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COMPARATIVE STUDY OF AST: ALT RATIO IN LIVER DISEASES IN A TERTIARY CARE HOSPITAL IN BAREILLY

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Abstract:

Background: Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT), the enzymes predominantly found in the hepatocytes, exhibit specific elevations in serum levels in different liver diseases. The ratios of their serum levels (AST: ALT ratio or De Ritis ratio) also exhibit specific patterns providing important diagnostic clues. The objective of the study is to establish the diagnostic utility of the AST: ALT ratio in liver diseases.

Material and methods: The present study was conducted to measure the serum levels of these enzymes from the blood samples collected from a total of 60 patients with diagnosis of Alcoholic Hepatitis (AH, n= 18), Viral Hepatitis (VH, n= 18), Obstructive Jaundice (OJ, n= 06) and Chronic Hepatitis (CH, n= 18) to calculate their ratio as Mean ± SD, separately in each disease group. 24 normal healthy individuals were studied as control group. The data was analyzed using SPSS (Version 17.0) software and 'p' values were elicited using student-'t' test.

Results: An AST: ALT ratio of 2.005±0.833, 0.648±0.228, 0.865±0.147 and 1.314±0.305 was observed in AH, VH, OJ and CH respectively. Control group showed a mean AST: ALT ratio of 1.001±0.158. A significant difference ($p<0.05$) was observed when each case group was compared with control except OJ vs Control where the 'p' value was observed >0.05. A significant difference ($p<0.05$) was observed when comparison was done between any two of the disease groups.

Conclusion: AST: ALT ratio can be useful in differentiating the liver diseases.

Key words: AST:ALT ratio, De Ritis ratio, Alcoholic Hepatitis, Viral Hepatitis, Obstructive Jaundice and Chronic Hepatitis.

Introduction

Liver is a complex internal organ with interdependent metabolic, excretory and defense functions. The use of several screening tests improves the detection of hepato-biliary abnormalities, helps to differentiate the basis for clinically suspected diseases and to determine the severity of liver diseases[1]. Liver associated enzyme tests are used to detect, specifically diagnose, and to estimate the severity of hepatic diseases. Recognizing the different patterns of liver injury can be used as a guide to direct further evaluation of diseases that affect the liver[2]. Aminotransferases (previously called transaminases) are commonly employed liver enzymes to ascertain liver function. Increase in aminotransferase level is the first and only signal of liver disease[3]. A single laboratory liver test is of little value in screening for liver disease as many serious liver diseases may be associated with normal levels and abnormal levels

might be found in asymptomatic healthy individuals[4] therefore it is essential in studying liver disease to determine the activities of both aminotransferases (SGOT or AST and SGPT or ALT), as well as the AST:ALT ratio, for if only one were measured this would give much more limited diagnostic information (particularly in the case of AST) and might thus become a source of error. Simultaneous determination of the AST and ALT levels and of the AST:ALT ratio makes the diagnosis easy in more than 97% of the cases of viral hepatitis and in more than 95% of the cases of cholestatic jaundice. The transaminase (or aminotransferase) test is valuable not only in the clinical study of viral hepatitis but also as an epidemiological aid in detecting anicteric cases of hepatitis by mass screening of population groups and in identifying possible virus carriers among blood donors. AST and ALT determinations should be compulsory for all blood donors[5]. The ratio of AST:ALT in serum may help in the diagnosis of some liver diseases[6].

Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) are normally intracellular enzymes. They are involved in catalyzing chemical reactions in which amino groups of aspartate and alanine are transferred to the α-keto group of ketoglutaric acid, particularly during gluconeogenesis. AST and ALT are widely distributed in the cells throughout the body and are found in liver, heart, skeletal muscle, kidney, brain, and pancreas. ALT is found primarily in the liver and kidney, with only minute amounts in heart and skeletal muscle[7].

Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) are the most commonly used indicators of cell necrosis. They are present in high concentration in the liver cells. Injury to liver cell membranes causes leakage of aminotransferases into the circulation. Nonhepatic causes of raised aminotransferase levels include celiac sprue, hyperthyroidism & hypothyroidism, and transient elevations are observed following laparoscopic cholecystectomy[8]. Common hepatotoxic drugs which increase the serum aminotransferase levels are acetaminophen, NSAIDs, antibiotics, methotrexate and isoniazid[7], ACE inhibitors and inhibitors of Hydroxymethylglutaryl co-enzyme A[8]. Acetaminophen toxicity can result in AST and ALT levels greater than 50 times normal[9]. Increased levels of ALT are generally a result of primary liver disease such as cirrhosis, carcinoma, viral or toxic hepatitis. ALT level is normally elevated during second trimester in asymptomatic normal pregnancy[4]. Its decreased levels may be observed in renal dialysis patients and in those with vitamin B_6 deficiency. Increased levels of AST are associated with liver disease or damage, myocardial infarction, muscular dystrophy and cholecystitis. Its decreased levels are observed in undergoing renal dialysis and in those with vitamin B_6 deficiency[10]. AST is present in both mitochondria (80 %, mAST- mitochondrial iso-enzyme form) and cytoplasm (20%, cAST- cytoplasmic iso-enzyme form). In contrast, ALT is confined to the cytoplasm[8]. In alcoholism, the alcohol is responsible for (i) selective mitochondrial injury leading to release of mAST[11], (ii) depletion of pyridoxal-5'phosphate in the liver[12-14] & development of hypoglycemia[15], leading to reduced production of ALT than AST; resulting in raised AST: ALT ratio[14]. An elevated serum AST in relation to ALT has been proposed as an indicator that alcohol has induced organ damage[16]. Typically, aminotransferase levels are less than 300 IU/L in alcohol induced liver injury[17] or no higher than 6 or 7 times normal in 98 % of cases [13]. Normal value of AST:ALT ratio is slightly <1[13,18] or slightly >1[5,14] .In most liver diseases, the ratio is <1[14,19]. In alcoholic liver diseases, the ratio is always >1[14] and a ratio of >1.5[16] or >2[11,13,19,20-24] or >3[1] is highly suggestive of ALD. Measurements of mitochondrial AST may have diagnostic utility , but such determinations are not in routine use, in part because of inconvenient assay techniques and the lack of commercially available reagents[25]. The ratio of mAST to total over 4 is highly suggestive for alcohol related liver injury[26]. Large increases in mitochondrial AST occur in serum after extensive tissue necrosis and because of this, assay of mitochondrial AST have been advocated in myocardial infarction[27]. Wilson's disease can cause the ratio to exceed 4.5 and similar such altered ratio is found even in hyperthyroidism[4]. In acute viral hepatitis, there is considerable increase in both AST and ALT activities (upto 40 times the normal figures) with a large relative increase in ALT as compared with AST and a consequent decrease in AST:ALT ratio to figures considerably less than one[5]. AST:ALT ratios just below one cannot be considered as characteristic of viral hepatitis if the absolute figures for the two enzyme activities are normal or moderately increased[5].

MATERIAL AND METHODS:

The present case control study was conducted in the Department of Biochemistry, Rajshree medical research institute, Bareilly, U.P, India from January 2018 to March 2019 after getting approval from Institutional Ethical Committee. Blood samples were collected from a total of 60 patients with diagnoses of Alcoholic Hepatitis (AH, n=18), Viral Hepatitis (VH, n=18), Obstructive Jaundice (OJ, n=06) and Chronic Hepatitis (CH, n=18). 24 normal healthy individuals were studied as control group. The diagnoses were confirmed on the basis of biochemical, radiological, microbiological assessment and clinical correlation with the clinician. **Inclusion criteria**: The diagnosed cases of alcoholic hepatitis, acute viral hepatitis, obstructive jaundice and chronic hepatitis were included. **Exclusion criteria**: Individuals with other diseases associated with or without hepatitis and with H/O taking any drug altering serum AST and / or ALT levels, pregnant women and individuals with family history of liver disorder. **Biochemical analysis** included estimation of AST & ALT from fresh serum, by IFCC, kinetic method[3,16]. **Statistical analysis** was done using SPSS (Version 17.0) software and results expressed as mean ± SD. Comparison of variables between two groups were performed with student-'t' test. 'p' values <0.05 were considered significant.

RESULTS:

An AST: ALT ratio of 2.005±0.833, 0.648±0.228, 0.865±0.147 and 1.314±0.305 was observed in AH, VH, OJ and CH respectively. Control group showed a mean AST:ALT ratio of 1.001±0.158. A significant difference ($p<0.05$) was observed when each case group was compared with control except OJ vs Control where the 'p' value was observed >0.05. A significant difference ($p<0.05$) was observed when comparison was done between any two of the disease groups (Table-1).

Table: 1 showing the difference between the different groups-

Comparison of AST: ALT ratio between the groups					
	AH(n=18)	**VH(n=18)**	**OJ(n=06)**	**CH(n=18)**	**CONTROL(n=24)**
MEAN±SD	2.005±0.833	0.648±0.228	0.865±0.147	1.314±0.305	1.001±0.158
'p' value	**AH v/s VH** P< 0.0001 t = 6.6663 **AH v/s OJ** P=0.0034 t = 3.2876 **AH v/s CH** P=0.0022 t = 3.3048 **AH v/s CONTROL** t=5.7902 P<.0001	**VH v/s OJ** t=2.1681 P=0.041 **VH v/s CH** t=7.4202 P<0.0001 **VH v/s CONTROL** P< 0.0001 t = 5.9300	**OJ v/s CH** t=3.4371 P=0.002 **OJ v/s CONTROL** P=0.0666 t = 1.9089	**CH v/s CONTROL** P< 0.0001 t = 7.3242	

Table 2 showing absolute levels of aminotransferases in different groups-

	AST(MEAN±SD) (IU/L)	ALT(MEAN±SD)(IU/L)
Alcoholic Hepatitis (AH)	109.9±99.9	51.0±40.4
Viral Hepatitis (VH)	455.2±358.7	684.0±470.7
Obstructive Jaundice (OJ)	49.2±10.3	59.1±18.3
Chronic Hepatitis (CH)	55.8±61.1	56.5±81.5
Control group	28.0±6.8	28.7±8.6

Table 3: showing the mean age and male female ratio in different groups-

	MEAN AGE (years)	MALE (No.)	FEMALE (No.)
AH (n=18)	47	18 (100%)	00 (00 %)
VH (n=18)	40	14 (77.8%)	04 (22.2%)
OJ (n=06)	43	04 (66.7%)	02 (33.3%)
CH (n=18)	31	12 (66.7%)	06 (33.3%)
CONTROL (n=24)	39	17 (70.8%)	07 (29.2%)

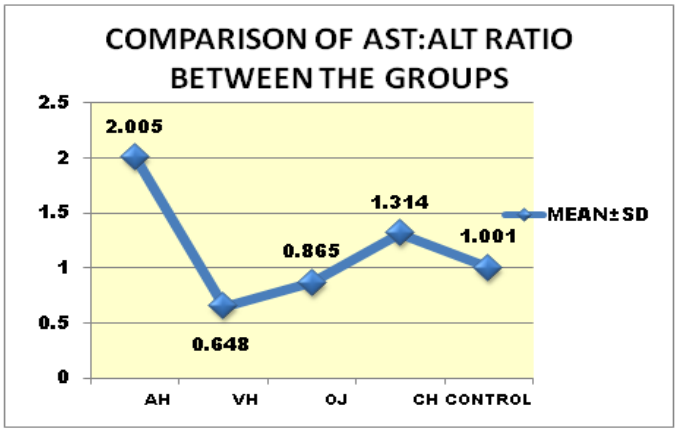

Figure 1:

DISCUSSION

Serum aminotransferases such as AST and ALT indicate the concentration of hepatic intracellular enzymes that have leaked into the circulation. These are the markers for hepatocellular injury[1].

The highest serum aminotransferase levels were observed in VH (AST 455.2± 358.7 IU/L and ALT 684±470.7 IU/L)[1]. In AH (AST 109.9±99.9 IU/L and ALT 51.0±40.4IU/L), ALT is not elevated to the extent as AST, but elevations in both the enzymes are less than 300 IU/L. The absolute enzyme elevations (AST 55.8±61.1 and ALT 56.5±81.5) in serum in CH were around four times the mean values in control group. Lower levels (less than 100IU/L) were observed in cases of OJ (AST 49.2±10.3 IU/L and ALT 59.1±18.3 IU/L). In VH and OJ, ALT activity was significantly greater than AST. In AH and CH, AST activity was significantly greater than ALT.

In our study, the mean AST/ALT ratio of 1.001±0.158 was observed in control group which is comparable with the studies of Dr. G. Vijaya Benerji[1]; Philip Hall and Johnny Cash[13]; R. Ferrari et al[18]; Subir Kumar Das, D. M. Vasudevan[14]; and Fernando De Ritis et al.[5].

The mean AST/ALT ratio in AH in our study was obtained 2.005±0.833 which is consistent with the results obtained by Gavin Arteel et al[20]; Bouneva et al[11]; Philip Hall & Johnny Cash[13]; Fuad A.M. Hasan, Salim Owyed[19]; and Sorbi D, Boynton J, Lindor KD[21].

We observed in 16 cases (88.8% of total AH cases) of AH the ratio of >1, in 12 cases (66.6%) >1.5, in 8 cases (44.4%) >2.0, in 7 cases (38.8%) >2.5 and in 2 cases (11.1%) the ratio of >3.0.

We observed in 6 cases (33.3% of total VH cases) the ratio of >1 and in 12 cases (66.7%) the ratio of <1.

Obstructive group showed the AST: ALT ratio of >1 in 2 cases (33.3%) and <1 in 4 cases (66.7%).

4 cases (22.2%) among CH group showed the ratio of >1 and 14 cases (77.8%) showed <1.

Our results of AST:ALT ratio in VH (0.648± 0.228) are similar to the results obtained in the studies of R. Ferrari et al[18]; Jerold A. Cohen and Marshall M. Kaplan[28]; and others[14] and the results in OJ (0.865± 0.147) and CH group (1.314± 0.305) are consistent with the study of Jerold A. Cohen and Marshall M. Kaplan[28] (0.81 ±0.06 and 1.3 ± 0.17 respectively). The raised AST/ALT ratio in chronic cases may be due to the fact that Mitochondrial AST is also increased in chronic liver disease as documented by B.R. Thapa and Anuj Walia[27].

CONCLUSION

The AST/ALT ratio (along with the activities of AST and ALT in serum) may contribute in differentiating the cases of liver diseases into Alcoholic Hepatitis, Viral Hepatitis, Obstructive Jaundice and Chronic Hepatitis.

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