An Investigation of the Relationship Between Liver Enzymes and Alcohol Use with Regard to High-Density Lipoprotein Cholesterol

Adil Hussain Gounchoo[1] , Balwinder kaur [2] Seema rani ,[3]

1. Student of Medical Microbiology at Desh Bhagat University Mandigobindgarh .
2. Assistant Professor at Desh Bhagat University Mandigobindgarh
3. Assistant Professor at Desh Bhagat University Mandigobindgarh

ABSTRACT.

Health problems related to lifestyle and behavior are steadily more common in modernized societies. Recent studies have indicated that the common liver enzymes, gamma- gutamyltransferase (GGT),asparatate aminotransferase (AST), Alkaline phosphatase (ALP) and alinine aminotransferase (ALT) are elevated in alcoholics. In this study, we investigate blood sample of chronic alcoholics. Alcohol consumption, smoking, coffee drinking, income, education, food habits were analyzed using detailed questionnaires. The mean age of study groupwas 41.95 ± 8.45 years. Serum AST was 36.92 ± 26.35 U/L. Serum ALT was 53.59 ± 31.24 U/L,serum ALP was 102.47 ± 29.03 U/L, serum GGT was 66.63 ± 30.96 U/L and Serum HDL- Cholesterol was 44.68 ± 11.66 mg/dl. The result shows that alcoholics had increased serum liver enzymes and decreased serum HDL- Cholesterol.

Keywords: - Liver enzymes ,Alcohol, High density lipoprotein, Alcohol liver disease, High density lipoprotein.

INTRODUCTION

ALCOHOL

Alcohol are the organic molecules assembled from the carbon oxygen and hydrogen atoms. An active drug found in drinks that contain alcohol is a chemical called ethanol, Alcohol or ethanol is an intoxicating ingredient found in beer, wine and liquor. When yeast acts together with sugars in grains,fruits and vegetables. It causes them to ferment and breakdown This results in two by products – ethanol and carbon dioxide.

ALCOHOLISM

Alcohol is absorbed into a persons body primarily through the small intestines and also the stomach.Any drinking of alcohol results in significant mental or physical health problems, it's a serious disease where people where people gain control over the desire for physical and mental effects of drinking alcoholic beverages. Chronic alcohol abuse can lead the feeling of guilt and shame which leads to broken relationships due to family's lack of control over the alcohol intake. Alcoholism has injurious effects on one's overall health. Organs such as brain, liver, heart, kidneys and stomach are most affected.

LIVER ENZYMES

Prolonged alcohol consumption affects the liver enzymes. Four enzymes are measured in the laboratory to evaluate function of the liver. These enzymes include Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), and Gamma Glutamyl- Transferase (GGT). The first two are known together as transminases and second two are known together as cholestatic liver enzymes. Elevation in any of these enzymes can indicate the presence of liver disease. Elevation of the transminases can occur with alcoholic liver disease and fatty liver, conditions that can result from excessive alcohol intake. Elevation of the cholestatic liver enzymes can also occur with alcoholic liver disease.

Aspartate amino Transferase (AST)

AST catalyse transmination reaction. AST exists in two different isoenzyme forms, which are genetically distinct, the mitochondrial and cytoplasmic form. AST is found in highest concentration in heart compared with other tissues of the body such as liver, skeletal muscle and kidney. Normal level of serum AST is 0-40U/L. Elevated mitochondrial AST is seen inextensive tissue necrosis during myocardial infarction and also seen in chronic liver disease.

About 80% of AST activity of the liver disease is contributed by mitochondrial isoenzyme. However the ratio of mitochondrial AST to total AST activity has diagnostic importance in identifying the liver cell necrotic type condition and alcoholic hepatitis.

Alanine amino Transferase (ALT)

ALT is found in kidney, heart, muscle and highest concentration in liver compared with other tissues of the body. ALT is purely cytoplasmic catalyzing the transminase reaction . Normal level of serum ALT is 0-40U/L. Any type of cell injury can increase ALT levels. Viral hepatitis like A, B, C, D, and E may be responsible for a marked increase in aminotransferase levels. The increase in ALT associated with hepatitis C infection tends to be more than associated with hepatitis A or B. In a recent study it was found that the hepatic fat accumulation in childhood obesity and nonalcoholic fatty liver disease causes serum ALT elevation.

Gamma-Glutamyl-Transferase (GGT)

Gamma-glutamyl-transferase, catalyzes the transfer of the gamma-glutamyl group from peptides and compounds that contain it to the same accepters. The gamma-glutamyl accepter is the substrate itself, some amino acid or peptides or even water in which case simple hydrolysis takes place. Even though renal tissue have the highest concentration of GGT, the enzyme present in serum appears to originate primarily from the hepatobiliarysystem.GGT is a sensitive indicator of the presence of hepatobiliary disease, being elevated in most subjects regardless of cause.

Alkaline Phosphatase (ALP)

ALP (orthophosphoric monoester phosphohydrolase) is found across a multitude of organisms , prokaryotes, and eukaryotes alike with the same general functions, but in different structural forms suitable to the environment. Alkaline phosphatase is found in the periplasmic space of E.coli bacteria. This enzyme is heat stable and has its maximum activity at high Ph. In humans, it's found in many forms depending on its origin with the body. ALP is a protein found in all body tissues. tissues with higher amount of ALP include the liver, bile ducts, and bone. High doses of alcohol damages the liver and early symptoms of liver diseases include changes in routinely assessed liver enzymes.

HIGH DENSITY LIPOPROTEIN CHOLESTEROL

HDL is the lipoprotein with the highest density and the largest ratio of proteins to lipids. Due to the strong negative relationship between HDL cholesterol levels and the risk of atherosclerosis, HDL is of great importance in medicine. High-density lipoproteins cholesterol (HDL-C) is one of the five major groups of lipoproteins. Lipoproteins are complex particles composed of lipids and proteins in varying proportions, which transport lipids from one tissue to the other through plasma.HDL-C serves as carrierof cholesterol from peripheral tissues to liver for its degradation and excretion (Scavenger action). HDL contains apoproteins AI and AII.

Oxidative pathway

The oxidative pathway of alcohol metabolism involves three enzymes, viz: Alcohol dehydrogenase (ADH) in the cytosol, Cytochrome P450 and Catalase in the microsomes . In the cytosol ADH converts alcohol to acetaldehyde and other metabolites. Oxidation of ethanol by alcohol dehydrogenase leads to excess production of reduced nicotinamide adenine dinucleotide $NADH^+$. The $NADH^+$ generated competes with reducing equivalents from other substrates, including fatty acids, for the respiratory chain, inhibiting their oxidation and causing increased esterification of fatty acids to form triacylglycerol, resulting in the fatty liver. Some metabolism of ethanol takes place via a cytochrome P450-dependent microsomal ethanol oxidizing system (MEOS) involving NADPH and O_2. This system increase inactivity in chronic alcoholism and may account for the increased metabolic clearance in this condition.

Alcohol oxidizes into acetaldehyde and water by hydrogen peroxide (H_20_2) in the presence of catalase enzyme. Acetaldehyde is highly reactive toxic by- product in hepatocytes that may promote glutathione depletion, lipid peroxidation and mitochondrial damage . It also contributes to the changes in the redox state of the cell and the formation of reactive oxygen species (ROS).The product of acetaldehyde breakdown is rapidly removed from the liver and is metabolized into CO2 via theTricarboxylic acid cycle(TCA) in the heart, skeletal muscle and brain. Genetic variation in Alcohol dehydrogenase (ADH) and Aldehyde dehydrogenase (ALDH)influence susceptibility of developing alcoholism and alcohol related liver injury .

MATERIAL AND METHODS

Blood samples were collected from chronic alcoholic subjects visitingthe psychiatry department of Punjab Institute of Medical Sciences(PIMS), Jalandhar. Informed written consent was obtained from all participants. In this survey 132 alcoholic subjects and 108 non-alcoholic subjects were included.

Control: About 108 subjects aged between 20 to 60 years who had come for routine checkup and were non alcoholic, were selected as controls. Informed written consent was also obtained from these subjects.

Inclusion criteria

Subjects between 20 to 60 years taking at least 150 ml of alcohol daily for one year and above were included in the study.

Exclusion criteria

In this study, pregnant women, elderly (above 60 years) and children below 20 were excluded. A subject addicted to any other drug was also excluded from the study. Patients suffering from liver cancer and chronic heart disease were also not included in the study.

Laboratory measurements

The various biochemical parameters were measured in the laboratory of the Punjab Institute of Medical Sciences using standard clinical chemical methods. Serum AST, ALT, ALP and GGT activities were measured by standard kinetic methods following the recommendations of the test according to International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), and Serum high-density lipoprotein cholesterol (HDL-C) activity was measured by HDL- C Immuno FS homogeneous method using BS 400 clinical chemistry analyzer(fully automatedMindray Machine).

Statistical methods

Values are expressed as means ± SD or means ± 95% confidence interval (CI), as indicated. Logarithmic transformation of AST, ALT, ALP, GGT and HDL data was used to obtain non- skewed distributions with homogeneity of variance. Differences between the groups were determined withLevene's test for the equality of variance (Indentpen*t* test) using the parameters comparisons. Differences between correlations were analysed with the t-test for comparison between alcoholics and non-alcoholic parameters. The SPSS 24 version, statistical software
packages for Windows was used for the statistical analyses (SPSS Inc., Chicago, IL, USA), p-value of < 0.05 was considered statistically significant.

RESULTS.

One hundred and thirty two alcoholics were enrolled in this study. The mean age of the alcoholics was 41.95 ± 4.45 years .All the subjects were male. The longest duration of alcohol abuse was 15 years while the shortest duration of abuse was 2 years. Majority of the study population ingested at least 150 ml of alcohol daily. Majority of the study population had studied uptoclassXII. Few subjects of the study population were cigarette smokers. Average income of the study population was above 30,000 rupee per month. Majority of study population had no physical activity. Around 50% of the alcoholic subjects hadhypertension.More than 25% of the study population had either parent suffering from diabetics.
Hundred and eight males of age group 20 to 60 years acted as controls. They had no history of alcoholism. The liver enzymes, (AST, ALT, GGT, ALP) and HDL-C concentration in the controlsubjects was within the normal reference rang

GROUP STATISTICS				
	GROUP	**N**	**Mean**	**Std. Deviation**
AGE	ALCOHOLIC	132	41.95	8.45
	CONTOL	108	41.03	9.44
AST	ALCOHOLIC	132	36.92	26.35
	CONTOL	108	24	4.62

ALT	ALCOHOLIC	132	53.59	31.24
	CONTOL	108	27.52	7.22
ALP	ALCOHOLIC	132	102.47	29.03
	CONTOL	108	71.95	9.93
GGT	ALCOHOLIC	132	66.63	30.96
	CONTOL	108	29.42	7.38
HDL	ALCOHOLIC	132	44.68	11.66
	CONTOL	108	50.9	7.26

DISCUSSION

The study shows that alcoholics have higher value of liver enzymes such as AST, ALT, ALP and GGT, when compared with non-alcoholic, age matched subjects. A brief dietary history showed that alcoholics consumed more of dietary fats, had less physical activity leading to positive calorie balance and obesity.Batic- mujanovic et al shows that cigarette smoking adversely affects HDL-C by lowering its level, further increasing the risk for coronary heart disease.According to the Heart UK: the cholesterol charity association, acrolein is a chemical, which is found in cigarettes. This substance decreases plasma HDL cholesterol and thus decreased transport of cholesterol to the liver. In our study 18.9% of subjects were alcoholics and smokers.There was an increase in the value of AST by 26.5%, ALT by 68.1%, ALP by66% and GGT by 58.3%in alcoholics.Teddy Charles Adias et al in a study found that the value of prothrombintime, activated partial thromboplastin time, and ALT, AST, GGT were highly elevated in chronicalcoholics.

CONCLUSION

From the result of this study, it can be concluded that alcohol has detrimental effects on the liver. It was observed that the liver enzymes (AST, ALT, ALP and GGT), were raised above the reference range in the alcoholic subjects. This rise is due to the deleterious effect of ethanol on hepatocytes, causing leakage of cytosolic enzymes into the blood stream. Also a decrease in high density lipoprotein cholesterol (HDL-C), in sera of alcoholic subjects.

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