists using standard imaging protocols. LVEF was calculated using the modified Simpson method.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as frequencies and percentages. Group comparisons were performed using the Student's t-test or Mann–Whitney U test for continuous variables, depending on the distribution. Categorical variables were analyzed using the chi-square or Fisher's exact test, as appropriate.

Correlation analyses were conducted to assess the association between the AST/ALT ratio and functional parameters (NYHA class and LVEF). Pearson or Spearman correlation coefficients were used based on variable characteristics. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using SPSS version 25.0.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of the Government Thiruvallur Medical College and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all the participants.

Results

Baseline Characteristics

A total of 75 patients with HFrEF were included in this analysis. The mean age of the study population was 58.4 ± 11.2 years, and the majority were men. Patients were divided into two groups based on the AST/ALT ratio: 33 patients with AST/ALT <1 and 42 patients with AST/ALT ≥1.

Patients with AST/ALT ≥1 were significantly older than those with AST/ALT <1. The prevalence of ischemic heart disease was higher in the AST/ALT ≥1 group, whereas the distribution of dilated cardiomyopathy was similar between the groups. Guideline-directed medical therapy was comparable between the two groups.

Biochemical Profile

Mean AST levels were significantly higher in the AST/ALT ≥1 group, whereas ALT levels did not differ significantly between the groups. This pattern indicates that the elevation of the AST/ALT ratio was primarily driven by increased AST levels rather than by reduced ALT levels.

Table 1. Baseline Clinical and Biochemical Characteristics of the Study Population According to AST/ALT Ratio

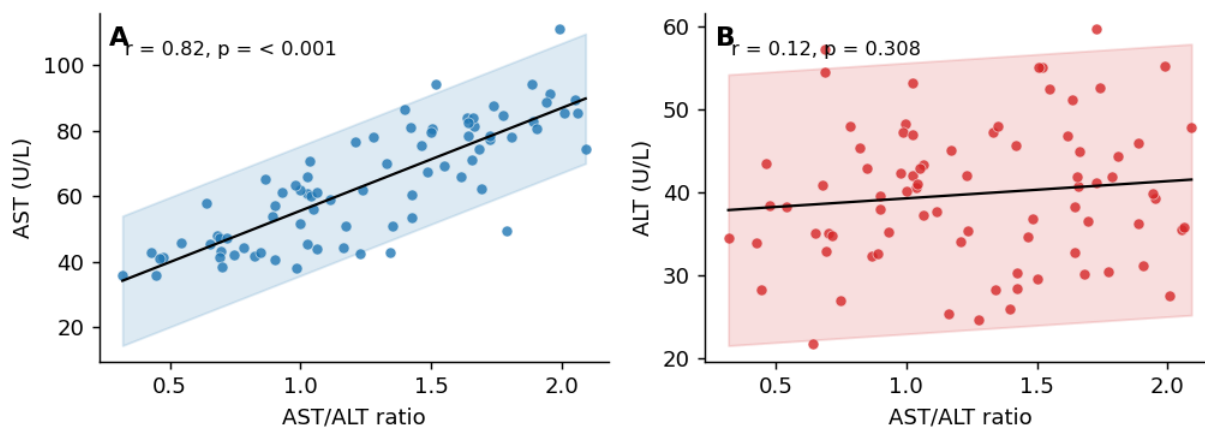
Variable	AST/ALT < 1 (n = 33)	AST/ALT ≥ 1 (n = 42)	p value
Age (years)	53.1 ± 10.5	62.3 ± 9.8	<0.001
Female sex, n (%)	8 (24.2)	16 (38.1)	0.20
Ischemic heart disease, n (%)	13 (39.4)	27 (64.3)	0.03
Dilated cardiomyopathy, n (%)	10 (30.3)	12 (28.6)	0.86
AST (U/L)	28.6 ± 10.3	48.2 ± 22.4	<0.001
ALT (U/L)	32.8 ± 12.6	35.1 ± 15.2	0.47
AST/ALT ratio	0.87 ± 0.11	1.34 ± 0.29	<0.001
LVEF (%)	31.2 ± 7.1	29.4 ± 6.8	0.23
NYHA Class I, n (%)	11 (33.3)	4 (9.5)	—
NYHA Class II, n (%)	16 (48.5)	26 (61.9)	—
NYHA Class III, n (%)	6 (18.2)	12 (28.6)	0.18†

Functional Severity

Patients with AST/ALT ≥ 1 showed a higher proportion of NYHA class II and III symptoms than those with AST/ALT < 1. However, these differences were not statistically significant. Similarly, the mean LVEF was numerically lower in the AST/ALT ≥ 1 group, but the difference was not statistically significant.

The AST/ALT ratio showed a significant positive correlation with AST levels but not with ALT levels (Figure 1), indicating that the ratio elevation was predominantly driven by increased AST levels.

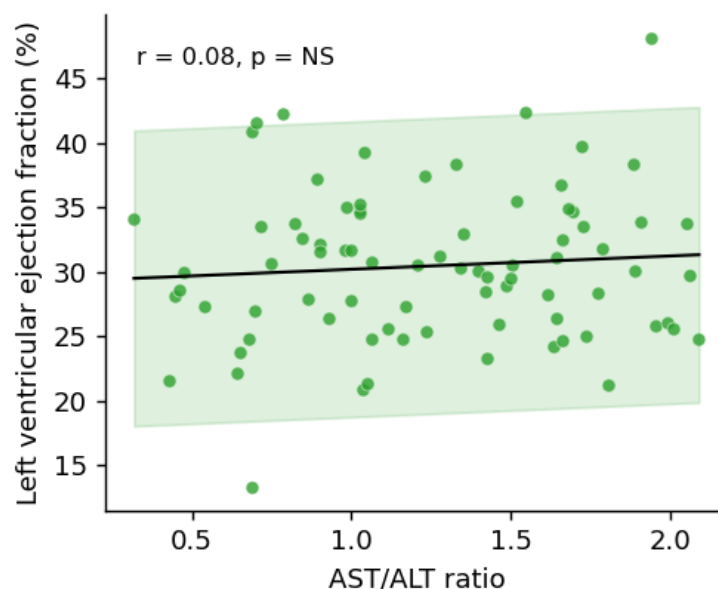
Relationship Between AST/ALT Ratio and Serum Aminotransferase Levels



Correlation Analysis

No significant correlation was observed between the AST/ALT ratio and the NYHA functional class. Similarly, there was no significant correlation between the AST/ALT ratio and the LVEF.

No significant correlation was observed between AST/ALT ratio and left ventricular ejection fraction (Figure 2).



The AST/ALT ratio was significantly positively correlated with absolute AST levels, whereas its correlation with ALT levels was weak and not statistically significant. These findings suggest that this ratio reflects AST elevation rather than an independent biochemical pattern of liver injury.

Discussion

This cross-sectional study evaluated the association between the AST/ALT ratio and functional severity in patients with HFrEF. The principal finding was the absence of a significant association between the AST/ALT ratio and established measures of functional severity, namely, the NYHA class and LVEF. These findings suggest that the AST/ALT ratio is not an independent marker of functional impairment in HFrEF.

The liver is frequently affected by heart failure due to chronic venous congestion and reduced perfusion. Elevated liver enzymes, particularly AST, are commonly observed in patients with advanced heart failure. However, the present study indicates that while the AST/ALT ratio reflects hepatic enzyme alterations, it does not directly correspond to symptomatic severity or systolic dysfunction.(1,8–10)

The observed elevation of AST in patients with higher AST/ALT ratios likely reflects hepatic congestion or hepatocellular injury related to systemic venous hypertension. (11,12)AST is present in both cytosolic and mitochondrial compartments and is expressed in extrahepatic tissues, including the cardiac and skeletal muscles. Therefore, its elevation may represent a nonspecific marker of systemic illness rather than isolated liver pathology.(13,14)

The lack of correlation between the AST/ALT ratio and LVEF is noteworthy. LVEF is a measure of systolic function but does not fully capture the hemodynamic complexity of heart failure, particularly right-sided pressure and systemic congestion. Similarly, NYHA classification, while clinically useful, is subjective and influenced by multiple factors beyond cardiac performance alone.(15)

These findings align with the concept that hepatic involvement in HFrEF represents a parallel pathophysiological process rather than a direct surrogate of cardiac functional severity. Consequently, the AST/ALT ratio should be interpreted as an adjunctive laboratory finding, rather than a marker of functional class or systolic impairment.

Clinical Implications

From a clinical perspective, the AST/ALT ratio is a readily available and inexpensive laboratory parameter. An elevated ratio may prompt clinicians to consider hepatic congestion or multiorgan involvement in patients with HFrEF. However, reliance on this ratio to infer functional severity or guide prognostic decisions is not supported by our data.

Limitations

This study has several limitations. The single-center design and modest sample size limit the generalizability of the findings. The cross-sectional nature of this study precludes the assessment of temporal relationships or prognostic implications. Multivariate analyses were limited, and residual confounding could not be excluded from the study. Additionally, the AST/ALT cutoff used was not specifically validated for heart failure populations.

Conclusion

In this cohort of patients with heart failure and reduced ejection fraction, the AST/ALT ratio was not independently correlated with functional severity, as assessed by the NYHA class or left ventricular ejection fraction. Elevation of the ratio was primarily driven by increased AST levels, suggesting hepatic enzyme involvement rather than a direct reflection of cardiac functional impairment. These findings support the role of the AST/ALT ratio as an adjunctive marker of hepatic involvement in HFrEF, while underscoring its limitations as a measure of functional severity. Further longitudinal studies are required to clarify its prognostic significance in this population.

References

1. Ewid M, Allihimy AS, Sherif H, Abazid R, Alkuraydis SA, Alharbi SA, et al. AST/ALT ratio predicts the functional severity of chronic heart failure with reduced left ventricular ejection fraction. *BMC Res Notes*. 2020 Mar 24;13(1).
2. Bhuiyan T, Maurer MS. Heart Failure with Preserved Ejection Fraction: Persistent Diagnosis, Therapeutic Enigma. *Curr Cardiovasc Risk Rep*. 2011 July 6;5(5):440–449.
3. Rosenkranz S, Gomberg-Maitland M, Howard LS, Hooper MM. Systemic Consequences of Pulmonary Hypertension and Right-Sided Heart Failure. *Circulation*. 2020 Feb 24;141(8):678–693.
4. Kubo SH. Liver Function Abnormalities in Chronic Heart Failure. *Arch Intern Med*. 1987 July 1;147(7):1227.
5. Yokoyama M, Watanabe T, Otaki Y, Takahashi H, Arimoto T, Shishido T, et al. Association of the Aspartate Aminotransferase to Alanine Aminotransferase Ratio with BNP Level and Cardiovascular Mortality in the General Population: The Yamagata Study 10-Year Follow-Up. *Disease Markers*. 2016 Jan 1;2016(10):1–9.
6. Samsky MD, Patel CB, Armstrong PW, Schulte PJ, Wilson Tang WH, Butler J, et al. Liver function tests in patients with acute heart failure and associated outcomes: insights from ASCEND-HF. *European J of Heart Fail*. 2015 Dec 28;18(4):424–432.
7. Bozkurt B, Anker SD, Kinugawa K, Lam CSP, Teerlink JR, Gomez-Mesa J, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese. *European J of Heart Fail*. 2021 Mar 1;23(3):352–380.
8. Khaidirman SK, Hasan H, Andra CA, Lubis HA, Dangana A, Haykal TB. Relationship of left ventricular diastolic dysfunction with quality of life in heart failure patients with reduced ejection fraction (HFrEF). *Narra J*. 2024 June 19;4(2):e707.
9. Giannini E, Testa R, Malfatti F, Chiarbonello B, Romagnoli P, Risso D, et al. Validity and Clinical Utility of the Aspartate Aminotransferase–Alanine Aminotransferase Ratio in Assessing Disease Severity and Prognosis in Patients With Hepatitis C Virus–Related Chronic Liver Disease. *Arch Intern Med*. 2003 Jan 27;163(2):218.
10. Bosch L, Ng TP, Sim D, Yeo D, Jaufeerally F, Leong KTG, et al. Right ventricular dysfunction in left-sided heart failure with preserved versus reduced ejection fraction. *European J of Heart Fail*. 2017 June 8;19(12):1664–1671.

11. Nathwani RA, Kaplowitz N, Pais S, Reynolds TB. Serum alanine aminotransferase in skeletal muscle diseases†. *Hepatology*. 2005 Jan 1;41(2):380–382.
12. Liu H, Zhu L, Ding C, Zhou W, Bao H, Wang T, et al. The association between AST/ALT ratio and all-cause and cardiovascular mortality in patients with hypertension. *Medicine*. 2021 Aug 6;100(31):e26693.
13. Ndrepepa G. Aspartate aminotransferase and cardiovascular disease—a narrative review. *J Lab Precis Med*. 2021 Jan 1;6:6.
14. Liu H, Zheng X, Zheng Y, Chen J, Huang Y, Yan H, et al. Association of AST/ALT ratio with 90-day outcomes in patients with acute exacerbation of chronic liver disease: a prospective multicenter cohort study in China. *Front Med*. 2024 Mar 21;11.
15. Gehlken C, Screever EM, Van Der Meer P, Coster JE, Westenbrink BD, Meijers WC, et al. Left atrial volume and left ventricular mass indices in heart failure with preserved and reduced ejection fraction. *ESC Heart Failure*. 2021 Jun 4;8(4):2458–2466.