Original Article

Aminotransferases in Chronic Active and Chronic Persistent Hepatitis

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Abstract:

Chronic active hepatitis (CAH) and chronic persistent hepatitis (CPH), the two histologically distinct forms of viral hepatitis present with variable clinical features. So liver function tests play the key role in diagnosis and prognosis of these disorders. Among the liver function tests, determination of serum aminotransferases: aspartate aminotransferase (AST), alanine aminotransferase (ALT) and AST/ALT ratio are still popularly used. In fact over the transaminase tests no other enzymatic tests have any particular value. In infiltrative disorders there is damage to both mitochondrial and cytoplasmic membranes. Therefore there is a proportionally greater increase in plasma AST activity than ALT. This comparative study was carried out in the department of Biochemistry, Sir Salimullah Medical College, Dhaka from January 2007 to December 2007 to observe the role of aminotransferases and AST/ALT ratio in CAH and CPH. With prefixed inclusion and exclusion criteria a total of 44 age and sex matched subjects were purposively enrolled in the study. Out of them 20 were CAH and 24 were CPH. Serum AST, ALT and total bilirubin were measured and AST/ALT ratio were calculated. Mentioned parameters were compared between groups. Unpaired student's t-test and chi (x^2) square test were done to detect the significant difference between the groups using SPSS version 12.0. Mean age of the study subjects in CAH and CPH group were 32.20 ± 10.65 years (20-50 years) and 32.83 ± 10.68 years (20-49 years) respectively. There was no significant difference regarding age and sex distribution between the groups ($p > 0.05$). Mean ± SD serum AST was 295.08 ± 153.77 IU/L and 73.38 ± 45.72 IU/L and ALT was 352.44 ± 206.95 IU/L and 121.01 ± 58.77 IU/L in CAH and CPH respectively and both were statistically highly significant ($p < 0.01$). Mean ± SD of AST / ALT ratio in CAH and CPH were 0.87 ± 0.14 and 0.59 ± 0.14 respectively and was highly significant ($p < 0.01$). There was no significant difference in serum bilirubin level between the groups (20.78 ± 14.16 µmol/L vs. 19.25 ± 15.90 µmol /L) ($p > 0.05$).

Keywords: CAH, CPH, serum aminotransferases, AST / ALT ratio.

Introduction:

Symptomatic, biochemical or serologic evidence of continuing inflammatory hepatic disease for more than six months without steady improvement is taken to mean chronic hepatitis.[1] Chronic viral hepatitis is actually three different diseases caused by three distinct viruses chronic type B hepatitis, chronic type D hepatitis (Delta hepatitis), and chronic C hepatitis (NANB hepatitis). These three diseases are clinically similar, but each has distinctive serological markers and a separate pathogenesis.[2]

Histologically three forms of viral hepatitis have been recognised chronic persistent hepatitis (CPH), chronic active hepatitis (CAH) and chronic lobular hepatitis (CLH). CPH produces either few or no symptoms. Patients appear entirely normal on examination and their aminotransferase levels are only slightly elevated. In CLH, relapses may be associated with elevations of aminotransferase levels that are consistent with acute hepatitis. Symptoms of acute hepatitis may accompany these relapses. In CAH, the clinical and laboratory features are variable. Many patients are asymptomatic or have few complaints like chronic fatigue, malaise, weakness, mild Jaundice, or signs of liver disease such as oedema and ascites. Other evidences are prolongation of the prothrombin time, decreased serum albumin level, with nearly normal or moderately elevated serum alkaline phosphatase level.[2,3]

5-10% of the adults, 20-30% of young children and 80% of infants exposed to HBV become chronic carrier whereas 50% of the hepatitis C runs to chronic infection and <5% cases of co-infection and 80% cases of superinfection of HDV runs to chronicity.[1,2,4,5]

Liver function tests are designed to detect the presence of liver disease and distinguish among different types of liver diseases along with their prognosis. Since the liver performs multiple functions, many tests are now available to the different functional disturbances. But the so called 'Liver function (LFTS)' are not tests of function at all; rather they detect hepatocellular and biliary channel patency of the liver.[6] Among the liver function tests, determination of serum aminotransferases (alanine arninotranferae - ALT or serum g1utarnic pyruvic

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transarninase - SGPT and aspartate ammotransferase AST or serum glutamic oxaloacetic transaminase - SGOT) are still popularly used by the clinician to assess the liver function, because of their simplicity and ease of availability, and these tests as the first line of investigation in the day to day care of patients with liver disorders.[7]

Although many studies were done and many review articles have been published in the past years dealing with multiple clinical applications of transaminase (ALT, AST) determinations, a precise revaluation of their use and study is still indicated to find their usefulness in liver disorders. Over the transaminase tests (ALT and AST), no other enzymatic tests have any particular value.[7]

The transaminase test is valuable in the clinical study of viral hepatitis- diagnosis and follow-up of cases, evaluation of the activity of subacute and hepatitis, effectiveness of drug treatment and also as an epidemiological detecting anicteric cases of hepatitis by mass screening of population and in identifying possible virus carriers among blood donors.[8] Liver cells contain more AST than ALT, but ALT is confined to the cytoplasm in which its concentration is higher than that of AST. In inflammatory or infective conditions, such as viral hepatitis, the cytoplasmic membrane sustains the main damage. Therefore leakage of cytoplasmic contents causes a relatively greater increase in plasma ALT than AST activities. In infiltrative disorders there is damage to both mitochondrial and cytoplasmic membranes. Therefore there is a proportionally greater increase in plasma AST activity than ALT. This relative plasma activities of ALT and AST (AST/ALT ratio) may help to indicate the type of cell damage.[9] Serum AST and ALT are cleared at different rates. ALT disappears more rapidly than AST. Turnover rate of ALT is three times more than AST. Therefore, increases in AST are more marked in chronic liver cell damage.[6,10]

The present study was designed to find out the pattern of the aminotransferases and usefulness AST/ALT ratio in chronic active and persistent viral hepatitis. This study may help to arrest further progression of the chronic hepatitis to its end stage cirrhosis.

Materials and Methods:

This comparative study was undertaken during the period of January 2007 to December 2007 in the department of Biochemistry, Sir Salimullah Medical College, Dhaka. Forty four biopsy proven diagnosed age matched cases of chronic active and persistent viral hepatitis without cirrhosis of both sex were selected purposively. Chronic hepatitis B was diagnosed on the basis of elevated serum aminotransferase activities, the presence of hepatitis B surface antigen (HbsAg) in serum for atleast 6 months, the absence of antibody to the hepatitis D virus (AntiHDV ab) and compatible hepatic histology. Chronic D hepatitis was diagnosed on the basis of elevated serum aminotransferase activities, presence of hepatitis B surface antigen in serum together with high titre of antibody to HDV (AntHDV ab) and compatible hepatic histology. Chronic hepatitis C was diagnosed on the basis of a definite history of parenteral drug abuse or history of transfusion of blood/blood products, elevations in serum aminotransferase activities and high titre of antibody to hepatitis C virus (Anti HCV ab) for at least 6 months and compatible hepatic histology. Alcoholic subjects were excluded from this study.

Diagnosed chronic viral hepatitis subjects were grouped into chronic active hepatitis and chronic persistent hepatitis on the basis of histological findings and duration of persistent elevation of biochemical markers.

Blood sample was collected after taking full aseptic precautions and sera were separated by centrifugation. Samples were stored in a refrigerator at 0-4°C.

Serum alanine aminotransferase (ALT) was determined by kinetic- ultraviolet method according to the recommendations of International Federation of Clinical Chemistry-IFCC.[11] Serum aspartate aminotransferase (AST) was determined by kineticultravilet method according to the recommendations of the expert panel of International Federation of Clinical Chemistry-IFCC.[12] Serum total bilirubin was determined by method of Malloy and Evelyn.[13] Viral serology of the patients were done in the AFIP (Armed Forces Institute of Pathology), Dhaka Cantonment, Dhaka. Histopathological examinations of Liver tissues were done in the Delta Medical Centre, Dhaka.

Data were analyzed by SPSS version 12 for Windows. Unpaired Student's t-test and chi (x^2) square test were done to detect the significant difference between the groups. $p < 0.05$ was considered as level of significance.

Results :

A total of 44 cases were studied which were diagnosed histopathologically, biochemically and serologically as chronic viral hepatitis. Among the chronic viral hepatitis patients, 24 patients (54.55%) were of chronic persistent hepatitis (CPH) and 20 patients (45.45%) were of chronic active hepatitis (CAH) for comparative study of serum AST, serum ALT, AST/ALT ratio and serum total bilirubin.

The mean age ± SD of CAH and CPH group were 32.20 ± 10.65 years and 32.83 ± 10.68 years with age range of 20-50 years and 20-49 years respectively. No significant difference was observed between the groups ($p > 0.05$). Regarding gender distribution, in CAH group 14 were male and 6 were female. On the other hand 20 were male and 4 were female in CPH group. These data revealed no significant difference regarding sex distribution between the groups ($p > 0.05$). (Table I)

Table I: Distribution and comparison of age and sex

Group	Age (years) Mean ± SD	t/p	Sex		x^2 / p
			Male	Female	
CAH (n = 20)	32.20 ± 10.65	0.196 / > 0.05	14	6	1.10 / > 0.05
CPH (n = 24)	32.83 ± 10.68		20	4	

Mean ± SD serum AST and ALT concentrations in CAH and CPH were measured and compared. Mean ± SD serum AST was 295.08 ± 153.77 IU/L and 73.38 ± 45.72 IU/L with range of 96.30-590.00 IU/L and 26.00-201.56 IU/L in CAH and CPH respectively which was statistically significant ($p < 0.01$). Whereas mean ± SD serum ALT was 352.44 ± 206.95 IU/L and 121.01 ± 58.77 IU/L with range of 119.60-776.00 IU/L and 78.00-286.00 IU/L in CAH and CPH respectively which was also statistically significant ($p < 0.01$). Serum AST / ALT ratio were calculated and compared between the groups. Mean ± SD serum AST / ALT ratio in CAH and CPH were 0.87 ± 0.14 and 0.59 ± 0.14 with range of 0.67-1.07 and 0.33-0.81 respectively and was statistically significant ($p < 0.01$). Serum bilirubin was also measured and compared between the groups. Mean ± SD serum bilirubin was 20.78 ± 14.16 µmol/L and 19.25 ± 15.90 µmol /L with range of 10.00-51.30 µmol /L and 10.00-67 µmol /L in CAH and CPH respectively which was not statistically significant ($p > 0.05$).

Table II: Distribution and comparison of studied biochemical parameters

Parameters	Group		t-value	p-value
	CAH (n = 20) Mean ± SD	CPH (n = 24) Mean ± SD		
Serum AST (IU/L)	295.08 ± 153.77	73.38 ± 45.72	-6.222	< 0.001
Serum ALT (IU/L)	352.44 ± 206.95	121.01 ± 58.77	-4.839	< 0.001
AST/ALT ratio	0.87 ± 0.14	0.59 ± 0.14	-6.870	< 0.001
Serum bilirubin (µmol/L)	20.78 ± 14.16	19.25 ± 15.90	-.333	> 0.05

Discussion:

In this study we found significantly higher serum AST, ALT and AST/ALT ratio in chronic active hepatitis than that of chronic persistent hepatitis with no significant difference in serum total bilirubin concentration. These findings are consistent with the findings of other studies.[2,14] All the studied parameters were higher than normal reference limit. Though mean AST/ALT ratio showed no alteration but the ratio was closer to 1 with more active disease.[15,16,17]

Serum transaminase elevation is a good indicator of hepatic cell damage or necrosis and the degree of elevation also represents the disease activity. The findings of this study strongly support the natural course of the disease process i.e. progressive liver functional impairment is associated with an increase in AST/ALT ratio. So it is obvious that clinicians can get a non-invasive handy tool to predict progression to cirrhosis in chronic hepatitis patients where chronic active hepatitis poses the greater risk. The effort should be given to halt the progression otherwise irreversible stage that is cirrhosis could ensue.

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