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Gamma Glutamyl Transferase As A Diagnostic Marker in Alcohol Induced Hepatotoxicity

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Abstract: *Liver disease is a general term for any damage that reduces the functioning of the liver. As a large organ the liver shares with many other abilities to perform its functions with extensive reserve capacity. Gamma glutamyl transferase (GGT) is a membrane bound enzyme that plays a key role in the synthesis of the antioxidant glutathione. The current study on fifty two subjects have undertaken to explore serum gamma glutamyl transferase as a diagnostic marker in alcohol induced hepatotoxicity..It was observed that serum levels of GGT usually showed a marked rise in alcoholic liver disease. It is suggested that measurement of serum levels of GGT is particularly helpful in the clinical assessment of alcoholic cirrhosis and in the diagnosis of primary and secondary hepatic neoplasm.*

Keywords: *Alcoholic liver disease, Cirrhosis of liver, Gamma Glutamyl transferase (GGT).*

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I. Introduction

Chronic liver disease is defined as a series of liver disorders with varying etiologies and severities, with which hepatic inflammation and necrosis continue for at least 6 months[1]. A variety of biochemical parameters like serum bilirubin, serum proteins, transaminases, gamma glutamyl transferase (GGT), prothrombin time, etc are evaluated to assess the liver cell damage[2]. The hydrolysis of glutathione is mainly done by gamma glutamyl transferase, which is a membrane bound glycoprotein and it also catalyses the transfer of the glutamyl groups from one peptide to another[3]. The GGT activity is considered as a sensitive index of the hepatobiliary dysfunction than alkaline phosphatase, due to its presence in the microsomes and the plasma membranes of hepatocytes[4].Gamma glutamyl transferase (GGT) is a membrane-bound enzyme that is essential for the synthesis of glutathione (GSH), a key antioxidant[5]. In clinical practice elevated serum GGT is generally used as an indicator of liver disease, such as biliary obstruction, alcohol consumption, and exposure to certain medical drugs[6]. Recently, several epidemiological studies have shown that a higher serum GGT level, even within the normal range, is associated with cardiovascular risk factors such as hypertension, hypertriglyceridemia, obesity, type 2 diabetes mellitus and stroke, as well as certain types of cancer[7,8]. In contrast to these studies, we observed that after surgery for ruptured abdominal aortic aneurysm or after liver resection[9], GGT is transiently increased in patients who had a good outcome. In these short-term observational studies GGT level was inversely related to other liver laboratory parameters such as aspartate amino transferase (ALT), alanine amino transferase (AST) as well as total bilirubin[10,11]. The aim of study was to evaluate the serum GGT levels in patients with alcoholic liver diseases and to show that it can be used as a diagnostic biomarker for the diagnosis of alcoholic liver diseases.

II. Material and Methods

The present study was conducted at Muzaffarnagar Medical College Muzaffarnagar, U.P. India from September 2015 to December 2016. Fifty two subjects diagnosed as alcohol induced hepatotoxicity and fifty healthy controls were enrolled in this study. The data on personal history, regarding the onset of the disease, alcohol consumption and treatment history of liver disease were collected through standard questionnaire. 10 ml of venous blood samples were collected in plain tubes, the serum was separated by centrifugation and the obtained serum was used for the estimation of Gamma Glutamyl transferase[12].The patients with renal, pancreas, respiratory, cardiac and neurological diseases, who presented with icterus , who were taking alcohol of more than 20 gm/day, who were on drugs like anti epileptics, amiodarone, tamoxifen and steroids and who had undergone biliopancreatic surgeries were excluded from the study by taking a proper history and by doing a proper examination and investigations

III. Stastical analysis

Data analysis was performed using Epi info software version 3.5.1. Descriptive statistics, including mean, range, and standard deviations, were calculated for all variables. Proportions were compared using Chi-square tests and chi square for trend at 0.05 level of significance.

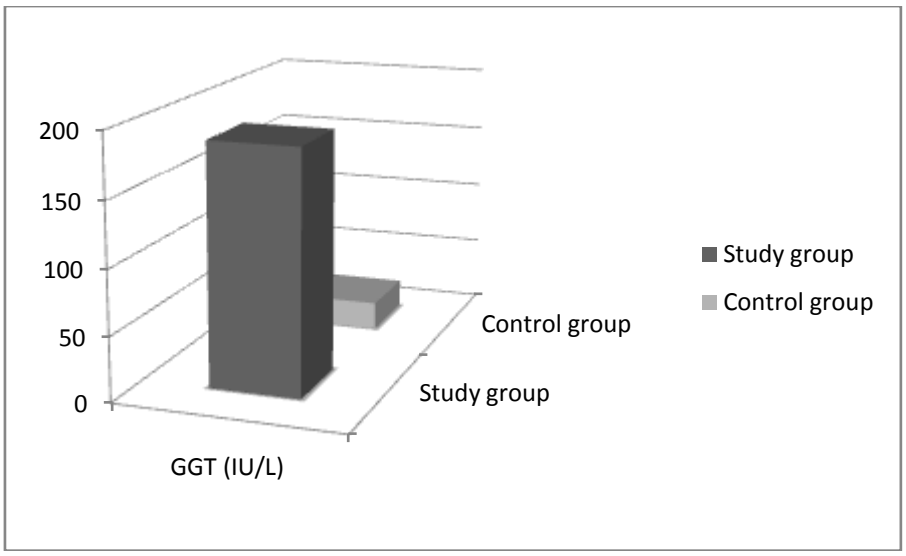
IV. Finding

The study was conducted on 52 patients (male) of different age groups. 50 healthy subjects were randomized selected as control group. The bio-chemical findings of this study are expressed in as mean and SD, the normal values of control group is used to compare value with study group.

4.1The serum GGT level in alcoholic hepatitis as study group and in normal control group.

Parameter (IU/L)	**Study group (no=52) Mean ± S.D.**	**Control group (no=50) Mean ±S.D.**	**P value**
Gamma Glutamyl transferase (GGT).	186.93 ±21.37	21.84± 9.28	$p < 0.0001$

It is evident from our findings there was significantly increased GGT in alcoholic hepatitis subjects (186.93 ±21.37 IU/L) as compared to healthy control (21.84± 9.28 IU/L).



V. Discussion

As a result of efforts by the World Health Organization, the National Council on Alcoholism and others, it is now recognized that alcoholism is an illness which is treatable. Effective treatment, however, is greatly dependent on early detection of liver involvement before permanent damage has occurred. Furthermore, it has been demonstrated that afflicted individuals are more likely to abstain from alcohol if objective evidence of liver damage can be demonstrated[13,14].The determination of gamma-glutamyl transferase (GGT) activity in the serum is commonly used as a screening test for alcoholism, since striking elevations of serum GGT activities can be observed in patients with a high alcohol intake over a prolonged period[15]. Enhanced serum enzyme activities are also found in patients with various stages of alcoholic liver disease including alcoholic fatty liver, alcoholic hepatitis, alcoholic liver fibrosis and cirrhosis[16]. Since enzyme alterations in the serum are commonly observed even during the early stage of alcoholic liver disease, such as alcoholic fatty liver, the determination of GGT activity in the serum is a useful test for early recognition of alcoholism. Moreover, the assessment of the adult and fetal form of GGT in the serum facilitates a clear dissociation between early stages of alcoholic liver diseases, such as alcoholic fatty liver, and late stages such as alcoholic liver cirrhosis[17]. Recent studies have suggested that the activity enhancement in the serum is primarily due to hepatic enzyme induction, rather than to liver cell injury, and can be ascribed to the action of ethanol itself but not to dietary imbalance with respect to carbohydrates[18]. The activity of GGT is increased after chronic alcohol consumption in plasma membrane and microsomal fractions of the hepatocyte[19].

This suggests that GGT is primarily induced in the endoplasmic reticulum and subsequently transported to plasma membranes via Golgi apparatus and/or microtubuli. In the presence of ethanol, GGT of the plasma membrane may then be solubilized and released into the blood.

However, the results of the present investigation signify the importance of measurement of serum GGT as a diagnostic marker in alcoholic hepatitis. This marker may be very useful in opportunistic case finding, in motivating patients to change drinking habit and in monitoring the treatment response.

VI. Conclusion

Serum Gamma Glutamyl transferase levels were estimated in 52 subjects of chronic alcoholics. The serum levels of GGT usually showed a marked rise in alcohol induced hepatotoxicity. It is suggested that measurement of serum levels of GGT is particularly helpful in the clinical assessment of alcoholic cirrhosis and in the diagnosis of primary and secondary hepatic neoplasm.

1. Conflict of interest - None
2. Source of funding – Self
3. Ethical clearance – Taken

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