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Original Article

Ratio Of Ast/alt And Serum Gamma Glutamyl Transferase (ggt) Activity In Chronic Alcoholics And Acute Viral Hepatities."

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ABSTRACT

Background:. Liver enzymes AST, ALT, Gamma Glutamyl Transferase (γ-GT), ALP activity in serum is assayed in Controls, Chronic alcoholics and Acute viral hepatitis and controls. Analysis was done to find the comparative level of liver associated enzymes among chronic alcholics and viral hepatitis. Materials and Methods: Fifty-one chronic male alcoholics aged between 30-60 years, and thirty six patients with viral hepatitis who were admitted to the medicine ward, were the subjects. Forty Eight Age-matched, normal, healthy controls were also included in the study. GGT, ALT, AST and ALP were assayed in the clinical biochemistry laboratory using auto analyser by kit method Results: Chronic alcoholics (n=51) subjects shows increased in serum levels of GGT (185.42±58.32), ALT (83.43±32.48), AST (139.29±64.34), ALP (173.42±31.62), as compared to controls which was statistically significant. In Acute Viral hepatitis (n=36), all enzymes levels were statistically increased significant as compared to controls. But the levels of GGT (108.47±31.54) & ALT (293.43±54.62) were more significant in viral hepatitis as compared to controls and chronic alcoholics. Ratio of AST/ALT was significantly increased (1.66) as compared to controls (0.92). But the ratio of AST/ALT was more significantly decreased (0.49) in acute viral hepatitis as compared to chronic alcoholics.Conclusion: Serum GGT and the ratio of AST/ALT increased much more in chronic alcoholics than viral hepatitis. In Viral hepatitis the GGT increased but not more than in chronic alcoholics, while level of ALT most significant in viral hepatitis.

1. Introduction

Introduction-Gamma Glutamyl Transferase (GGT), also known as Gamma Glutamyl Transpeptidase, is a micorsomal enzyme with a wide tissue distribution. GGT is present in the cell membranes of many tissues, including the kidneys, bile duct, pancreas, gallbladder, spleen, heart, brain, and seminal vesicles.[1]It is involved in the transfer of amino acids across the cellular membrane[2] and leukotriene metabolism.[3] It is also involved in glutathione metabolism by transferring the glutamyl moiety to a variety of acceptor molecules including water, certain L-amino acids, and peptides, leaving the cysteine product to preserve intracellular homeostasis of oxidative stress.[4,5] GGT is predominantly used as a diagnostic marker for liver disease, latent elevations in GGT are typically seen in patients with chronic viral hepatitis infections often taking 12 months or more to present.[6]

Elevated serum GGT activity can be found in diseases of the liver, biliary system, and pancreas. In this respect, it is similar toalkaline phosphatase (ALP) in detecting disease of the biliary tract. Indeed, the two markers correlate well, though there is conflicting data about whether GGT has better sensitivity.[7,8] In general, ALP is still the first test for biliary disease. The main value of GGT over ALP is in verifying that ALP elevations are, in fact, due to biliary disease; ALP can also be increased in certain bone diseases, but GGT is not.[8] More recently, slightly elevated serum GGT has also been found to correlate with cardiovascular diseases and is under active investigation as a cardiovascular risk marker. GGT in fact accumulates in atherosclerotic plaques,[9] suggesting a potential role in pathogenesis of cardiovascular diseases,[10].

Patients with alcoholic liver disease may exhibit increased serum activities of various enzymes including gamma-glutamyltransferase (GGT).,[11] alkaline phosphatase (ALP),[12] aspartate aminotransferase (AST)[11,13] alanine aminotransferase (ALT)[11] and glutamate dehydrogenase (GDH)[11]. A few population studies [14–17] have examined the relationship between serum GGT and all-cause mortality, focusing on GGT as an indicator of alcohol consumption. Serum GGT has been found to predict morbidity and mortality independent of alcohol consumption and liver pathology[18].

The AST/ALT ratio is the ratio between the concentrations of the enzymes aspartate transaminase (AST) and alanine transaminase(ALT) in the blood of a human or animal. It is measured with a blood test and is sometimes useful in medical

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diagnosis to differentiate between causes of liver damage, or hepatotoxicity.[19,20,21] Most causes of liver cell injury are associated with an AST that is lower than the ALT. An AST to ALT ratio of 2:1 or greater is suggestive of alcoholic liver disease, particularly in the setting of an elevated gamma-glutamyl transferase.[22]

However, the AST to ALT ratio is occasionally elevated in an alcoholic liver disease pattern in patients with non alcoholic steatohepatitis, and it is frequently elevated in an alcoholic liver disease pattern in patients with hepatitis C who have developed cirrhosis. In addition, patients with Wilson's disease or cirrhosis due to viral hepatitis may have an AST that is greater than the ALT, though the ratio typically is not greater than two.

Present study was conducted to find the comparative level of liver associated enzymes among Viral Hepatitis, Chronic Alcoholic and their significance in this diseases.

MATERIALS AND METHODS

Fifty-one chronic male alcoholics (with a history of alcohol abuse for five years or more) aged between 30-60 years, and thirty six patients with viral hepatitis who were admitted to the medicine ward, were the subjects. Patients, who had severe somatic complications, necessitating treatment in medical wards, were excluded. Forty Eight Age-matched, normal, healthy controls were also included in the study. GGT, ALT, AST and ALP were assayed in the clinical biochemistry laboratory using auto analyser by kit method.

Ethical approval was obtained from concerned authority and informed consent was taken from each participant.

Statistical Analysis -Biostatistical Analysis was done by using Microsoft Office Excel with Windows operating system and using Graph Pad Prism software.

Results expressed as (mean ±SD). Comparison of between controls and chronic alcoholics, viral hepatitis groups performed with student t-test. The p values < 0.05 were considered statically significant

Results

Chronic alcoholics (n=51) subjects (Table No-1) & (Fig-1)shows increased in serum levels of GGT (185.42±58.32), ALT (83.43±32.48), AST (139.29±64.34), ALP (173.42±31.62), as compared to controls which was statistically significant. In Acute Viral hepatitis (n=36), all enzymes levels were statistically increased significant as compared to controls. But the levels of GGT (108.47±31.54) & ALT (293.43±54.62) were more significant in viral hepatitis as compared to controls and chronic alcoholics.

Ratio of AST/ALT was significantly increased (1.66) as compared to controls (0.92). But the ratio of AST/ALT was more significantly decreased (0.49) in acute viral hepatitis as compared to chronic alcoholics (Fig-2).

Table 1: Enzymes value (Mean±SD) among controls and chronic alcoholic, patients' viral hepatitis

Enzymes(U/IL)	Control(48)	Chronic Alcoholics(51)	Viral Hepatitis(36)
GGT	29.73±3.92	185.42±58.32*	108.47±31.54**
ALT	13.28±2.38	83.43±32.48*	293.43±54.62**
AST	12.32±4.25	139.29±64.34*	145.72±47.63
ALP	41.47±8.48	173.42±31.62*	218.34±71.47
AST/ALT	0.92	1.66*	0.49**

*p- value significant change as compared to controls. **p-value more significant change as compared to chronic alcoholics.

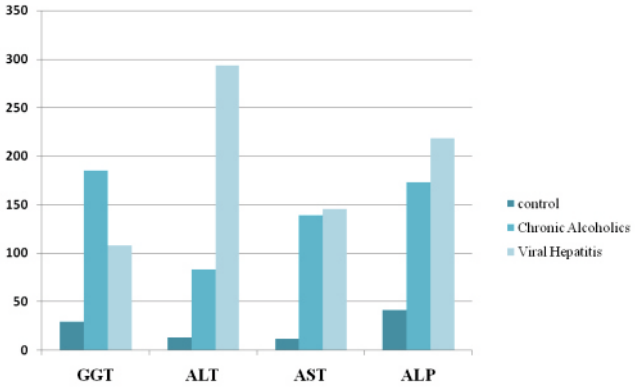

Fig .1-Enzymes levels in controls, chronic acholics, viral hepatitis

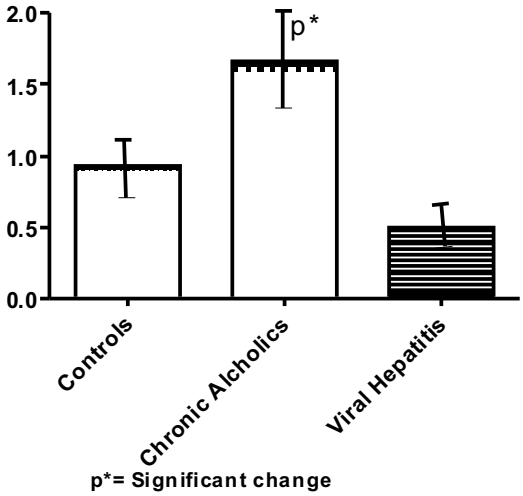

Fig:2 - Ratio of AST/ALT

DISCUSSION

The enzymes, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase(ALP) and gamma glutamyl transferase (GGT) are increased in alcoholic liver diseases and viral hepatitis. In the present study all these enzymes were increased. These enzymes are measures of liver homeostasis [23]. Serum amino transferases such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) indicate the concentration of hepatic intracellular enzymes that have leaked into the circulation. These are the markers for hepatocellular injury [24].

The aminotransferases (transaminases) are sensitive indicators of liver cell injury and are most helpful in recognizing acute hepatocellular diseases such as hepatitis. The pattern of the aminotransferase elevation can be helpful diagnostically. In most acute hepatocellular disorders, the ALT is higher than or equal to the AST.

In this study AST, ALT ALP, GGT levels were significantly raised in viral hepatitis, chronic alcoholic liver disease patients as compared to control. In viral hepatitis AST, ALT Levels were more significantly high as compared to chronic alcoholic liver. In

viral hepatitis ALT is greater than AST. The peak levels of transminases have been reported to vary from 400-4000 IU/l or more [25]. In alcoholic liver disease AST activity has been reported to be greater than ALT and usually does not exceed 300 IU/L.

In patients with increased serum aminotransferase activity, the predominance of AST over ALT in alcohol-related liver disease was first reported by Harinasuta et al. in 1967. However, it became more widely recognized only with the paper by Cohen and Kaplan in 1979. The diagnostic significance of a high AST/ALT ratio for alcoholic liver disease was recently underscored in the Practical Guidelines for Alcoholic Liver Disease published by the American College of Gastroenterology in 1998 (McCullough and O'Connor, 1998). An AST: ALT ratio>2:1 is suggestive while a ratio >3:1 is highly suggestive of alcoholic liver disease. The AST in alcoholic liver disease is rarely >300 U/L and the ALT is often normal. A low level of ALT in the serum is due to an alcohol induced deficiency of pyridoxal phosphate [26]. In this study, Table 1 shows the AST: ALT ratios 0.92 for normal, 0.49(<1) for viral hepatitis, consistent with F .DE RITIS et al[27], < 2 for chronic alcoholics group, which similar to reported by several other studies conducted earlier [28] and others . This helps to differentiate ALD from other liver diseases. AST/ALT ratio is greater than 2 because of existing mitochondrial damage [25, 29].

The ALP activity has been reported by various workers , minimally increased usually up to 200 -300 U/L in viral hepatitis and in alcoholic liver disease ALP usually up to 300 U/L. Elevation of ALP is observed in patients who have some form of extra hepatic and intra hepatic bile duct obstruction. Any mechanism that impaired excretion of ALP in bile will result in regurgitation of enzyme into circulation via the hepatic sinusoid. The increased ALP present in the patients with disease closely resembles the ALP that can be extracted from liver. The increased cholestatis stimulates the synthesis of ALP by the bile ductules cell providing more ALP which ultimately enters the bloods, the amphillic nature of bile salts facilitates the release of ALP from its membranes bound site and entry into blood [30] .

CONCLUSION

Serum GGT and the ratio of AST/ALT increased much more in chronic alcoholics than viral hepatitis. In Viral hepatitis the GGT increased but not more than in chronic alcoholics, while level of ALT most significant in viral hepatitis.

To conclude, most patients with chronic alcoholic consumption have an AST/ALT ratio above 1. A high AST/ALT ratio is suggestive of advanced alcoholic liver disease.

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