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Original Research Article

Serum Levels of Gamma-Glutamyl Transferase, Aspartate Aminotransferase (AST), alanine Transaminase (ALT), AST: ALT, and Bilirubin in Patients with Chronic Hepatitis: A Hospital Based Comparative Study.

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Conflict of interest: Nil

Abstract:

Objectives: The present study was to evaluate and compared the serum levels of gamma-glutamyl transferase, aspartate aminotransferase (AST), alanine transaminase (ALT), AST: ALT, and bilirubin in patients with chronic Hepatitis with control.

Methods: 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 For the evaluation of blood serum GGT, AST, ALT, AST:ALT ratio, and bilirubin, 5 ml blood sample was withdrawn from the anticubital vein of all participants and were collected in a sterile, dry, and plain vial.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. The IFCC method was used to estimate the serum levels of the parameter using a commercially available kit from Transasia Pvt. Ltd. The tool used was an ERBA 5 chem semi-auto analyser.

Results: A total of 50 chronic hepatitis patients were enrolled in a case group and 50 healthy individuals were included as control group. Mean age of the patients in case group was 50 ± 12.87 years. And mean age of healthy individual in control group was 48 ± 14.76 years. In case group, males were 37(54%) and females were 23(46%). And in control group, males were 28(56%) and females were 22(44%). When we compared the Gamma-glutamyl transferase between case and control. which was highly significant differences (P<0.0001). Similarly other enzymes such as Aspartate aminotransferase, Alanine transaminase, and AST: ALT were also highly significant differences (P<0.0001) between cases and control. Serum level of Bilirubin was also highly significant differences (p<0.0001) in case as compared to control subjects. When we correlated the different parameter of chronic hepatitis patients. GGT level was not significant differences (p=0.868). ALT level was highly significant differences (p<0.000). AST level (P=0.000), AST: ALT ratio (P=0.020) and bilirubin level was significant differences (P=0.012).

Conclusions: Gamma-glutamyl transferase, Aspartate aminotransferase, Alanine transaminase, AST: ALT ratio and serum level of bilirubin was extreme significantly higher in patients with chronic hepatitis as compared to control (healthy subjects). Hence, GGT, AST, ALT, AST:ALT ratio, and bilirubin, are prominent indicators of chronic hepatitis.

Keywords: Chronic hepatitis, Gamma-glutamyl Transferase, Aspartate Aminotransferase (AST), Alanine Transaminase (ALT), AST: ALT, and Bilirubin.

Introduction

Liver disease develops silently; there may be no signs or symptoms until the complications of liver failure or portal hyper tension develop. At this late, often pre-terminal stage, the tests of liver function—bilirubin, albumin, international normalised ratio (INR) and platelet count—may be abnormal. In necro-inflammatory hepatitic diseases liver enzymes are frequently elevated [1,2].

Chronic hepatitis B virus (HBV) infection is a serious health problem worldwide, and it can cause a series of manifes tations, including liver cirrhosis, liver failure, and hepato cellular carcinoma [3]. Antiviral therapy can prevent disease progression and reduce the risk of adverse events in pa tients with chronic hepatitis B (CHB) [4,5]. Patients with either hepatitis B e antigen (HBeAg)-positive or -

negative immune active phase are recommended antiviral treatment, according to current guidelines [4,5]. However, a substantial number of HBeAg-negative CHB patients with detectable HBV DNA and normal alanine aminotransferase (ALT) levels are not recommended antiviral treatment [4,5]. Previous studies have reported that normal ALT levels do not mean the absence of significant liver injury [6,7]. In addition, high HBV DNA levels were associated with significant liver inflammation and fi brosis in HBeAg-negative CHB patients with normal ALT levels [8]. A retrospective study that enrolled 286 patients with HBeAg-negative CHB showed that nearly a third of patients with normal ALT levels had significant liver inflammation or fibrosis [9]. Choi et al. [10] reported that untreated HBeAg-negative CHB patients with normal ALT and high HBV DNA levels had a higher risk of advanced events than treated immune active CHB patients did. Thus, identifying the stages of liver inflammation and fibrosis in these patients is crucial to guide their clinical management.

Several markers for high alcohol consumption per se have been studied e.g. carbohydrate deficient transferrin (CDT), gamma glutamyl transferase (GGT) and aspartate aminotransferase (AST). Most have fairly low sensitivities and specificities (Conigrave et al., 2002) [11]. The use of test combinations significantly improves the information received with single serum enzyme determinations. An elevated serum AST in relation to serum ALT (alanine aminotransferase) has been proposed as an indicator that alcohol has induced organ damage. Thus, when AST/ALT ratio is >1.5, this is considered as highly suggestive that alcohol is the cause of the patient's liver injury [12]. Objectives of our study was to evaluate and compare the serum levels of gamma-glutamyl transferase, aspartate aminotransferase (AST), alanine transaminase (ALT), AST: ALT, and bilirubin in patients with chronic Hepatitis with control (healthy subjects).

Material & Methods

The present study was conducted in the Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar during a period from January 2021 to July 2021.

The case group comprised 50 clinically diagnosed patients of chronic hepatitis were reported in the Medicine OPD or admitted in Medicine ward of Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar. And a total of 50 age- and sex-matched healthy controls with no previous history of hepatitis were selected from the general population.

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.

Methods

Anti-HCV ELISA and HBs Ag ELISA tests 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.

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. The IFCC method was used to estimate the serum levels of the parameter using a commercially available kit from Transasia Pvt. Ltd. The tool used was an ERBA 5 chem semi-auto analyser.

Statistical Analysis: Data was analysed by using SPSS software. Mean ± Standard deviations were observed. Pearson's correlation coefficients were obtained. P-value was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Results

A total of 50 chronic hepatitis patients were enrolled in a case group and 50 healthy individuals were included as control group. Mean age of the patients in case group was 50 ± 12.87 years. And mean age of healthy individual in control group was 48 ± 14.76 years. It was not statistically significant (p=0.471). In case group, Males were 37(54%) and females were 23(46%). And in control group, males were 28(56%) and females were 22(44%).

Table 1: Mean age of subjects in case and control.

Subjects	Case (N=50)	Control	p-value
Age	50 ± 12.87	48 ± 14.76	0.471
Gender			
Male	27(54%)	28(56%)	0.841
Female	23(46%)	22(44%)	0.841
Total	50(100%)	50(100%)	

In the present study, when we compared the Gamma-glutamyl transferase between case and control. P-value was found to be <0.0001. which was highly significant differences. Similarly other enzymes such as Aspartate aminotransferase, Alanine transaminase, and AST: ALT was also highly significant differences (p=<0.0001) between cases and control. Serum level of Bilirubin was also highly significant differences (p<0.0001) in case as compared to control subjects.

Table.2. Comparison of various enzymes, AST:ALT ratio and serum levels of bilirubin.

Groups	Gamma-glutamyl transferase (U/L)	Aspartate aminotransferase (U/L)	Alanine transaminase (U/L)	AST: ALT	Bilirubin (mg/dL)
Group I (cases) n = 50	89.34 ± 24.67	75.89 ± 26.78	43.86 ± 21.45	3.12 ± 0.96	4.21 ± 2.72
Group II (controls) n = 50	37.64 ± 9.12	20.68 ± 11.25	24.76 ± 12.43	1.01 ± 0.24	0.86 ± 0.16
p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

In the present study, when we were correlated the different parameter of chronic hepatitis patients. GGT level was not significant differences (p=0.868). ALT level was highly significant differences (p=<0.000). AST level (p=0.000), AST: ALT ratio (p=0.020) and bilirubin level was significant differences.

Table 2: Correlation of different parameters of chronic hepatitis cases.

Parameters	R	p-value
GGT	0.024	0.868
AST	–0.453	0.000
ALT	0.612	<0.000
AST: ALT	–0.328	0.020
Bilirubin	–0.352	0.012

Discussions

Gamma-glutamyl transferase (GGT) is used in clinical practice as a biochemical indicator of liver injury although it lacks specificity to aetiology [13,14]. Numerous studies have shown that higher GGT concentrations associate with higher risk of liver disease, cardiovascular disease (CV) and all-cause mortality [15,16]. Clinical guide lines recommend assessment for liver disease aetiology and fibrosis stage in patients with abnormal liver enzymes including GGT [17]. Prospective studies show a positive association between GGT and incident myocardial infarction (MI), [18,19] heart failure (HF), [20] and cardiovascular mortality [21].

The present study 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 was increased highly significantly ($p < 0.0001$) 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.

Prati et al [22] propose that it is prudent to reconsider the established thresholds for ALT levels in patients diagnosed with chronic HCV infection or non alcoholic fatty liver disease [22]. Previous studies have shown that even if the ALT level is within the normal range, the ALT level correlates with the degree of liver inflammation and fibrosis.

Sonneveld et al [23] showed that 52% of 168 patients without liver fibrosis and 82% of 66 patients with significant liver fibrosis with normal ALT levels had mild and moderate inflammation [23]. More importantly, even if the ALT level is within the normal range, higher ALT levels have a higher incidence of decompensated cirrhosis and HCC. Compared to patients with ALT levels < 0.5 × ULN (53 U/L and 31 U/L for males and females, respectively), patients with ALT levels of 0.5-1 × ULN had an increased risk for the development of complications including ascites, spontaneous bacterial peritonitis, oesophageal varices, encephalopathy and HCC [24]. Similarly, REVEAL-HBV research demonstrated that compared to ALT < 15 U/L, patients with ALT 15-44 U/L had an increased risk of cirrhosis (aHR = 1.97, 95%CI: 1.56-2.48) and HCC (aHR = 2.45, 95%CI: 1.74-2.48) [25].

Patil et al. [26] 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 [26,27]. In case with AVH, GGT levels are observed to be raised negligibly with respect to peak levels. In their investigation, Batta et al. [27] 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.

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) [30,31]. 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 [28,29].

The liver associated enzymes, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), and gamma glutamyl transferase (GGT) are measures of liver homeostasis [32]. 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 [29]. This study also confirms that in cirrhosis AST and ALT levels are normal or slightly elevated. If the etiological factors were present or with active alcohol abuse increases AST and ALT levels [33]. The ALP activity has been reported by various workers, minimally increased usually upto 200 -300 U/L in viral hepatitis and in alcoholic liver disease ALP usually up to 300 U/L. In cirrhosis ALP is either normal or slightly elevated, increased in serum ALP is associated with liver disease is caused by intra or extra hepatic cholestasis and some destruction of hepatic cell membrane [34]. Elevation of ALP is observed in patients who have some form of extra hepatic and intra hepatic bile duct obstruction [35].

Conclusions

The present study concluded that the Gamma-glutamyl transferase, Aspartate aminotransferase, Alanine transaminase, AST: ALT ratio and serum level of bilirubin was extreme significantly higher in patients with chronic hepatitis as compared to control (healthy subjects). Hence, GGT, AST, ALT, AST:ALT ratio, and bilirubin, are prominent indicators of chronic hepatitis.

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