Original Article

Development of Diabetes Mellitus in Alcoholic Cirrhotic Patients

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Abstract

Background: Diabetes mellitus and chronic liver disease (CLD) have a complex bidirectional relationship. Up to 80% of patients with liver cirrhosis experience glucose metabolism disorders, known as "hepatogenous diabetes". Coexistence accelerates liver damage and increases mortality risk, making specialized, individualized management essential. The damaged liver struggles to clear insulin and store glucose, leading to peripheral insulin resistance and impaired glucose tolerance (IGT). Type 2 diabetes promotes chronic inflammation, fibrosis, and oxidative stress, which accelerate the progression of CLD to cirrhosis and increase the risk of hepatocellular carcinoma. Traditional diagnostic markers are often skewed in CLD patients. Fasting blood glucose may be artificially low due to decreased glucose production by the failing liver. Glycosylated haemoglobin (HbA1c) is generally unreliable because of shortened red blood cell lifespans and anemia in advanced liver disease. Oral Glucose Tolerance Testing (OGTT) is the most accurate diagnostic tool for these patients. In management, focus should be on frequent, small meals with a balance of complex carbohydrates and proteins. Strict fasting or severe calorie restriction should be avoided to prevent malnutrition and muscle wasting. Metformin once thought to be strictly contraindicated in severe liver disease due to lactic acidosis risk, recent studies suggest it can be safely used in early CLD and may even reduce the risk of hepatocellular carcinoma. Insulin is often the preferred choice, particularly in advanced cirrhosis. Certain GLP-1 receptor agonists and SGLT2 inhibitors are showing promise due to their efficacy in reducing liver fat and fibrosis, though careful monitoring is required depending on the severity of the liver impairment. The aim and objective is to determine prevalence of Diabetes Mellitus in Alcoholic liver disease patients at tertiary care center of Northern India. **Material and Methods:** Over the course of 10 years, from May 1, 2016, to April 30, 2026, a prospective study was carried out at the Department of Medical Gastroenterology, Post Graduate Institute of Medical Sciences (PGIMS), Rohtak. The 100 confirmed alcoholic liver disease (ALD) patients were enrolled in the study, and all were cirrhotic (fibroscan greater than 12.2 Kpa). Only those patients who had no past history of diabetes mellitus and at-least three years or more duration of being diagnosed with ALD, were enrolled in the study. This was done with aim of giving ample time for developing diabetes mellitus, so as to decrease false negative rate. Patients were labelled to be having diabetes mellitus on basis of clinical symptoms (Polydipsia, Polyphagia, Polyuria), blood sugar fasting & post prandial levels (>126 mg/dl and >180 mg/dl respectively) and HbA1C (>6). **Results:** Our all 100 ALD patients were male, predominantly belonging to rural background. The maximum percentage (82.67%) were above 40 yrs of age; the peak age group was between 41-60 yrs (52%). Out of these 100 patients, 16 (16%) developed diabetes mellitus. The average time period for developing DM after being diagnosed as cirrhotic varied between 3- 6 years. **Conclusion:** Patients of ALD are at high risk of developing type 2 diabetes mellitus, mainly in cirrhotic stage. The prevalence of DM increase with progression of decompensation. Hence, it's anticipation by the treating team is mandatory which can be achieved by regularly testing for both fasting and post-prandial sugar levels, along with HbA1C levels. Moreover, patients should also be motivated for being watchful for polydipsia, polyurea and polyphagia which are manifestations of development of diabetes mellitus. Timely detection and appropriate treatment of diabetes mellitus can lead to reduction in morbidity and mortality associated not only with chronic liver disease but also with diabetes mellitus.

Keywords: Diabetes Mellitus, HbA1C, Blood Sugar level, Alcohol, Polydipsia, Polyphagia.

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Introduction

Thirty percent of patients with liver cirrhosis have overt diabetic mellitus (DM), and about eighty percent of patients may have problems with glucose metabolism. DM has been linked to a higher incidence of hepatic problems and death in people with liver cirrhosis, according to prospective studies. DM damages the liver by increasing mitochondrial oxidative stress, which is mediated by adipokines, and causing inflammation and fibrosis. Therefore, the management of hyperglycemia has a beneficial influence on these patients' development. Nevertheless, only a small number of therapeutic studies have assessed the safety and efficacy of antidiabetic medications as well as the influence of DM treatment on liver cirrhosis patients' morbidity and mortality.[1] Liver cirrhosis and diabetes mellitus have a reciprocal relationship: type 2 diabetes is a risk factor for CLD.[2-4] On the other side, cirrhosis can lead to DM. Those with de novo diabetes mellitus were more likely to develop cirrhosis and other hepatic sequelae in a cohort of people with HBV-induced liver infection.[5] Diabetes mellitus (DM) was

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found to be an independent predictor of hepatic sequelae in patients with chronic hepatitis C, including ascites, spontaneous bacterial peritonitis, renal failure, and hepatocellular carcinoma.[6] Type 2 Diabetes Mellitus (T2DM) is highly prevalent in patients with metabolic dysfunction-associated steatohepatitis (MASH), formerly known as NASH. The prevalence of diabetes mellitus (DM) in patients with alcoholic liver disease ranges from 15% to 30%. Up to 80% of patients with advanced chronic liver disease experience some form of glucose intolerance, often termed hepatogenous diabetes. Diabetes and alcohol-associated liver disease (ALD) are closely intertwined. Alcohol disrupts glucose homeostasis. Concurrently, the presence of diabetes promotes liver inflammation and fibrosis, multiplying the risk of severe liver disease. Hepatic damage decreases insulin clearance, leading to chronic hyperinsulinemia and insulin resistance. The combination of diabetes and ALD significantly increases the risk of liver-related mortality and progression to end-stage liver failure compared to ALD alone.

Aims and Objectives: To determine prevalence of Diabetes Mellitus in Alcoholic liver disease patients at tertiary care center of Northern India.

Materials and Methods

Over a ten-year period, from May 1, 2016, to April 30, 2026, the Department of Medical Gastroenterology at the Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, undertook this prospective study. The 100 confirmed alcoholic liver disease (ALD) related cirrhotic patients were enrolled in the study. Only those patients who had no past history of diabetes mellitus and at-least three years or more duration of being diagnosed with ALD, were enrolled in the study. This was done with aim of giving ample time for developing diabetes mellitus, so as to decrease false negative rate. Patients were labelled to be having diabetes mellitus on basis of clinical symptoms (Polydipsia, Polyphagia, Polyuria), blood sugar fasting & post prandial levels (>126 mg/dl and >180 mg/dl respectively) and HbA1C (>6).

Statistical Analysis: Microsoft Excel was used to enter all of the data, and SPSS 15.0 was used for analysis.

Results

Our all 100 ALD patients were male, predominantly belonging to rural background. The maximum percentage (82.67%) were above 40 yrs of age; the peak age group was between 41-60 yrs (52%). The chances of developing DM were 16% in cirrhotic stage.

Table 1: Displaying the Age, Sex, and Geographic Distribution of the ALD Group.

ALD Patients	Male	Female	Rural	Urban	20-40 yrs	41-60 yrs	61-80 yrs
100 (100%)	100 (100%)	0 (0%)	60 (60%)	40 (40%)	18 (18%)	52 (52%)	30 (30%)

Table 2: Showing prevalence of Development of Diabetes Mellitus in ALD Patients

Total ALD Cirrhotic Patients	Developed Diabetes Mellitus	Not Developed Diabetes Mellitus
100	16 (16%)	84 (84%)

Discussion

The most prevalent liver conditions include severe disease stages like NASH, cirrhosis, liver failure, and HCC, as well as fatty liver diseases including alcoholic and MAFLD, infections with HAV, HBV, and HCV, and hemochromatosis.[7] IR and other liver illnesses are closely related, according to recent research. IR has also been linked to chronic hepatitis, such as that brought on by HBV, HCV, hemochromatosis, cirrhosis, and HCC. The World Health Organization recognizes "hepatogenous diabetes," a term used by certain authors to describe the development of type 2 diabetes brought on by cirrhosis.[8] Excessive drinking is linked to cirrhosis in about 25% of patients with ALD. The pancreas immediately metabolizes ethanol's byproducts and metabolites, which could harm acinar cells.[9,10] Extracellular matrix (ECM), acetaldehyde, and reactive oxygen species (ROS) are produced and deposited as a result of inflammatory responses and endothelial dysfunction. This further activates the transcription factors that make up nuclear factor κB (NF-κB) and activator protein-1 (AP-1).[10,11] An multinational multi-center cohort of individuals with ALD confirmed by biopsy is part of the Worldwide Alcohol-related Liver Disease Outcomes (WALDO) project. It was noted whether DM was present at baseline or during follow-up. A total of 712 patients were monitored for a median of 4.8 years (IQR: 1.2–9.5), with a median age of 52 years. 113 individuals (15.9%) and an additional 56 patients (7.8%) had DM at baseline.[12] In one study, Israelsen et al. found that insulin resistance was the best indicator of hepatic inflammation and fibrosis stage in patients with ALD.[13] Alcohol and metabolic dysfunction are known to cause liver damage on their own, and having both risk factors raises the likelihood of developing chronic liver disease.[14–16] Åberg et al,[16] found that both alcohol consumption and the presence of diabetes mellitus (DM) doubled the population-level risk of serious liver disease. Alcohol consumption and the risk of acquiring diabetes mellitus have been the subject of numerous research.[17-19] In our geographical area, most common cause of cirrhosis is alcoholic liver disease, constituting 50 % of total load. There is clear-cut male predominance, as still culture of drinking alcohol in females, is mainly seen in affluent societies only. Our study group analysis reveals that chances of developing DM in initial stages of ALD like fatty liver or alcoholic hepatitis are not increased and are comparable to chances in normal population. Once, ALD patient crosses significant fibrosis stage (>F2), then there is mild increase for development of DM. The main burnt of developing DM occurs in cirrhotic which increases in direct proportion, as decompensation increases. The same rule applies to pre-diabetic stage which no doubt is more commonly seen than DM in all three stages of ALD but maximally is seen in

decompensated cirrhotic.

Conclusion

Patients of alcoholic liver disease are at high risk of developing type 2 diabetes mellitus, mainly in cirrhotic stage, chances of which increase with progression of decompensation. Hence, it's anticipation by the treating team is mandatory which can be achieved by regularly testing for both fasting and post-prandial sugar levels, along with HbA1C levels. Moreover, patients should also be motivated for being watchful for polydipsia, polyurea and polyphagia which are manifestations of development of diabetes mellitus. Diabetes mellitus and chronic liver disease-related morbidity and death can be reduced with prompt diagnosis and proper treatment.

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Conflicts of interest

There are no conflicts of interest.

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