Original Research Article

Effect of alcohol in south Indian diabetic patients: A Prospective Study

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ABSTRACT:

Introduction: There is a delicate balance between the harmful effects and the beneficial effects of Alcohol on Diabetes Mellitus.

The aim of the study was to analyse, the effect of alcohol and liver functions in diabetic patients.

Materials & Methods: A prospective study was performed on 210 consecutive patients with diabetics with alcoholism. This study was conducted in various Medical Colleges in Tamil Nadu and Kerala The patients were studied on the basis of a specific questionnaire and hospital records.

Results: Of 210 enrolled patients, 124 are daily consuming alcohol.66 more than twice a week 20 drinks once in a week. The amount varies from, one large 45pts(60ml) to one full32pts(720ml), majority of them drinks a half of a quarter133 (90ml) daily. 102 patients had more than 5 episodes of hypoglycaemia, 28 had three episodes and 41 had 2 episodes of hypoglycaemia requiring admissions in a year. A high prevalence of abnormal LFTs (56%) was observed in patients in our study. ALP was the most commonly affected liver function parameter. This was followed by abnormalities in AST, ALT, and albumin in that order.

Conclusion:Alcoholism causes more hypoglycaemic episodes and altered LFTs in south Indian patients with diabetes mellitus with increased frequency and severity resulting frequent absenteeism for work and decreased productivity. Hence reduction of alcohol consumption and de addiction treatment is must.

Key words ; Diabetes Mellitus ,Alcoholism, LFT, Hypoglycaemia

Introduction:

Diabetes mellitus (DM) is recognized clinically as a complication of alcoholism, and both alcoholism and DM affect a large population worldwide Chronic, heavy alcohol consumption, an independent risk factor for type 2 diabetes mellitus disrupts the glucose homeostasis and is associated with development of insulin resistance , heavy amounts of alcohol show direct diabetogenic effects with its contribution to excess caloric intake and obesity, induction of pancreatitis, disturbance of the carbohydrate and glucose metabolism and the impairment of the liver function, which affects the blood glucose levels, which causes hypoglycemia.

When a shortage of glucose is impending, glucose will be secreted from glycogen stores in the liver, but glycogenolysis is also impaired by alcohol in which normal blood glucose levels cannot be maintained by the depletion of stores and hypoglycemia, which consequently may occur. Besides, continued alcohol metabolism

causes diminished gluconeogenesis. Both the depletion of glycogen and diminished gluconeogenesis lead to lower blood glucose levels, as well as insulin secretion that is also reduced as the level of blood glucose falls.

Diabetic with chronic alcohol consumption showed lower fasting plasma glucose level, but significantly higher postprandial plasma glucose level that was difficult to return to baseline levels than the non-drinking diabetic. Alcoholic patients with T2DM have repeatedly been found to have deregulation of the ghrelin and leptin systems, as indicated by impaired insulin secretion, increased hepatic glucose production and decreased peripheral glucose utilization, BDNF, and hippocampal LTP, which play important roles in the brain and insulin sensitivity, could become possible candidates for mediation that links T2DM and alcohol consumption. The novel mechanisms of these two appetite regulating peptides, BDNF and hippocampal LTP are widely involved in the neurobiology of alcohol dependence and T2DM.

The organ which plays a key role in diabetes is liver It has an important role in maintaining basal and postprandial glucose concentrations.

The effect of liver enzymes on the incidence of type 2 diabetes has been reported Alanine amino transferase (ALT) is a specific marker of liver pathology, as it is found primarily in the liver. ALT is considered to be the marker most closely correlated to liver fat and reported to be related to hepatic insulin sensitivity On the other hand,ALP, γ-glutamyltransferase (GGT) and aspartate aminotransferase (AST) are less specific markers of liver disease, as they are found in other tissues as well as the liver. High-dose statin therapy is associated with more frequent abnormalities of LFTs, although they are generally still relatively infrequent

Individuals with type 2 diabetes have a higher incidence of LFT abnormalities than individuals who do not have diabetes. The most common abnormality is elevated ALP & ALT. Any diabetic patient found to have a mild chronic elevation of ALT, or elevation of ALT ≤ 250 units/l for > 6 months should have screening for treatable causes of chronic liver disease, particularly hepatitis B, hepatitis C, and hemochromatosis, which are found with increased incidence in type 2 diabetes. Elevation of ALT within three times the upper limit of normal is not a contraindication for starting any oral anti diabetic or lipid-modifying therapy. In contrast, antidiabetic agents have generally been shown to decrease ALT levels as tighter blood glucose levels are achieved.

Liver function tests in alcoholism :

Alcohol is a hepatotoxin that is commonly consumed worldwide and is associated with a spectrum of liver injury including simple steatosis or fatty liver, alcoholic hepatitis, fibrosis, and cirrhosis.which are more common in indians than western countries Excessive or harmful alcohol use is ranked as one of the top five risk factors for death and disability globally and results in 2.5 million deaths and 69.4 million annual disability adjusted life years.

Approximately 60%-90% of individuals who drink more than 60 g of alcohol per day have been shown to have hepatic steatosis However, less than half of individuals with alcoholic steatosis, who continue to drink alcohol, will progress to fibrosis and only 10%-20% will eventually progress to cirrhosis Nonetheless, once steato hepatitis has developed, the risk of development of cirrhosis is increased compared with simple steatosis.

The biochemical markers for chronic alcohol consumption that have been most commonly studied are serum GGT, AST, ALT,ALP, mean corpuscular volume (MCV) and carbohydrate-deficient transferrin (CDT) An AST to ALT ratio over 2 is highly suggestive of ALD. Most patients with non-ALD have AST to ALT ratios below one. Specific IgA antibodies directed towards acetaldehyde-derived protein modifications are frequently

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seen alcoholics and thus IgA levels are increased in chronic ALD. An increased ratio of IgA to IgG is highly suggestive of ALD.

Chronic alcohol consumption is known to induce a rise in serum GGT and is a widely used index for excessive alcohol use. However, elevated GGT alone has both low sensitivity and specificity for alcohol abuse GGT is not specific to alcoholism and is increased in many conditions such as obesity, advanced age, moderate alcohol consumption, all forms of liver disease including fatty liver and in particular intra and extra hepatic biliary obstruction, hepato cellular carcinoma and phenytoin use The sensitivity of GGT as a marker for alcohol consumption in young adults has been showed to be particularly poor even in cases of documented alcohol dependence.

Sensitivity and specificity of biomarkers in detecting harmful or heavy alcohol consumption.

Biomarker	**AST/ALP**	**ALT**	**MCV**	**CDT**	**CDT + GGT**	**CDT + GGT + MCV**
Sensitivity	47%-68%	32%-50%	45%-48%	63%-84%	83%-90%	88%
Specificity	80%-95%	87%-92%	52%-94%	92%-98%	95%-98%	95%

AST: Aspartate aminotransferase;ALP;Alcaline phosphatase ALT: Alanine aminotransferase; MCV: Mean corpuscular volume; CDT: Carbohydrate-deficient transferring; GGT: Gamma-glutamyltranspeptidase

Clinical findings may be minimal or absent in early ALD characterized only by hepatic steatosis, whereas in cirrhosis there will be typical signs and symptoms of cirrhosis and portal hypertension. Laboratory studies characteristic of ALD include elevated transaminase levels with AST greater than ALT but also increased,ALP, MCV, GGT, and IgA to IgG ratio.

Liver function tests in diabetic and alcoholic:

- Tests indicative of:
- 1) liver inflammation: ALT (alanine aminotransferase) and AST (aspartate aminotransferase).
- 2) cholestasis or biliary obstruction: bilirubin (total includes both direct and indirect bilirubin), ALP (alkaline phosphatase) and GGT (gamma-glutamyltransferase).
- 3) Synthetic function: albumin and PT (prothrombin time).
- Abnormal liver function due to non-alcoholic fatty liver disaese is common in diabetes.fibroscan is used to assess the presence of liver fibrosis.
- Symptoms suggestive of liver disease: jaundice, dark urine, or light-colored bowel , loss of appetite, fatigue, vomiting of blood, bloody or black tarry stools, swelling or pain in the abdomen, unusual weight changes.
- Signs suggestive of liver disease: hepatomegaly, ascites
- Exposure to people that have viral hepatitis, excessive alcohol consumption.
- Presence of additional comorbid conditions associated with liver disease among persons with diabetes: extreme obesity, hypertriglyceridemia, alcohol use

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Differential diagnosis

- Increased AST: primary liver disease, acute myocardial infarction, muscle trauma and diseases, pancreatitis, intestinal surgery, burns, renal infarction, pulmonary embolism.
- Increased ALT: primary liver disease, biliary obstruction, and pancreatitis. ALT > AST viral hepatitis, AST> ALT alcoholic liver disease.
- Increased ALP: biliary obstruction, primary liver disease (changes parallel GGT), infiltrative liver disease, bone diseases, hyperparathyroidism, hyperthyroidism Diabetes mellitus.
- Increased GGT: biliary obstruction, primary liver disease (changes parallel ALP), alcohol consumption, pancreatitis.
- Increased bilirubin: biliary obstruction, primary liver disease, hemolytic anemias, hypothyroidism.
- Medications: may cause increases in one or more liver chemistry tests because of direct hepatotoxicity or cholestasis.
- ALT and AST are abundant liver enzymes. AST is also present in heart, muscle. ALP is present in nearly all tissues, primarily bone and liver. GGT is abundant in liver, kidney, pancreas and intestine.
- ALT and AST normal ranges vary depending on lab, in general: ≤ 40 U/L.
- ALT and AST less than 5 times the upper limit of normal (ULN)) should be rechecked before extensive work-up is undertaken. Possible causes: chronic hepatitis C or B, acute viral hepatitis, NAFLD, haemo chromatosis, autoimmune hepatitis, medications, alcohol-related liver injury, Wilson's disease.
- Moderately elevated ALT and AST (ALT and AST 5-15 times the ULN) should be investigated without waiting to confirm the persistence of abnormal ALT, possible causes: entire spectrum of liver diseases that may cause either mild or severe elevations.
- Severe ALT and AST elevations (ALT and AST greater than 15 times the ULN) suggest severe acute liver cell injury: acute viral hepatitis, ischemic hepatitis or other vascular disorder, toxin-mediated hepatitis, acute autoimmune hepatitis.
- Bilirubin is a heme degradation product excreted in the bile, it requires conjugation in the liver before its secretion.
- Hyperbilirubinemia: Investigate if caused by direct (conjugated) or indirect (unconjugated) fraction of bilirubin. Pre-hepatic causes (increased production, decreased liver uptake) cause increase of indirect. Intra-hepatic or post-hepatic causes (decreased hepatic excretion), increase of direct. Increased production: hemolysis. Decreased liver uptake: Gilbert Syndrome, found in 5% population, benign. Decreased hepatic excretion: bile duct obstruction, primary biliar cirrhosis, primary sclerosing cholangitis, benign recurrent cholestasis, hepatitis, cirrhosis, medications, sepsis, total parenteral nutrition, Dubin-Johnson Syndrome, medications Increased GGT: Alcohol consumption
- Increased ALP and GGT: bile duct obstruction, primary biliary cirrhosis, primary sclerosing cholangitis, benign recurrent cholestasis, infiltrative disease of the liver (sarcoidosis, lymphoma, metastasic disease)
- Isolated elevated ALP (extra-hepatic disease): bone disease, pregnancy, chronic renal failure, lymphoma, congestive heart failure.
- Abnormal PT (expressed in seconds or as INR) and albumin levels: indicate severe hepatic synthetic dysfunction and indicates progression to cirrhosis or impending hepatic failure.

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- Other commonly used tests to assess potential causes of hepatic diseases include: viral markers (IgM Hepatitis A Virus, HBsAg, Total Anti-HBc, IgM anti-HBc, anti-hepatitis C antibody), immunologic markers (ANA, SMA, anti-LKM-1, AMA), genetic diseases (hereditary hemochromatosis: transferrin saturation, ferritin, hepatic iron index; Wilson's disease: serum ceruloplasmin, urinary copper; a1-antitrypsin deficiency: serum electrophoresis), hepatocellular carcinoma marker (AFP: alfa-Fetoprotein) and imaging studies (ultrasound, CT, MRI).
- Poor correlation between ALT and AST levels and hepatic fibrosis. Patients with cirrhosis may have normal or only mildly elevated ALT.
- For ALT, AST, ALP and bilirubin samples, hemolysis can cause significant increases. Samples need to be stable at 0 to 4 ° C over 1 to 3 days.
- ALT and AST: increase with strenuous exercise and muscle injury. Meals have no effect. ALT is increased with higher BMI.
- ALP levels increase with food intake, pregnancy and smoking.
- Bilirubin levels increase with fasting. Light exposure decrease bilirubin.

Results:

Characteristics	**Category**	**Frequency**
Age (years)	**30-39**	**69**
	40-49	**61**
	50-59	**58**
	≥ 60	**42**
Frequency of drinking	**daily**	**124**
	Weekly twice	**66**
	Weekly Once	**20**
Body Mass Index (kg/m^2)	**19-25**	**94**
	>25	**116**
Duration of diabetes	**Less than 5 yrs**	**74**
	More than5	**136**
Duration of alcohol intake	**Less than 5yrs**	**111**
	More than 5	**99**
Daily Exercise, Walking	**Yes**	**40**
	No	**170**
Family Type	**Nuclear**	**119**
	Joint	**91**
Family Income in rupees per annum	**≤ 1,00,000**	**59**
	>1,00,000	**151**
Other Health Problems	**Yes**	**30**

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Characteristics	Category	Frequency
	No	180
Abnormal, ALP AST, Abnormal ALP,AST,&ALT,ALBU Abnormal ALP, AST,ALT,GGT&ALBU	30% 17% 9%	63 36 19
Total	56%	118

Of 210 enrolled patients, 124 are daily consuming alcohol.66 more than twice a week 20 drinks once in a week. The amount varies from, one large to one full, majority of them drinks a quarter daily. 102 patients had more than 5 episodes of hypoglycaemia, 28 had three episodes and 41 had 2 episodes of hypoglycaemia requiring admission.

Discussion:

Diabetics need to control their diet and avoid sugar. But can they consume alcohol ? The most important rule is to keep alcohol consumption moderate. Studies have shown that moderate alcohol consumption may have positive health effects like raising HDL cholesterol and lowering the risk of cardiovascular disease. Other studies suggest that moderate alcohol consumption may even reduce risk of type 2 diabetes.

The American Heart Association defines moderate alcohol consumption as 1 drink a day for women and 2 drinks a day for men. For reference, a single drink is measured as a 12 oz. beer, a 5 oz. glass of wine, or 1 ½ oz. of distilled spirits i.e. vodka, whisky, gin etc.

However, excessive alcohol consumption or binge drinking in which a person consumes more than 5 drinks in a two hour span of time for men and 4 for women, can increase the risk of heart disease, type 2 diabetes, and metabolic syndrome. Alcohol in excess can further increase your weight which can lead to insulin resistance making glucose control more challenging but in India drinking and not eating any food causes loss of weight, hypoglycaemia and alcoholic liver diseases ,fatty liver, cirrhosis, and its complications.

The American Diabetes Association recommends that individuals living with diabetes be able to recognize and manage delayed hypo glycaemia when drinking alcohol especially if these individuals use insulin or other medications that can cause blood sugar levels to drop.

Since alcohol consumption can result in increased insulin production which can lower blood sugar levels, education is vital for safety .Diabetics should avoid sugary drinks mixed with processed juices, added sugars and artificial syrups which can add high doses of processed sugars. Such beverages can cause blood glucose spikes and weight gain if consumed in excess. Alcoholic beverages like wine, champagne or distilled alcohol mixed with water or soda are better options for diabetics only way to know what works for you is to monitor blood sugar more often while drinking alcohol. Even 24 hours after drinking, alcohol can cause a drop in blood sugar.

A high prevalence of abnormal LFTs (56%) was observed in patients with type 2 DM in our study. ALP was the most commonly affected liver function parameter. This was followed by abnormalities in AST, ALT, and albumin in that order. The results in our study were similar to those reported in other populations where ALP was highlighted as the most commonly elevated liver enzyme in diabetics. However, this is not a

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universal finding, and some other studies have detected abnormalities in the values of aminotransferases (i.e. AST and/or ALT) to be the most commonly deranged LFT in type 2 diabetes.

In many studies they state that the proportion of abnormal liver functions tests varied in a gender-wise manner. In females, ALP was the most commonly affected parameter. On the other hand, in males, the most commonly deranged parameter was ALT. Furthermore, the proportion of normal and abnormal values for the enzymes AST and ALT varied significantly between males and females. It is increasingly believed that abnormal hepatocellular functions are strongly related to type 2 DM. Analytical studies have linked elevated liver enzymes with hyperglycemia and/or insulin resistance. Abnormal LFTs in type 2 DM have also been attributed to factors like non-alcoholic fatty liver disease and underlying hepatitis C infection. Our study reaffirms the close relationship between type 2 DM and liver dysfunction.

In Indian diabetics, deranged LFTs have been reported at a frequency of 50–70%.This is remarkably higher than the values from Europe and the United States, where derangements in LFTs in diabetics have been reported in the range of 7.8–22.9%.The considerably high frequency of deranged LFTs in type 2 diabetics in the current study and other Indian studies is possible because of co-existence of conditions such as alcoholic liver disease, non-alcoholic fatty liver disease, and other chronic liver diseases. Reasons for these differences between the Indian and non-Indian studies. Our findings underscore the importance of hepatic function monitoring and subsequent workup in diabetics. The currently many of of diabetic subjects did not seek medical attention for hepatic problems. Liver dysfunction assessment often does not figure in the workup of diabetic patients as opposed to assessment of the involvement of other organ systems such as the heart, nervous system, retina, or the kidneys. This is especially true in the primary care setting, which caters to a large chunk of the diabetic patients. However, a high co-existence of liver function derangements in type 2 diabetics, as seen in our study, has important implications because it may influence prognosis and clinical outcomes, and improve patient care. Detailed workup of such patients may offer opportunities for hepatic case finding. Further, the fact that many anti-diabetic agents have hepatotoxic effects and that liver diseases modulate insulin sensitivity may necessitate adapting the management protocol keeping in view the hepatic derangements. Moreover, as several liver function parameters were found to be independently associated with fasting glucose levels in our study, it would be interesting to note if improvements in the LFTs would bring about better glycemic control in type 2 diabetics.

Conclusion:

The current study highlights the importance of liver function monitoring in patients with type 2 DM and alcoholic. It reveals widely co-existent derangements in LFTs in the DM with Alcoholism, very few reports are available about abnormalities of LFTs in these type of patients from India People with diabetes should be particularly cautious when it comes to drinking alcohol because alcohol can make some of the complications of diabetes worse. First of all, alcohol impacts the liver in doing its job of regulating blood sugar. Alcohol can also interact with some medications that are prescribed to people with diabetes. frequent checking of blood sugar and regular LFT is must.

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