

Effect of AST/ALT Ratio on Prognosis of Alcohol Induced Cardiomyopathy in Chronic Alcoholic Patients: A Cross Sectional Study in a Tertiary Care Centre

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ABSTRACT

Background: Alcohol-induced cardiomyopathy (ACM) is an acquired form of dilated cardiomyopathy resulting from prolonged heavy alcohol consumption. Chronic ethanol exposure produces myocardial oxidative stress, mitochondrial dysfunction, myocyte injury, ventricular remodeling and progressive systolic dysfunction. The aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio, also known as the De Ritis ratio, is traditionally used as a marker of hepatocellular injury but may also reflect systemic tissue injury and impaired cardiovascular function. Evidence regarding its relationship with severity of alcohol-induced cardiomyopathy remains limited. **Materials and Methods:** A cross-sectional observational study was conducted in the Department of Medicine at a tertiary care hospital. One hundred adult patients with chronic heavy alcohol consumption and echocardiographically documented alcohol-induced cardiomyopathy were included. Serum AST and ALT were measured and the AST/ALT ratio was calculated. Patients were categorized into two groups according to an AST/ALT ratio <1 or ≥ 1 . Echocardiography was performed to assess left ventricular ejection fraction (LVEF), LV dimensions and associated structural abnormalities. For this cross-sectional analysis, poorer cardiac prognosis was operationalized by severe systolic dysfunction and advanced NYHA functional class. **Results:** Of the 100 patients, 35 had an AST/ALT ratio <1 and 65 had a ratio ≥ 1 . Patients with a ratio ≥ 1 demonstrated lower mean LVEF than those with a ratio <1 ($34.7 \pm 7.8\%$ vs. $43.8 \pm 8.6\%$, $p < 0.001$) and had a greater frequency of NYHA class III–IV symptoms (49.2% vs. 14.3% , $p < 0.001$). Advanced ventricular dilation, atrial enlargement and clinically significant arrhythmias were also more frequent in the higher-ratio group. The AST/ALT ratio demonstrated an inverse correlation with LVEF ($r = -0.52$, $p < 0.001$). On multivariable analysis, AST/ALT ratio ≥ 1 was independently associated with severe cardiac dysfunction after adjustment for age, duration of alcohol exposure, hypertension and serum albumin. **Conclusion:** An elevated AST/ALT ratio was associated with poorer cardiac functional status, reduced LVEF and advanced NYHA class among chronic alcoholic patients with alcohol-induced cardiomyopathy. The ratio is inexpensive and routinely available and may serve as an adjunctive marker for identifying patients requiring more intensive cardiovascular assessment. Prospective longitudinal studies are required to determine whether it independently predicts hospitalization or mortality.

Keywords: Alcohol-induced cardiomyopathy, alcohol cardiomyopathy, AST/ALT ratio, De Ritis ratio, left ventricular ejection fraction, heart failure, chronic alcoholism, prognosis.

INTRODUCTION

One significant modifiable factor contributing to cardiovascular morbidity is alcohol use. Long-term heavy alcohol consumption is known to develop acquired dilated cardiomyopathy and can directly cause

cardiac damage. In the absence of another adequate cause of dilated cardiomyopathy, alcohol-induced cardiomyopathy is characterized by ventricular dilatation and reduced myocardial contractility following prolonged excessive alcohol intake. Although

susceptibility varies greatly between individuals, current reviews often define chronic intake of more than about 80 g ethanol/day for at least five years as a classical exposure related with the illness. [1,2]

Alcohol-induced cardiomyopathy has a complex pathogenesis. Oxidative stress, mitochondrial dysfunction, altered calcium handling, decreased sarcomere function, apoptosis, and myocardial fibrosis can all be brought on by ethanol and its metabolite acetaldehyde. Nutritional disorders and neurohormonal stimulation may exacerbate cardiac damage. Individual variations in the onset and severity of cardiomyopathy may also be influenced by genetic predisposition. [1,3,4] Clinically asymptomatic early cardiac problems are possible. Increased LV mass, ventricular enlargement, and reduced systolic or diastolic function have all been shown by prior echocardiographic studies in chronic alcohol users; some research have linked the severity of myocardial dysfunction to cumulative alcohol intake. [5-7] Patients may exhibit peripheral edema, tiredness, arrhythmias, exertional dyspnea, and signs of congestive heart failure once symptomatic cardiomyopathy develops.

The De Ritis ratio, also known as the AST/ALT ratio, was first created as a biochemical marker for liver illness. While ALT is comparatively more liver-specific, AST is found in a variety of tissues, including skeletal muscle and the heart. Therefore, rather than being just indicative of liver illness, a high ratio may also indicate tissue damage, mitochondrial damage, or altered hepatic metabolism. [8]

The De Ritis ratio has been studied outside of hepatology, according to growing evidence. Higher AST/ALT ratios have been linked in cardiovascular disease studies to unfavorable outcomes, such as heart failure severity and cardiovascular mortality. [9-12] The AST/ALT ratio was elevated in patients with decreased systolic function, however its discriminatory performance for severity was low, according to a recent prospective cross-sectional Indian study comprising 100 patients with chronic heart failure and decreased LVEF. [13]

Because alcohol affects both the liver and the heart, alcoholic cardiomyopathy is a particularly pertinent context where the AST/ALT ratio may have clinical importance. However, liver disease, malnourishment, muscular damage, renal failure, and systemic sickness can also contribute to a high ratio in an alcoholic patient. Therefore, rather than being evaluated alone, its association with cardiac severity should be investigated in conjunction with clinical and echocardiographic characteristics.

AIM AND OBJECTIVES

Aim: To evaluate the association of the AST/ALT ratio with cardiac severity and prognostic markers in chronic alcohol patients with alcohol-induced cardiomyopathy.

Objectives

1. To determine the AST/ALT ratio among chronic alcohol patients with alcohol-induced cardiomyopathy.
2. To compare clinical and echocardiographic characteristics between patients with AST/ALT ratio <1 and ≥ 1 .
3. To assess the relationship between AST/ALT ratio and LVEF.
4. To evaluate whether an elevated AST/ALT ratio is associated with advanced NYHA functional class and severe LV systolic dysfunction.

MATERIALS AND METHODS

A hospital-based cross-sectional observational study was conducted in the Department of Medicine at a tertiary care teaching hospital. The proposed study population consisted of adult chronic alcohol users diagnosed with alcohol-induced cardiomyopathy. One hundred consecutive eligible patients were included in the study.

Inclusion criteria

1. Age ≥ 18 years.
2. History of chronic heavy alcohol consumption.
3. Alcohol exposure consistent with clinically suspected alcohol-induced cardiomyopathy.
4. Echocardiographic evidence of dilated cardiomyopathy with impaired LV systolic function.
5. No adequate alternative explanation for the cardiomyopathy.
6. Willingness to participate and provide informed consent.

Exclusion criteria

1. Known significant coronary artery disease or recent acute myocardial infarction.
2. Significant primary valvular heart disease.
3. Congenital heart disease.
4. Known myocarditis.
5. Severe chronic kidney disease requiring dialysis.
6. Active viral hepatitis or acute liver failure.
7. Active malignancy.
8. Recent major trauma or skeletal muscle injury.
9. Use of drugs known to cause cardiomyopathy.
10. Incomplete biochemical or echocardiographic records.

Clinical Assessment

A detailed history was obtained regarding age, sex, duration of alcohol consumption, approximate daily

ethanol intake, smoking, hypertension, diabetes and previous cardiac symptoms. Alcohol intake was converted to grams of ethanol per day using standard conversion principles.

Clinical examination included pulse rate, blood pressure, body mass index, signs of congestive heart failure, cardiomegaly, peripheral edema, hepatomegaly and evidence of chronic liver disease.

NYHA functional class was recorded at the time of evaluation.

Patients were divided into:

- **Group A:** AST/ALT ratio <1.
- **Group B:** AST/ALT ratio $\geq$ 1.

The threshold of 1 was selected because it is widely used in clinical studies evaluating the De Ritis ratio and because ratios $\geq$ 1 are common in advanced alcohol-related hepatic injury and have been investigated as markers of cardiovascular risk. [8-12]

Echocardiographic assessment

Two-dimensional transthoracic echocardiography was performed using a standard echocardiography system. LVEF was calculated using the Simpson biplane method where feasible. LV end-diastolic diameter, LV end-systolic diameter, left atrial size and right ventricular function were also assessed.

For analysis, severe LV systolic dysfunction was defined as LVEF <35%. The 2022 AHA/ACC/HFSA framework

classifies LVEF $\leq$ 40% as heart failure with reduced ejection fraction. [7]

Statistical analysis

Data were analyzed using appropriate statistical software. Continuous variables were expressed as mean $\pm$ standard deviation and categorical variables as frequency and percentage. Continuous variables were compared using Student's t-test or Mann-Whitney U test depending on distribution. Categorical variables were compared using chi-square test. Pearson correlation was used to evaluate the relationship between AST/ALT ratio and LVEF. Multivariable logistic regression was performed to identify independent associations with severe cardiac dysfunction. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

A total of 100 patients with chronic alcohol exposure and alcohol-induced cardiomyopathy were evaluated. The mean age of the study population was approximately 51 years. Most participants were male, reflecting the demographic distribution commonly observed among patients with chronic heavy alcohol exposure.

Thirty-five patients had an AST/ALT ratio <1, while 65 had a ratio $\geq$ 1. Patients in the higher-ratio group had longer alcohol exposure, higher mean AST and lower serum albumin concentrations. The differences in age and sex distribution were not statistically significant.

Table 1. Baseline characteristics according to AST/ALT ratio

Parameter	AST/ALT <1 (n=35) A	AST/ALT $\geq$ 1 (n=65) B	p-value
Age, years	49.1 $\pm$ 8.7	52.4 $\pm$ 9.3	0.086
Male sex, n (%)	31 (88.6)	59 (90.8)	0.739
Duration of alcohol use, years	14.2 $\pm$ 5.8	17.6 $\pm$ 6.2	0.008
Alcohol intake, g/day	91.4 $\pm$ 24.7	108.7 $\pm$ 31.5	0.006
AST, IU/L	49.8 $\pm$ 16.1	86.2 $\pm$ 35.7	<0.001
ALT, IU/L	62.4 $\pm$ 18.5	70.1 $\pm$ 26.4	0.112
Serum albumin, g/dL	3.72 $\pm$ 0.46	3.41 $\pm$ 0.52	0.004
Hypertension, n (%)	8 (22.9)	18 (27.7)	0.608
Diabetes mellitus, n (%)	5 (14.3)	12 (18.5)	0.586

Patients with AST/ALT $\geq$ 1 demonstrated significantly lower LVEF and larger LV dimensions. Mean LVEF was 34.7 $\pm$ 7.8% in the elevated-ratio group compared with 43.8 $\pm$ 8.6% among those with ratio <1 (p<0.001). Severe systolic dysfunction was observed in 53.8% of patients with ratio $\geq$ 1 compared with 20.0% in the ratio <1 group.

Table 2. Clinical and echocardiographic parameters

Parameter	AST/ALT <1 (n=35) A	AST/ALT $\geq$ 1 (n=65) B	p-value
LVEF, %	43.8 $\pm$ 8.6	34.7 $\pm$ 7.8	<0.001

LVEDD, mm	59.1 ± 6.7	64.8 ± 7.5	<0.001
LVEDS, mm	45.6 ± 6.4	51.7 ± 7.1	<0.001
Left atrial diameter, mm	40.3 ± 5.2	44.6 ± 6.1	0.001
LVEF <35%, n (%)	7 (20.0)	35 (53.8)	0.001
NYHA III–IV, n (%)	5 (14.3)	32 (49.2)	<0.001
Atrial fibrillation, n (%)	4 (11.4)	15 (23.1)	0.154
Ventricular arrhythmia, n (%)	6 (17.1)	25 (38.5)	0.028

There was a progressive relationship between increasing AST/ALT ratio and worsening cardiac functional status. The AST/ALT ratio showed a significant inverse correlation with LVEF ($r=-0.52$, $p<0.001$), indicating that patients with higher ratios tended to have lower systolic function.

Table 3. Relationship between AST/ALT ratio and markers of cardiac severity

Cardiac severity parameter	AST/ALT <1 A	AST/ALT ≥1 B	p-value
NYHA I–II, n (%)	30 (85.7)	33 (50.8)	<0.001
NYHA III–IV, n (%)	5 (14.3)	32 (49.2)	<0.001
LVEF ≥40%, n (%)	28 (80.0)	30 (46.2)	0.001
LVEF <40%, n (%)	7 (20.0)	35 (53.8)	0.001
LVEDD ≥60 mm, n (%)	13 (37.1)	42 (64.6)	0.009
Clinically significant arrhythmia, n (%)	10 (28.6)	29 (44.6)	0.116
Previous HF hospitalization, n (%)	4 (11.4)	24 (36.9)	0.007

In multivariable analysis, AST/ALT ratio ≥1 remained significantly associated with severe cardiac dysfunction after adjustment for age, alcohol consumption, duration of alcohol exposure, hypertension and serum albumin.

Table 4. Multivariable logistic regression for severe cardiac dysfunction

Variable	Adjusted OR	95% CI	p-value
AST/ALT ratio ≥1	3.21	1.42–7.25	0.005
Age ≥50 years	1.38	0.64–2.98	0.405
Alcohol intake ≥100 g/day	2.14	1.01–4.54	0.047
Alcohol duration ≥15 years	1.86	0.88–3.93	0.104
Hypertension	1.27	0.55–2.94	0.575
Serum albumin <3.5 g/dL	2.08	0.98–4.42	0.057

The elevated AST/ALT ratio demonstrated an adjusted odds ratio of 3.21 for severe cardiac dysfunction. These findings indicate an independent association, although the cross-sectional design prevents interpretation as a causal or prospective mortality effect.

DISCUSSION

In chronic alcoholic patients with alcohol-induced cardiomyopathy, the current study assessed the association between the AST/ALT ratio and indicators of cardiac severity. The main conclusion was that an AST/ALT ratio ≥1 was linked to higher LV dilatation, lower LVEF, and a more advanced NYHA functional class.

After extended exposure to high ethanol levels, alcohol-induced cardiomyopathy develops. Numerous intracellular mechanisms, such as oxidative stress, mitochondrial dysfunction, altered calcium homeostasis,

decreased protein synthesis, and direct effects on contractile proteins, are involved in the harmful consequences of alcohol. Heart failure, systolic dysfunction, and ventricular dilatation are eventually caused by persistent damage. [1,3,4] Patients with AST/ALT ≥1 had a substantially poorer mean LVEF in the current research. This group also had a much higher prevalence of LVEF <35%. A key factor in the categorization of heart failure is LVEF, a clinically validated indicator of LV systolic function. According to current guidelines, the primary imaging modality for evaluating the structure and function of the heart in

patients suspected of having heart failure is transthoracic echocardiography. [7-8] The current findings are biologically plausible based on evidence from other cardiovascular groups. In addition to providing predictive information beyond traditional cardiovascular risk variables, Ndrepepa et al. showed that an increased De Ritis ratio was linked to long-term mortality. [9] Increased AST/ALT ratios have been linked in other research to poor outcomes after acute myocardial infarction and cardiac arrest. [10,11] Higher De Ritis ratios have been linked to significant poor cardiovascular outcomes in individuals with acute decompensated heart failure, according to a recent study. [12]

Crucially, the connection between ventricular dysfunction and the AST/ALT ratio might not be unique to alcohol-induced cardiomyopathy. The AST/ALT ratio was found to be elevated and linked with indicators related to hepatic fibrosis in a recent Indian study of individuals with decreased LVEF and chronic heart failure. However, there was only a slight discrimination for heart failure severity in the reported ROC study. Therefore, rather than being a replacement for echocardiography or a thorough clinical evaluation, AST/ALT should be considered an additional biomarker [13].

Reducing or stopping alcohol consumption may potentially alter the clinical course of alcohol-induced cardiomyopathy. According to Nicolás et al., patients who abstained or significantly cut back on their alcohol use saw improvements in their LVEF, while those who continued to drink heavily were linked to further decline. [14] In addition to guideline-directed heart failure treatment, more recent research highlights alcohol abstinence as a crucial part of care. [1]

The severity of heart failure and ventricular size have historically been linked to the prognosis of alcohol cardiomyopathy. According to Kinney et al., survival in alcohol cardiomyopathy was linked to both inadequate mitral leaflet closure and enlarged LV end-diastolic dimension. [15] More recent cohorts have shown that long-term alcohol misuse is linked to worse ventricular function and unfavorable outcomes, but improvement may happen once alcohol exposure is reduced or stopped. [16]

However, there are a few restrictions to take into account. First, because the study was cross-sectional, it was unable to quantify long-term mortality or prove temporal causality. Second, skeletal muscle damage, liver disease, nutritional status, and other systemic factors affect AST/ALT. Third, self-report was used to determine alcohol consumption, which could lead to recall bias. Fourth, the sample came from a single tertiary center and was comparatively small. Lastly, the analysis did not include cardiac MRI, coronary angiography, or biomarkers such NT-proBNP.

STRENGTHS OF THE STUDY

1. The study specifically evaluated the association between the AST/ALT ratio and clinically relevant markers of cardiac severity in patients with alcohol-induced cardiomyopathy.
2. Both clinical and echocardiographic parameters were assessed, including NYHA functional class, LVEF, LV dimensions, left atrial size and clinically significant arrhythmias, providing a multidimensional assessment of cardiac involvement.
3. The study used a predefined AST/ALT ratio threshold of 1, allowing clinically meaningful comparison between patients with lower and higher ratios.
4. The analysis included multivariable logistic regression to evaluate whether an elevated AST/ALT ratio remained associated with severe cardiac dysfunction after adjustment for important clinical factors including age, alcohol exposure, hypertension and serum albumin.
5. AST and ALT are routinely available, inexpensive laboratory parameters, making the AST/ALT ratio potentially useful as an accessible adjunctive marker in resource-limited clinical settings.

FUTURE DIRECTIONS

Future prospective, multicentre studies with larger sample sizes should evaluate whether the AST/ALT ratio independently predicts clinically important outcomes such as heart-failure hospitalization, cardiovascular mortality and all-cause mortality in patients with alcohol-induced cardiomyopathy. Serial assessment of the AST/ALT ratio alongside LVEF, NT-proBNP and other cardiac biomarkers may help determine whether changes in the ratio correspond with changes in cardiac function. Further studies should also investigate the effect of alcohol abstinence or reduction on the AST/ALT ratio and cardiac recovery. Incorporation of cardiac magnetic resonance imaging and more comprehensive assessment of hepatic, nutritional and metabolic status may help clarify the mechanisms underlying the observed association. Development and external validation of prognostic models incorporating the AST/ALT ratio with established clinical and echocardiographic parameters may ultimately determine its practical value in risk stratification.

CONCLUSION

An AST/ALT ratio ≥ 1 was significantly associated with poorer cardiac functional status in chronic alcohol patients with alcohol-induced cardiomyopathy. Patients

with an elevated ratio had lower LVEF, greater LV dilation, more frequent severe systolic dysfunction and a higher prevalence of NYHA III–IV symptoms.

The AST/ALT ratio is inexpensive, readily available and may provide useful supplementary information during cardiovascular risk assessment in chronic alcohol users. However, it should not replace echocardiographic evaluation or established clinical prognostic parameters. Because the present design was cross-sectional, the observed association should not be interpreted as proof that an elevated AST/ALT ratio independently predicts future mortality. Prospective longitudinal studies are required to establish its true prognostic value.

DECLARATIONS

Ethics Approval and Consent to Participate

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of Hassan Institute of Medical Sciences, Hassan, Karnataka, India. Written informed consent was obtained from all participants before enrollment in the study.

Consent for Publication

Not applicable. No individually identifiable patient information or images are included in this manuscript.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request, subject to institutional and ethical restrictions.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

Dr.AkashNaik R: Conceptualization, study design, data collection, clinical assessment, data analysis, interpretation of results, manuscript drafting and revision.

Dr.Sowmyashree S N: Data collection, clinical assessment, literature review, interpretation of findings and manuscript review.

Dr.PrajwalNaik R: Data collection, echocardiographic data compilation, literature review, data organization and manuscript review.

All authors read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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AI Use Disclosure

The authors declare that no generative artificial intelligence tools were used to generate or substantially modify the scientific content of this manuscript.

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