Serum Aminotransferase Levels and Platelet Count as Predictive Factor of Fibrosis and Cirrhosis in Patients with Chronic Hepatitis C Infection

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Abstract

Objective: To assess the ratio of aminotransferases in combination with platelets count as a predictive factor for stages of fibrosis in patients with chronic hepatitis C virus infection.
Methods: A total of 266 patients were evaluated retrospectively who had undergone liver biopsy as a part of their evaluation for the management of chronic hepatitis C infection at Shifa International Hospital from 1998 to 2002. All these patients had complete blood counts and liver function tests including transaminases. The ratio of AST/ALT and platelet count of <150,000 were noted and degree of the fibrosis and cirrhosis on liver biopsies were matched. None of these patients had history of alcohol consumption. The fibrosis stages used were according to METAVIR score.
Results: An AST/ALT ratio of >1 and a platelet count of <150,000 had sensitivity of 85.6 and specificity of 90.0 with positive predictive value of 91.2 and negative predictive value of 83.4 for the fibrosis grade-Ill and IV. An AST/ALT ratio of <1 and a platelet count of >150,000 for grades 0-2, the sensitivity was 87.3, specificity 60.0, PPV 87.3 and NPV 48.0.
Conclusion: An AST/ALT ratio of >1 in combination with a platelet count of <150,000 can predict advance stage of fibrosis and cirrhosis in patients with chronic hepatitis C infection. In these patients, a liver biopsy may not be necessary (JPMA 53:101:2003).

Introduction

Hepatitis C has become a common problem worldwide and has been alarmingly increasing in Pakistan.[1] Degree of fibrosis in these patients has implications for management[2] and several consensus conferences.[3,4] have recommended a liver biopsy prior to initiation of anti viral therapy. Since liver biopsy does have some risks and complications[5], there have been attempts to evolve noninvasive means for evaluation of degree of fibrosis. Some of these attempts have used a high hyaluronic acid level, aspartate aminotransferase level and protime in addition to other markers.[6-8] More recently, there have been attempts of evaluate aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) as a ratio to evaluate stages of fibrosis and several of the studies[9-15] have shown that this ratio could be helpful in assessment of fibrosis and cirrhosis. However, others have failed to show the significance of the AST/ALT ratio in this situation.[16,17] Certain reports appeared that thrombocytopenia may be a strong predictive factor for cirrhosis in patients of chronic hepatitis C.[180] Low platelets when

combined with an AST/ALT ratio of >1 was noted to be helpful in predicting fibrosis[19] and it may not be necessary, in selected cases, to perform liver biopsy to evaluate this purpose.[20]
This study was undertaken to assess the AST/ALT ratio along with low platelets in predicting the degree of fibrosis and cirrhosis in Pakistani patients suffering from chronic hepatitis C.

Patient and Methods

This retrospective analysis included 266 patients of chronic hepatitis C who were seen at the outpatient clinic, —Shifa International Hospital Islamabad from 1998-2002. All had elevated ALT and anti HCV was found to be positive using second generation Elisa (Abbot Laboratories, North Chicago, IL, USA). They also had qualitative HCV RNA polymerase chain reaction positive (Roche Diagnostics, New Jersey. U.S.A). All patients had liver biopsies performed using either Menghini needle or 18 gauge spinal needle.[21] E 200000 These biopsy specimens were reported independently by a pathologist unaware of the patients clinical conditions or other laboratory values, using METAVIR score.[22] None of the patients admitted to consumption of alcohol. Serum AST, äserum ALT and platelet counts were performed using standard laboratory methods. All of them had less than 30 days time between these tests and the liver biopsy.
Statistical Analysis
Demographic values are shown as Mean ± SD. Sensitivities, specificities, positive predictive values (PPV) and negative predictive values (NPV) were calculated separately for patients with fibrosis score 0-2 and fibrosis score 3-4. They were also calculated with AST/ALT ratio and platelet counts of <0.05 was considered significant. Statistical analysis was performed using SPSS 10 (SPSS, Chicago, IL).

Results

There were 117 (44%) females and 149 (56°/o) males. The mean age for females was 43.14 ± 14.75 and for males 46.42 ± 13.10 years. The mean age of the entire patient population was 44.98 ± 13.92 years. Patient's fibrosis scores were as follows: Stage-0 33 (12.4 %), stage I = 21(7.9 %), stage 11 55 (20.7), stage III = 8(3.0%) and stage IV = 149 (56.0%). These numbers are depicted in Figure 1.

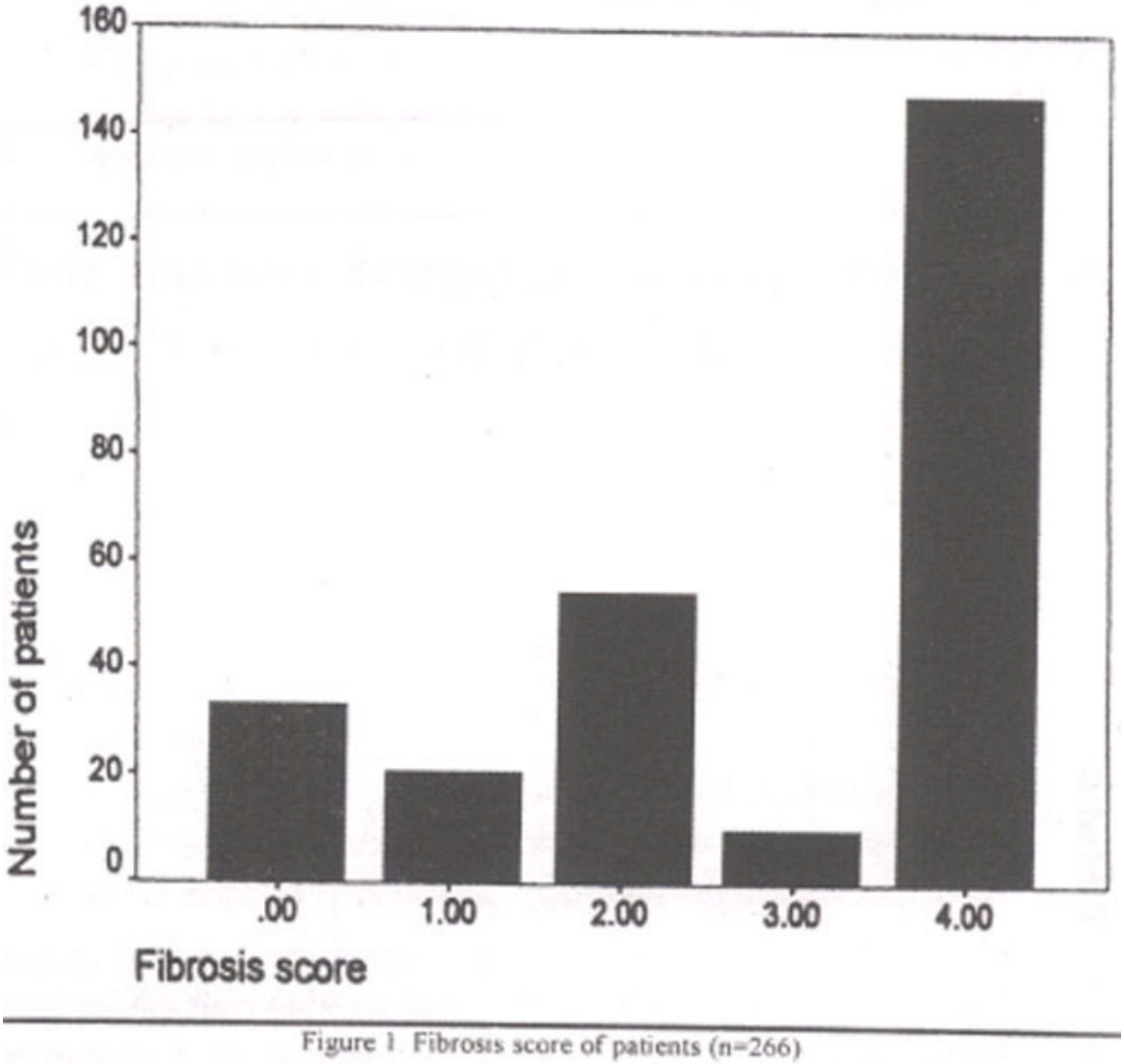

Figure 1 Fibrosis score of patients (n=266)

Mean fibrosis score was 2.82 ± 1.47 (95% CI 2.64 - 3.00). Mean necroinflammatory score was 1.88 ± 0.55 (95% CI 1.81-1.95).

Platelet counts of <150,000 were correlated with the degree of fibrosis as shown by correlation coefficient of -.776 (P<0.00) and the number continued to decrease with the progressive fibrosis, as shown in Figure 2.

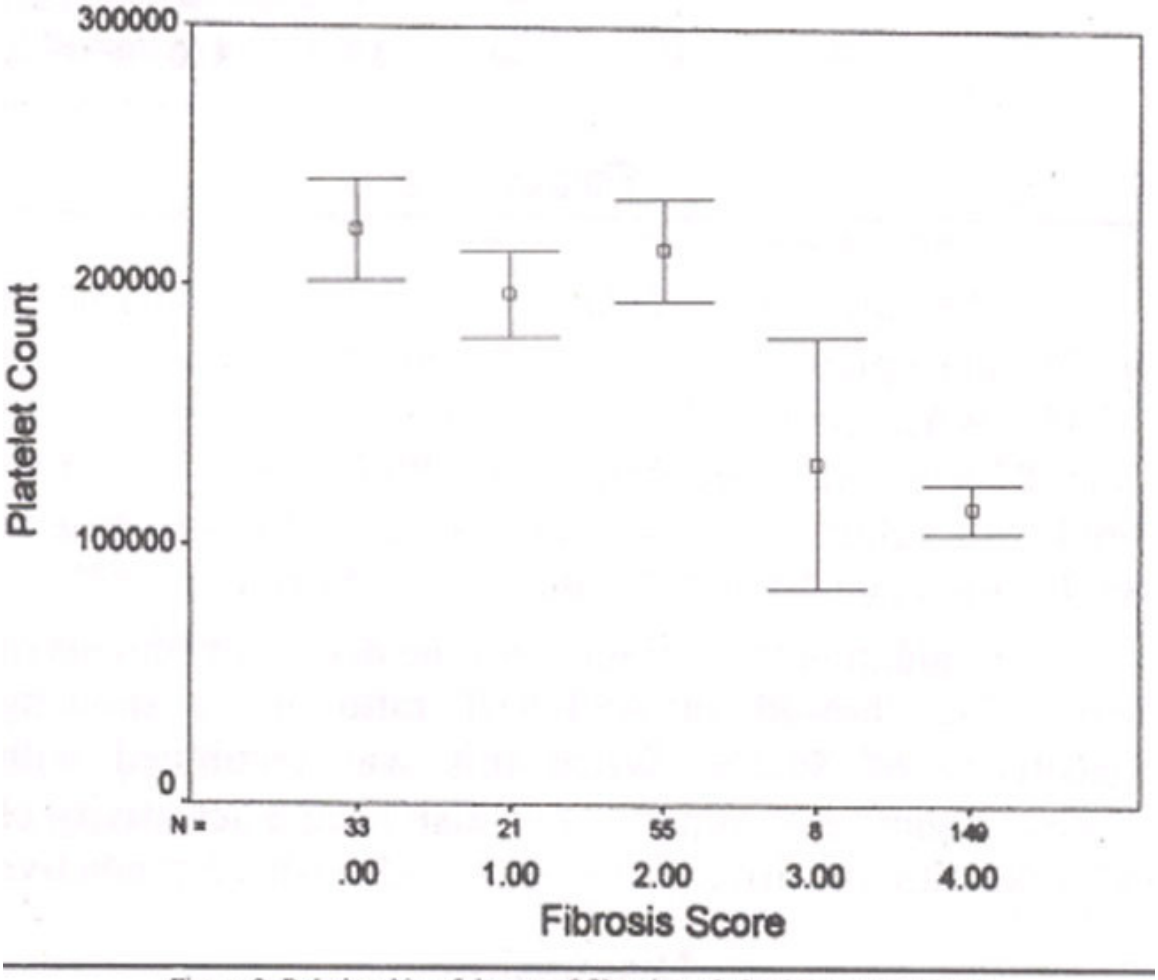

Figure 2. Relationship of degree of fibrosis and platelet count (n=266).

AST/ALT ratios were calculated and ratio of more than one was related to degree of fibrosis with correlation coefficient of .776 (P<0.00) and the ratio increased with the degree of fibrosis, as shown in Figure 3.

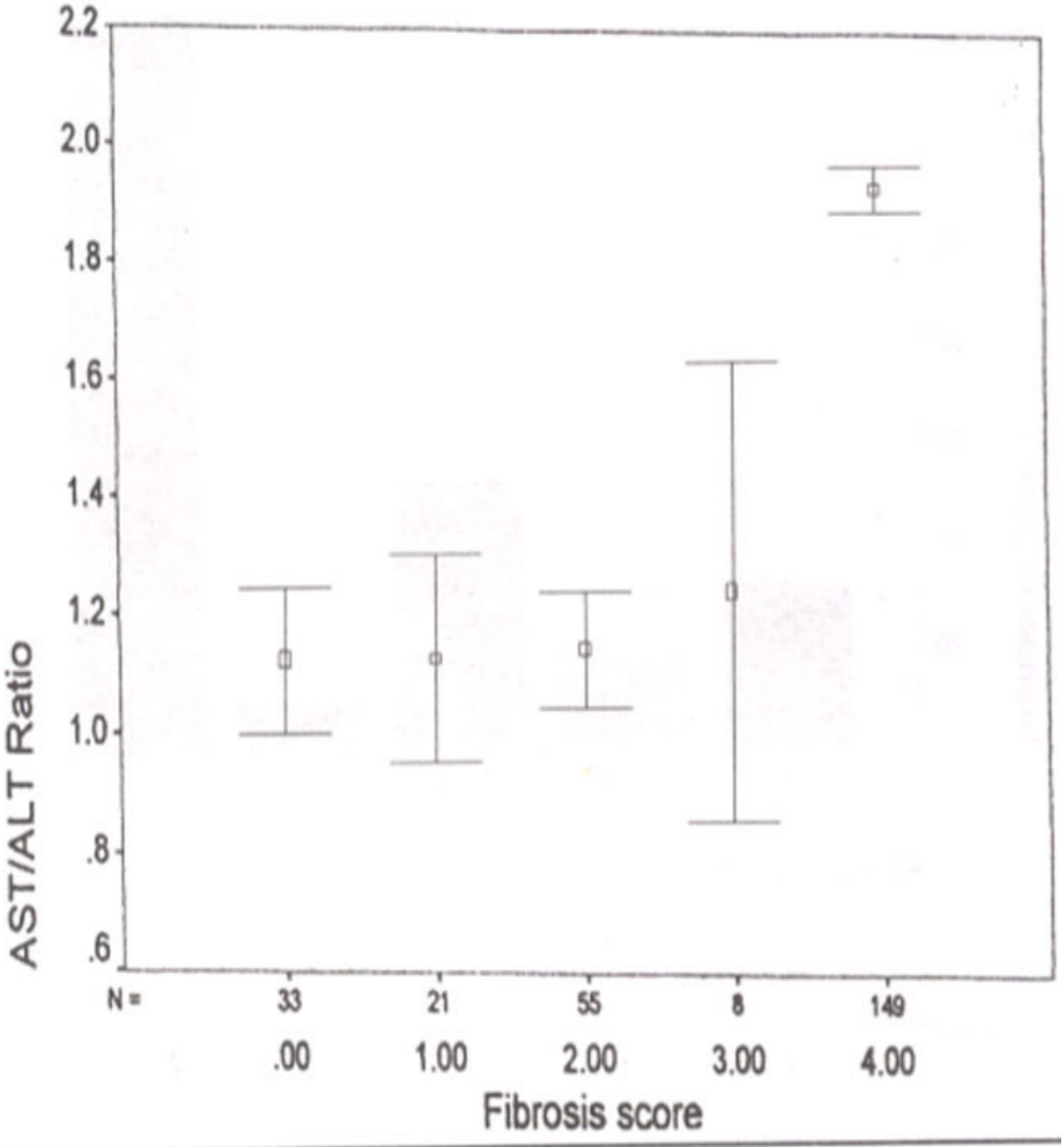

Figure 3. Relationship of fibrosis score and AST/ALT ratio (n=266)

The ratio of AST/ALT of >1 had sensitivity of 93.2% and a platelet count of<1 50,000 had a was 85.6% and specificity was 90.0% with positive predictive value of 91.2% and negative predictive value of 83.4°/o for stage-Ill and IV fibrosis (cirrhosis).
Evaluating these figures for the degree of fibrosis of stages 0-2 showed an AST/ALT ratio of <1 showing sensitivity of 86.2%. When this was combined with platelet count of>150,000/crnm it showed a sensitivity of 87.3 %.

Discussion

Several investigators have used AST/ALT ratio of >1 with specificity of 60.0% and positive predictive value of 87.3 % and negative predictive value of 48%. to predict fibrosis and cirrhosis in chronic hepatitis C patients.[9.12-14] Simple tests to predict degree of fibrosis had included platelet counts where levels of 1 50,000/cmm or less had been used and were found to indicate increasing fibrosis.[18] Recent study by Pohl et al[19] using AST/ALT ratio of>1 and platelet count of<150,000/cmm had a sensitivity of 4 1.2%, specificity of 99.1%. positive predictive value of 93.1% and negative predictive value of 85.0%. Present study showed sensitivity of 85.6 %. specificity of 90.0%. positive predictive value of 91.2% and negative predictive value of 83.4% using these parameters. Aspartate aminotransferase is a mitochondrial enzyme and HCV induced liver injury more extensively causes damage to mitochondria and increase in the AST level more than ALT and thus increasing AST/ALT ratio.[7] Also there is associated steatosis in patients with chronic hepatitis C which may raise AST levels. Low platelet levels have been noted to be present in patients of HCV infection especially those with history of blood transfusion, even in the absence of hepato cellular failure.[18]
Considering these factors it seems that these values have significant association in predicting the increasing stages of fibrosis. These figures are not as predictive in the stages 0-2 fibrosis if the AST/ALT ratio of< 1 and a platelet count of>150,000/cmm is considered. The findings of study can only be applied to the patients who do not consume alcohol as most of these patients would have a AST/ALT ratio of> 2 and will not be necessarily indicative of stage of fibrosis.[9]
This study, therefore, suggests that an AST/ALT ratio of>1 along with platelet count of<150,000/cmm can predict increasing fibrosis and cirrhosis at stages III and IV in patients with chronic HCV infection provided that there is no history of alcohol consumption. Thus, patients who fulfill this criteria may not necessarily be candidates for liver biopsy and could be spared of costs, inconvenience and its risks. However, in other patients it may be necessary to perform a biopsy to evaluate the liver histology, which will help in management of these patients.

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