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Comparative Study of Serum Levels of Gamma-glutamyl Transferase, Aspartate Aminotransferase (AST), Alanine Transaminase (ALT), AST: ALT, and Bilirubin in Patients with Chronic Hepatitis

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ABSTRACT

Introduction: Viral hepatitis and other liver-related diseases are mostly difficult to diagnose solely based on clinical regimes. Liver damage results in alterations in serum enzyme patterns which have been used to develop many enzyme-based assays.

Aim and objectives: The major clinical consequences of chronic liver disease can be evaluated by liver function tests like bilirubin, gamma- glutamyl transferase (GGT), aspartate aminotransferase (AST), and alanine transaminase (ALT). Alanine transaminase and AST changes indicate leakage from damaged hepatocytes. The present study was conducted to compare the serum levels of GGT, AST, ALT, AST:ALT ratio, and bilirubin in patients with chronic hepatitis.

Materials and methods: The study group comprised 100 clinically diagnosed patients with chronic hepatitis and 100 controls.

Results: Case–control comparison showed statistically higher values of GGT ($p < 0.01$), AST ($p < 0.05$), ALT ($p < 0.05$), AST: ALT ($p < 0.01$), and bilirubin ($p < 0.05$) in cases and serum levels of GGT, AST: ALT, and bilirubin were sensitive and specific when various parameters were compared with each other in various hepatitis and controls.

Conclusion: The present study indicates that the parameters GGT, AST, ALT, AST:ALT ratio, and bilirubin are associated with increased risk of hepatitis.

Keywords: Alanine transaminase, Aspartate aminotransferase, Bilirubin, Chronic hepatitis, Gamma-glutamyl transferase.

INTRODUCTION

Liver performs numerous metabolic, excretory, secretory, storage, & detoxifying functions. For reviewing liver function tests (LFTs), gamma-glutamyl transferase (GGT), alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), prothrombin time (PT), serum bilirubin, the international normalized ratio, and albumin are considered to be useful for examining the hepatic injury as well as pattern of elevation.[2] Hepatocytes, renal tubules, biliary epithelial cells, the pancreas, and the gut all contain the microsomal enzyme GGT. Several medications, including oral contraceptives and anticonvulsants, have the ability to activate it.[3] Numerous non-hepatic illnesses, such as chronic obstructive lung disease and renal failure, are associated with elevated GGT levels. Weeks after an acute myocardial infarction, it might still be there. Alcoholic liver disease (ALD) can cause increased blood levels due to enzyme induction and reduced clearance. In contrast to ALP levels, which may be normal or just mildly affected in these patients (GGT/ALP ratio >2.5), GGT serum levels can be considerably altered (>10 times the upper reference value). Any type of liver disease could be to blame for altered GGT serum levels, regardless of the source. More than 50% of patients with nonalcoholic fatty liver disease and roughly 30% of patients with chronic hepatitis C may have GGT levels that are 2–4 times higher than the upper reference limit, respectively.[4] Alanine transaminase and AST also termed as serum glutamic pyruvic transaminase and serum glutamic oxaloacetic transaminase, respectively, are widely distributed in the cells throughout the body. The equilibrium between the regular turnover of hepatocytes brought on by programmed cell death (apoptosis) and the removal of the enzymes from the plasma is represented by the normal levels of these enzymes in healthy persons.[5] The reticulo-endothelial system's breakdown of hemoglobin results in bilirubin. Unconjugated bilirubin is produced as a result of heme breakdown and is subsequently delivered to the liver. Water-insoluble unconjugated bilirubin is converted by uridine-5- diphospho (UDP) glucuronyl transferase in the liver to glucuronic acid, where it is subsequently expelled into the bile.[6] The present research was done to compare the serum levels of GGT, AST, ALT, AST:ALT ratio, and bilirubin in patients with chronic hepatitis.

MATERIALS AND METHODS

The present research was done in Basaveshwara medical college and Hospital, Chitradurga. The study group comprised 100 clinically diagnosed subjects of chronic hepatitis that belonged to three categories, i.e., 35 patients of viral hepatitis, 35 patients of alcoholic hepatitis, and 30 patients of idiopathic hepatitis reported in the Medicine OPD or admitted in Medicine ward. A total of 100

age- and sex-matched healthy controls with no previous history of hepatitis were recruited from the general population. Anti-HCV ELISA and HBs Ag ELISA tests (Meril Diagnostics) served as the defining criteria for chronic hepatitis and its subtypes, while controls were deemed to be in excellent health and had normal livers according to ultrasound examination. Individuals taking any drug (that can alter serum GGT, AST, ALT, and bilirubin levels) or those suffering from any kind of autoimmune diseases, metabolic disorder, diabetes mellitus, heart disease, etc. were excluded from the research. After getting informed consent, a detailed history of all the participants was taken on a pre-designed questionnaire. For the evaluation of blood serum GGT, AST, ALT, AST:ALT ratio, and bilirubin, 5 ml blood sample was withdrawn from the anticubital vein of all participants and were collected in a sterile, dry, and plain vial. The serum utilized in the estimation of biochemical assays was separated from the blood sample by centrifugation at 3000 rpm for 10 minutes.

RESULTS

In the present study, the range of age for cases and controls was 25–65 years. An equal number of male and female participants were enrolled in the study.

The comparison of various enzymes, AST:ALT ratio, and serum levels of bilirubin in patients and controls is illustrated in Table 1.

Table 1: Comparison of various enzymes, AST:ALT ratio, and serum levels of bilirubin in cases and controls (mean ± standard deviation along with CI)

Groups	*Gamma-glutamyl transferase (U/L)*	*Aspartate aminotransferase (U/L)*	*Alanine transaminase (U/L)*	*AST:ALT*	*Bilirubin (mg/dL)*
Group I (cases) *n* = 100	87.96 ± 21.14 (83.7–92.1)	77.63 ± 29.15 (73.8–81.4)	42.76 ± 20.76 (38.6–46.8)	2.14 ± 0.87 (1.9–2.3)	3.54 ± 1.26 (3.2–3.7)
Group II (controls) *n* = 100	35.44 ± 8.08 (33.8–37.04)	23.60 ± 10.56 (22.3–24.8)	26.17 ± 10.58 (24.0–28.2)	1.03 ± 0.46 (0.9–1.1)	0.95 ± 0.42 (0.9–1.0)
p-value	<0.01**	0.02*	0.03*	<0.01**	0.03*

It was observed that when control group was compared with the patients with hepatic disorders, the serum level of GGT, a marker of ALD, and AST:ALT ratio were increased highly significantly in patients as compared with controls. Similarly, serum levels of AST, ALT, and bilirubin were increased significantly as compared with controls.

The comparison of various enzymes, AST:ALT ratio, and serum levels of bilirubin in viral hepatitis, alcoholic hepatitis, idiopathic hepatitis, and controls is illustrated in Table 2.

Table 2: Comparison of various enzymes, AST:ALT ratio and serum levels of bilirubin in various types of hepatitis and control (mean ± standard deviation along with CI)

Parameters	*Viral hepatitis*	*Alcoholic hepatitis*	*Idiopathic hepatitis*	*Controls*	*p-value*
Gamma-glutamyl transferase (U/L)	81.34 ± 12.29 (77.1–85.5)	110 ± 11.6 (106–113.9)	69.97 ± 14.73 (64.5–75.4)	35.44 ± 8.08 (33.8–37.04)	<0.01**
AST (U/L)	93.31 ± 9.98 (89.9–96.7)	64.69 ± 17.99 (58.5–70.8)	94.43 ± 15.70 (68.6–80.2)	23.60 ± 6.32 (22.3–24.8)	0.02*
ALT (U/L)	32.11 ± 12.08 (29.3–34.8)	30.03 ± 13.86 (24.6–33.4)	70.03 ± 24.39 (65–75)	26.17 ± 11.58 (24.0–28.2)	0.02*
AST:ALT	3.02 ± 0.52 (2.5–3.2)	2.18 ± 0.52 (2.1–2.2)	1.08 ± 0.43 (0.9–1.1)	1.03 ± 0.46 (0.9–1.1)	<0.01**
Bilirubin (mg/dL)	4.76 ± 0.80 (4.4–5.0)	3.32 ± 0.72 (3.1–3.5)	2.38 ± 0.81 (2–2.7)	0.95 ± 0.42 (0.9–1.0)	<0.01**

It was observed that when all the hepatic disorders were compared with each other along with the controls, the serum level of GGT was highly significant, same is the case with the AST:ALT ratio and bilirubin, whereas the serum levels of AST and ALT showed the significant results.

Table 3: Correlation of different parameters of chronic hepatitis cases

Parameters	*r*	*p*
GGT	0.012	0.780
AST	–0.376	0.000
ALT	0.508	0.000
AST: ALT	–0.203	0.068
Bilirubin	–0.240	0.000

The statistical analysis revealed that AST, ALT and Bilirubin had a correlation with progression of chronic hepatitis (AST < 0.01, ALT<0.01, bilirubin <0.01).

DISCUSSION

Serum aminotransferases, bilirubin, and ALP are just a few of the liver biochemical tests referred to collectively as 'liver function tests' in medical terminology.[7] Hepatocytes contain aminotransferases, which were formerly known as transaminases and are sensitive markers of hepatocyte damage. They help in the early detection of acute hepatocellular disorders like hepatitis. They are made up of ALT and AST.[8] The test offering the best ease and sensitivity remains to be the traditional marker GGT. Combining it with other conventional markers like aminotransferases (AST, ALT) and certain measures that show the severity and prognosis, including total proteins, albumin, bilirubin, and PT, can improve its diagnostic accuracy.[9] Hence the present research was conducted to compare the serum levels of GGT, AST, ALT, AST:ALT ratio, and bilirubin in patients with chronic hepatitis. In the present study, it was observed that when control group was compared with the patients with hepatic disorders, the serum level of GGT a marker of ALD and AST:ALT ratio were increased highly significantly ($p < 0.01$) in patients as compared with controls. Similarly, serum levels of AST, ALT, and bilirubin were increased significantly ($p < 0.05$) in patients as compared with controls.

In the present study, AST and ALT were increased maximum in idiopathic hepatitis followed by viral hepatitis, whereas GGT was found maximum in alcoholic hepatitis followed by viral hepatitis and idiopathic hepatitis. Aspartate aminotransferase and alanine transaminase ratio and bilirubin were highest in viral hepatitis followed by alcoholic hepatitis.

Patil et al.[10] revealed similar results in their study. They claimed that moderate-to-heavy alcohol use and hepatobiliary diseases both resulted in an increase in serum GGT activity. When compared with healthy controls, individuals with acute viral hepatitis (AVH) and individuals with non-alcoholic cirrhosis, GGT was found to be considerably raised in patients with ALD in a study by Patil et al. Smooth endoplasmic reticulum has a significant amount of GGT, making it susceptible to hepatic microsomal activation by drugs and alcohol. Alcohol has an impact on GGT activity, hence GGT assays are thought as sensitive indicators of alcoholism. Numerous studies have linked high GGT levels (>25 IU/L) to ALD.

The early decline in GGT value is a good and specific indicator of alcohol misuse and, as a result, of the alcoholic etiology of the disease. Gamma- glutamyl transferase presents as a poor indicator of alcoholism with chronic liver diseases. The aminotransferases provide far better insight into the progression of the disease, but GGT has very little diagnostic value in acute hepatitis.[10,11] In case with AVH, GGT levels are observed to be raised negligibly with respect to peak levels. In their investigation, Batta et al.[11] found that the ALT was typically higher than or equivalent to the AST in most acute hepatocellular diseases. A ratio of greater 2:1 or 3:1 is predictive of ALD in terms of the AST: ALT ratio. Rarely is the AST in ALD greater than 300 U/L, although ALT is frequently normal. A pyridoxal phosphate deficit brought on by alcohol is the cause of a low level of ALT in the serum. In comparison to controls, patients with cirrhosis, ALD, and viral hepatitis had significantly higher serum levels of AST, ALT, ALP, and GGT. In comparison to cirrhosis and ALD, serum levels of AST, ALT, and ALP were much higher in viral hepatitis. In addition, patients with ALD had higher levels of AST, ALT, and ALP than those with cirrhosis. Alanine transaminase was higher than AST in cases of viral hepatitis. Transaminase peak values have been observed to the range from 400 to 4000 IU/L or higher.[12] Alcoholic liver disease has been associated with higher than average AST activity, which typically does not reach 300 IU/L.[13] Alcohol usage actively raises AST and ALT levels. Serum GGT levels in viral hepatitis are much lower than those in cirrhosis and higher than those with chronic and alcoholic hepatitis; also, cirrhosis has higher GGT levels than ALD. The extraordinarily sensitive enzyme GGT, which is found in the cell membranes of the hepatobiliary system, can detect both intra- and extra-hepatic cholestasis illness.[11] In various investigations, patients with viral hepatitis, alcoholic hepatitis, and chronic hepatitis, respectively, showed varying patterns of increasing GGT value. An increasing body of research indicates that up to 25% of people with chronic hepatitis C virus infection continue to have normal aminotransferase levels (10–40%, according to different studies).[14,15] The top limit of the normal range for healthy individuals is often set as the cutoff value for ALT in most nations. Men and women have normal ALT values of 23 and 18 IU/L, respectively.[12,13]

According to Patil et al.'s[10] study, patients with AVH had considerably higher ALT activity than those with ALD ($p < 0.001$). However, in AVH, ALT levels did not go above AST levels. When the AST/ALT ratio is more than 1, it may indicate extensive cell necrosis that is severe enough to release significant amounts of mitochondrial AST and a worse prognosis. Similar to this, a study by Nyblom et al.[16] revealed that the AST/ALT ratio considerably increased in patients with alcohol dependency (1.0 in 64% of patients), patients with withdrawal symptoms, cirrhosis, and other consequences (2 in 69% of patients), and patients with other difficulties (1.0 in 8% of patients). The majority of people who consume a lot of alcohol but do not have serious liver disease, do not have an AST/ALT ratio exceeding 1. A high AST/ALT ratio indicates advanced liver damage from alcohol.

Even though higher levels were noted in patients with ALD, an increased AST/ALT ratio in patients with increased serum aminotransferase activity has also been linked to the emergence of cirrhosis in non-alcoholic steatohepatitis. However, there was a defense made against the AST/ALT ratio being solely determined by the progression of cirrhosis. After the treatment, Nyblom et al.[16] shown that the ratio quickly fell in patients with ALD. This would imply that alcohol's direct harmful effect on the AST/ALT ratio is a factor. In the current investigation, viral hepatitis had the highest levels of bilirubin. According to Patil et al., patients with viral hepatitis have lengthier disease progression and more histological evidence of hepatocellular damage, the higher the serum bilirubin levels.[10]

CONCLUSION

From the study, it can be concluded that when all the parameters (GGT, AST, ALT, AST:ALT ratio, and bilirubin) were compared with each other in various hepatitis groups and controls, the increased serum levels of GGT, AST:ALT ratio, and bilirubin were seen in patients. The ratio of AST:ALT was high in viral hepatitis patients, whereas levels of GGT were high in patients with alcoholic hepatitis when compared with controls. Serum levels of AST were on higher side in idiopathic hepatitis as compared with controls. Thus, the present study suggests that the five markers, that is, GGT, AST, ALT, AST:ALT ratio, and bilirubin, are prominent indicators of chronic hepatitis and must be routinely used for clinical diagnosis.

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