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Evaluation of De Ritis Ratio, GGT, and hs-CRP as Biomarkers in Alcohol Dependence: A Case-Control Study

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ABSTRACT

Background: Alcoholic liver disease is characterized by elevated levels of liver enzymes and inflammatory markers. The aspartate transaminase (AST) to alanine transaminase (ALT) ratio, known as the De Ritis ratio, is altered in alcoholic liver disease. This study aimed to evaluate and compare the AST/ALT ratio, gamma-glutamyl transferase (GGT), and high-sensitivity C-reactive protein (hs-CRP) in individuals with alcohol dependence versus non-alcoholic controls. **Methods:** This case-control study was conducted at a tertiary care center in Aurangabad, Maharashtra, India. Sixty adult males aged 18 years and above with alcohol dependence, diagnosed per DSM-V criteria, were enrolled as cases from the Medicine ward or outpatient department. Sixty socioeconomic status-matched non-alcoholic males served as controls. Serum levels of AST, ALT, GGT, and hs-CRP were measured, and the AST/ALT ratio was calculated. Parameters were compared between groups using unpaired t-tests. **Results:** The mean AST was 206.81 ± 85.07 U/L in cases and 25.81 ± 8.31 U/L in controls. The mean ALT was 93.25 ± 39.17 U/L in cases and 30.82 ± 8.21 U/L in controls. The mean AST/ALT ratio was 2.18 ± 0.43 in cases and 1.27 ± 0.51 in controls. The mean GGT was 90.8 ± 24.8 U/L in cases and 30.8 ± 8.2 U/L in controls. The mean hs-CRP was 3.08 ± 1.1 mg/dL in cases and 0.15 ± 0.1 mg/dL in controls. All parameters were significantly higher in the alcoholic group compared to the control group ($p < 0.05$). **Conclusions:** The De Ritis ratio, serum AST, ALT, GGT, and hs-CRP are significantly elevated in individuals with alcohol dependence compared to non-alcoholic controls, suggesting their utility as markers of alcoholic liver disease.

KEYWORDS: De Ritis ratio, Liver enzymes, Alcoholic liver disease, Gamma-glutamyl transferase, High-sensitivity C-reactive protein, Alcohol dependence

INTRODUCTION

The liver, as the primary organ responsible for alcohol metabolism, is highly susceptible to alcohol-related tissue damage. Aspartate transaminase (AST) and alanine transaminase (ALT) are enzymes routinely measured in liver function tests. However, their elevation in the bloodstream primarily reflects hepatocellular injury or death rather than merely assessing liver function. De Ritis originally described the ratio of AST to ALT, noting that in acute viral hepatitis, ALT levels typically exceed AST levels. In contrast, in alcoholic hepatitis, the AST to ALT ratio is often greater than 1, with AST levels surpassing ALT levels. The De Ritis ratio has been demonstrated to be sensitive to various phases of alcoholic hepatitis. [1–3] Recent reviews have emphasized the need for longitudinal and comparative studies across diverse populations and geographical regions to elucidate the role of the De Ritis ratio in different pathological conditions. [4]

Gamma-glutamyl transferase (GGT) is another enzyme whose elevated activity serves as a valuable screening tool for liver dysfunction. Increased GGT levels are associated with oxidative stress, a critical mechanism underlying ethanol-induced tissue injury. [5] Additionally, high-sensitivity C-reactive protein (hs-CRP), an inflammatory marker, has been identified as a potential indicator of alcohol abuse and sensitivity. [6]

The present study aims to compare the De Ritis ratio, serum AST, ALT, GGT, and hs-CRP levels between individuals with alcohol dependence and non-alcoholic controls.

METHODS

Study Design: This was a case-control study conducted at a tertiary care center in Aurangabad, Maharashtra, India.

Study Participants: Sixty adult males aged 18 years and above, diagnosed with alcohol dependence according to DSM-V criteria, [7] were recruited as cases from the Medicine ward or outpatient department. Sixty socioeconomic status-matched non-alcoholic males were enrolled as controls. Exclusion criteria included individuals with alcohol delirium, seizures, hepatic encephalopathy, chronic psychiatric disorders, multiple substance abuse, those too ill to cooperate with the study, or those with a history of blood loss, melena, chronic liver disease unrelated to alcoholism, recent myocardial infarction, acute coronary syndrome, rheumatoid arthritis, rheumatic fever, neoplastic disease, hypertension, or hepatic failure.

Ethical Considerations: The study protocol was approved by the institutional ethics committee, and informed consent was obtained from all participants.

Study Parameters: Serum levels of AST, ALT, GGT, and hs-CRP were measured. The AST/ALT ratio was calculated from the AST and ALT values.

Sample Collection and Analysis: Approximately 5 mL of venous blood was collected from the anterior antecubital vein using a sterile needle and vacutainer. The blood was allowed to clot and then centrifuged at 3000 rpm for 10 minutes to separate the serum. Serum samples were stored at -20°C until analysis. AST and ALT levels were determined using the Vitros AST and ALT slide method on the Vitros 5600 integrated system, calibrated with the Vitros chemistry products calibrator kit three. GGT was measured using a kinetic test for quantitative determination of gamma-glutamyl transferase activity in serum. Hs-CRP was estimated using the Turbidimetric Immunoassay Method with the Tulip Diagnostics kit.

Statistical Analysis: Data were analyzed using unpaired t-tests to compare the means of AST, ALT, AST/ALT ratio, GGT, and hs-CRP between the alcoholic cases and non-alcoholic controls. A one-tailed hypothesis was applied, assuming higher levels in the alcoholic group, with a significance level of 0.05. Data were assessed for normality prior to analysis.

RESULTS

This case-control study included 60 adult males with alcohol dependence (cases) and 60 non-alcoholic controls. The age distribution of participants is shown in Table 1. Most participants in both groups were aged 31–50 years. However, the mean age of cases (44.12 ± 10.77 years) was higher than that of controls (37.47 ± 9.48 years), which may affect the interpretation of the findings.

Age Group (years)	Cases (n=60)	Controls (n=60)
18–30	8 (13.3%)	15 (25%)
31–40	16 (26.7%)	24 (40%)
41–50	21 (35%)	12 (20%)
51–60	11 (18.3%)	9 (15%)
>60	4 (6.7%)	0 (0%)
Mean ± SD	44.12 ± 10.77	37.47 ± 9.48

SD: Standard deviation

Table 1: Age Distribution of Study Subjects

The mean values of key parameters—serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), AST/ALT ratio, gamma-glutamyl transferase (GGT), and high-sensitivity C-reactive protein (hs-CRP)—were compared between cases and controls (Table 2). The AST/ALT ratio was significantly higher in cases (2.2 ± 0.4) than in controls (1.3 ± 0.5, p=0.02). Similarly, serum AST, ALT, GGT, and hs-CRP were significantly elevated in cases compared to controls (all p<0.001).

Parameter	Alcoholic Cases (n=60) (Mean ± SD)	Non-alcoholic Controls (n=60) (Mean ± SD)	p-value (Unpaired t-test)
Serum AST (U/L)	206.81 ± 85.07	25.81 ± 8.31	<0.001
Serum ALT (U/L)	93.25 ± 39.17	30.82 ± 8.21	<0.001
AST/ALT ratio	2.2 ± 0.4	1.3 ± 0.5	0.02
Serum GGT (U/L)	90.8 ± 24.8	27.1 ± 8.3	<0.001
Serum hs-CRP (mg/L)	3.08 ± 1.1	0.15 ± 0.1	<0.001

SD: Standard deviation

Table 2: Serum Parameters in Cases and Controls

DISCUSSION

This study demonstrates a significant elevation of serum AST, ALT, and the AST/ALT ratio in individuals with alcohol dependence compared to non-alcoholic controls. These findings are consistent with extensive prior research documenting liver enzyme abnormalities in alcoholic liver

disease. [8–10] The AST/ALT ratio, often termed the De Ritis ratio, was significantly higher in the alcoholic group (2.2 ± 0.4) than in controls (1.3 ± 0.5), aligning with reports that a ratio exceeding 1.5 or 2 is suggestive of alcohol-related liver injury. [11, 12] However, this ratio is not diagnostic on its own, as conditions like viral hepatitis can also influence it. [13]

The global rise in alcohol consumption, coupled with shifts in dietary patterns and increasing obesity, has contributed to a growing prevalence of liver disease. [5, 14–16] In this context, the AST/ALT ratio serves as a useful marker for identifying alcohol-related liver damage. Interestingly, ratios below 2 or even 1 have been observed in alcoholics with coexisting viral hepatitis, highlighting the importance of considering comorbidities when interpreting this marker. [13]

The elevated AST/ALT ratio in alcoholic subjects may result from multiple mechanisms. Chronic alcohol use can deplete vitamin B6, a cofactor essential for ALT activity, leading to relatively lower ALT levels. Additionally, alcohol-induced mitochondrial damage in hepatocytes increases the release of mitochondrial AST into the serum, further elevating the ratio. [2, 17–19] These processes account for the characteristic enzyme profile observed in alcoholic liver disease.

A high AST/ALT ratio is often associated with heavy, recent alcohol consumption or progression to advanced liver damage, such as cirrhosis. [20] Following abstinence or treatment, the ratio typically decreases, reflecting the shorter half-life of AST compared to ALT. [20] However, an Australian study reported unexpectedly low AST/ALT ratios (below 1) in alcoholics with biopsy-proven cirrhosis, possibly due to inclusion bias or the timing of blood sampling relative to alcohol intake. [21] This variability suggests that the ratio's utility may depend on the stage of liver disease and other clinical factors.

Serum GGT levels were markedly higher in the alcoholic group (90.8 ± 24.8 U/L) compared to controls (27.1 ± 8.3 U/L). GGT is sensitive to even moderate alcohol consumption, and its elevation in this study indicates either high alcohol intake or increased alcohol sensitivity. [6, 11] This supports the potential use of GGT in screening and deaddiction programs. Similarly, hs-CRP, an inflammatory marker, was significantly elevated in the alcoholic group (3.08 ± 1.1 mg/L vs. 0.15 ± 0.1 mg/L in controls). This elevation reflects systemic inflammation associated with chronic alcohol use, which may be particularly pronounced in individuals with depression, where alcohol can modulate inflammatory responses. [6, 22]

The high AST/ALT ratio observed here may indicate recent alcohol consumption (e.g., within the day prior to testing) or advanced alcoholic hepatitis. Elevated GGT and hs-CRP levels further suggest excessive alcohol use or heightened sensitivity, reinforcing the need for robust deaddiction and awareness initiatives.

Limitations of the Study

This study has several limitations: small sample size (n=60 per group) with convenience sampling, inclusion of only male subjects, exclusion of patients with hepatic encephalopathy or failure, and its single-center nature. Larger, longitudinal, multi-center studies are warranted to validate and expand upon these findings.

CONCLUSION

The estimation of AST, ALT, and the AST/ALT ratio is valuable for assessing liver damage in individuals with alcohol dependence. Elevated levels of these enzymes, alongside GGT and hs-CRP, indicate significant hepatic injury and systemic inflammation. These markers should be routinely included in the diagnostic and management protocols for alcoholic patients. Moreover, mass screening of alcohol consumers for liver enzymes and the De Ritis ratio could enable early detection of liver damage, facilitating timely interventions to prevent and manage liver dysfunction.

DISCLOSURE

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