

# ASPARTATE AMINOTRANSFERASE-ALANINE AMINOTRANSFERASE RATIO PREDICTS CIRRHOSIS IN CHRONIC HEPATITIS C PATIENTS

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## ABSTRACT

**Background:** Hepatitis C virus infection is on rise in Pakistan. **Objective:** To evaluate serum aspartate aminotransferase and alanine aminotransferase ratio (AST/ALT ratio) in predicting liver cirrhosis of chronic hepatitis C patients. **Patient and Methods:** Study Design: A prospective study. Place and Duration of Study: This study was done in Gastroenterology department at Sheikh Zayed Hospital Lahore. Duration of study was 6 months from 1<sup>st</sup> January to 30<sup>th</sup> June 2010. Total 80 patients of chronic hepatitis C confirmed by PCR were included in the study. The sera of the patients were tested for AST and ALT. Liver biopsy of each patient was performed. Histological Activity Index (HAI) of the specimens was scored on the basis of Knodell score. AST/ALT ratio was correlated with the histological stage (i.e. degree of fibrosis), and the histological grade (i.e. inflammatory activity). **Results:** The mean AST/ALT ratio in 40 cirrhotic patients ( $1.64 \pm 0.46$ ;  $p < 0.001$ ) was higher than in 40 noncirrhotic patients ( $0.88 \pm 0.34$ ;  $p < 0.001$ ). A ratio  $\geq 1$  has 96.38% specificity and 93.73% positive predictive value in distinguishing cirrhotic from noncirrhotic patients with 88.26% sensitivity and 94.84% negative predictive value. The ratio correlated positively with histological stage but not with the grade. Two patients out of 17 cirrhotic patients (12%) have no clinical or biochemical features suggestive of chronic liver disease except for an AST/ALT ratio more than one. **Conclusion:** It is concluded that AST/ALT ratio  $\geq 1$  is highly specific for the presence of cirrhosis in patients with chronic hepatitis C. This ratio reflects the fibrosis stage in these patients. This ratio may be considered as a marker of fibrosis in patients with chronic hepatitis C.

**Keywords:** Chronic Hepatitis, Aspartate Aminotransferase, Alanine Aminotransferase, Fibrosis

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## INTRODUCTION

Hepatitis C Virus (HCV) infection is a major cause of chronic liver disease in various parts of the world including Pakistan.<sup>1</sup> There are some 175 million chronic HCV carriers throughout the world.<sup>2</sup> About 85% HCV infected individuals become chronically infected, out of which 10-20% develop cirrhosis of liver. About 7 % of cirrhotic patients develop hepatocellular carcinoma.<sup>3</sup> Clinical examination is often unreliable in assessing the severity of disease in patients with chronic hepatitis C. The histological evaluation of a liver biopsy specimen remains the gold standard for determining the activity of HCV related liver disease and histological staging remains the only reliable predictor of prognosis and the likelihood of disease progression.<sup>4</sup> The invasive and costly procedure of liver biopsy is associated with risk of complications and discomfort. Considerable efforts are being made by research workers to find some simple, safe,

inexpensive means to non-invasively assess the severity of liver disease in patients with chronic hepatitis C.<sup>5</sup> Despite the lack of correlation between serum ALT concentrations and liver histology in chronic hepatitis C, some investigators have observed that the AST/ALT ratio may be useful for predicting the presence of cirrhosis. The assessment and usefulness of this ratio was confirmed in some other studies also.<sup>6-10</sup> However, few studies showed limited value of AST/ALT ratio in predicting the presence of cirrhosis.<sup>11-13</sup> Thus, the clinical utility of this ratio may remains uncertain and needs further study. The objective of this study was to assess the usefulness of AST/ALT ratio in predicting liver cirrhosis and to correlate the ratio with histological grade (inflammatory activity) and stage (degree of fibrosis) in chronic hepatitis C patients.

## PATIENTS AND METHODS

This study was conducted at Sheikh Zayed Hospital Lahore from 1<sup>st</sup> January to 30<sup>th</sup> June 2010. 80 patients, of chronic hepatitis C positive by PCR, were included in this study. For comparison thirty healthy control were also included in study. Patients of chronic hepatitis C were enrolled and admitted with symptoms and signs of chronic liver disease confirmed by serological tests and ultrasound. Patients having HBsAg +ve cases and those with the

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history of drugs or alcohol abuse, antiviral or immunosuppressive therapy and any serious medical illness like diabetes mellitus, chronic renal failure and advanced liver disease were excluded from the study. The biochemical parameters recorded for all the patients were serum transaminases, total proteins including albumin and globulin. The haematological parameters included prothrombin time with INR, Blood Hb, TLC, DLC, and platelet count. All the patients were thoroughly examined. Liver biopsy of the patients was done and evaluated for histological changes by classified pathologist. Histological Activity Index (HAI) was scored on the basis of Knodell score. The data was analyzed by SPSS version 15. Sensitivity, Specificity, positive predictive value and negative predictive value was calculated at AST/ALT ratio of one. A p value of  $< 0.05$  was taken as significant. ANOVA test was applied to compare mean level of AST and ALT in different in three HAI grades and Stages.

## RESULTS

**Table I: Diagnostic value of AST/ALT ratio at one**

Variable	Values
Sensitivity	88.26%
Specificity	96.38 %
Positive Predictive value	93.78%
Negative Predictive value	94.83%
Diagnostic efficacy	93.58%

There was poor correlation ( $r \geq 0.1$ ) found between AST/ALT ratio and grade of the liver biopsy but a significant correlation was found between AST/ALT ratio and the histological stage to indicate cirrhosis ( $r \geq 0.03$ ). The test characteristics of AST/ALT ratio for all patients (taking liver biopsy as gold standard to indicate cirrhosis), showed 96.38% specificity and 88.26 % sensitivity of AST/ALT ratio in predicting cirrhosis. (Table I).

Out of 80 patients, 40 patients (50.1%) were found as non cirrhotic and 40 (50.1%) were found cirrhotic on liver biopsy. The Knodell HAI score

(excluding fibrosis) was 1-3 in 16 patients, 4-8 in 13 patients and 9-12 in 11 patients. Stage 1 fibrosis was found in 16 patients, stage 3 fibrosis in 6 patients and stage 4 in 18 patients. Stage 0 (no fibrosis) was detected in biopsy specimen of 19 patients. (Table II).

**Table II: Histological activity index (HAI): distribution of patients in relation to histological grade and stage on liver biopsy**

HAI Grade	No of patients
1-3	16
4-8	13
9-12	11
HAI Stage	No of patients
0	19
1	16
3	6
4	18

**Table III: AST / ALT Ratio in patients with cirrhosis, chronic hepatitis C (without cirrhosis) and control groups.**

Variable	With Cirrhosis (n $\geq$ 40)	Control Group (n $\geq$ 30)	P. value
AST/ALT ratio	1.64 $\pm$ 0.46	1.00 $\pm$ 0.24	<.001
Variable	Without Cirrhosis (n $\geq$ 40)	Control Group (n $\geq$ 30)	P. value
AST/ALT ratio	0.88 $\pm$ 0.34	1.00 $\pm$ 0.24	<.001

## DISCUSSION

Clinical use of AST/ALT ratio in assessing severity of liver disease has been evaluated by many research workers in their retrospective studies. Most of the investigators demonstrated that an AST/ALT ratio  $\geq 1$  was a reliable marker for predicting the presence of cirrhosis.<sup>6-10</sup> In one study, it was found that an AST/ALT ratio  $\geq 1$  has 100% positive predictive value for the presence of cirrhosis.<sup>5</sup> In this study, we also confirmed the usefulness of AST/ALT ratio as a means of separating the patients with cirrhosis, from those without cirrhosis. We also verified the existence of relationship of this ratio with severity

of the liver disease. Generally, the levels of AST were raised in cirrhotic patients and ALT were raised in non-cirrhotic patients as compared to those with cirrhosis. This finding was consistent with an earlier local study.<sup>7</sup>

No significant association was found between the individual levels of ALT or AST with grade or stage on liver biopsy. In our study, a significant association was found between AST/ALT ratio and the histological stage on liver biopsy. Out of 17 patients with cirrhosis, AST/ALT ratio was  $\geq 1$  in 15 patients, and out of 38 non-cirrhotic patients, only one patient had AST/ALT ratio  $>1$ . Hence, the sensitivity, specificity and positive predictive value of this ratio were 88.23%, 97.36% and 93.75% respectively, so this ratio was found significant in separating the cirrhotic from non-cirrhotic groups. The results of this study were compared with international studies done by Sheth and colleagues,<sup>5</sup> and Reedy and colleagues.<sup>12</sup> The positive predictive values in the former two studies were 100% and 77% respectively, whereas our study has demonstrated 93% positive predictive value for the presence of cirrhosis. So, our results are more close to those of Sheth and colleagues. Our study revealed that the mean AST/ALT ratio among cirrhotic patients was elevated significantly ( $p < 0.05$ ) than the patients with chronic hepatitis. These findings were consistent with the study as conducted by Butt AR and colleagues.<sup>7</sup> Similar results were demonstrated by Giannini E and colleagues, as well as Sheth and colleagues.<sup>5,6</sup> This study confirms that the low cost, non-invasive parameter that is AST/ALT ratio is highly specific for the presence of cirrhosis in patients with chronic hepatitis C and may be considered as a marker of fibrosis in chronic hepatitis C patients.

## CONCLUSION

Liver biopsy is considered as gold standard for assessing the severity of liver injury but the invasive and costly procedure of liver biopsy is associated with risk of complications and discomfort. Our study revealed that AST/ALT ratio is useful marker of liver fibrosis. It is recommended that further research work should be done on large population samples to finally accept the usefulness of AST/ALT ratio as an

alternate to liver biopsy. Other non-invasive markers may be evaluated along with this ratio for more accurate results.

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