Original Article

Prevalence of Diabetes in Chronic Liver Disease Patients: A Cross-Sectional Study

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Abstract: Diabetes Mellitus (DM) is a complex metabolic disorder characterized by hyperglycemia and micro or macrovascular problems. DM causes micro or macrovascular problems, shortened life expectancy, and poor quality of life. Insulin sensitivity and secretion imbalances cause diabetes. The liver controls insulin response throughout the body. In certain liver conditions, diabetes is more common. Diabetes worsens liver injury. It's vital to note the link between diabetes and cirrhosis while analyzing research since those with more cirrhotic patients are more likely to uncover a link. Diabetics can develop nonalcoholic fatty liver disease, chronic viral hepatitis, hemochromatosis, alcoholic liver disease, and cirrhosis. This study determined the prevalence of diabetes in patients with CLD. This is a cross-sectional study. The study analyzed 48 patients with liver diseases. All the patients with cirrhosis of either gender fulfilling the inclusion criteria were enrolled in the study. Ethical approval was obtained. Laboratory parameters like, platelet count, fasting and post-prandial sugar, HbA1C, ultrasonography of abdomen, and upper gastro-intestinal tract endoscopy, prothrombin time, serum bilirubin, albumin was measured. Child Pugh Scores was calculated by adding the scores of the five factors (serum bilirubin, serum albumin, prothrombin time, grade of ascites and hepatic encephalopathy). Data entry was done in SPSS version 20 and statistical analysis was done with Chi Square test. Total 48 patients were enrolled in the test. DM was present in 10 (20.8%) of the CLD patients. The frequency of DM in CLD patients was highest in chronic hepatitis C related liver cirrhosis i.e.3 patients (30%) and the result were statistically significant with the p value of <0.00001. Child Pugh score C had highest frequency for DM occurrence i.e. 9(18.75%) than child Pugh A and B but this result was not statistically significant with p value 0.53. The prevalence of diabetes was highest in chronic hepatitis C related liver cirrhosis. As the severity of liver disease increases, higher chances of DM occurrence.

Keywords: diabetes mellitus, chronic liver disease, child Pugh score

1. INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders of carbohydrates, lipids and proteins characterized by hyperglycemia [1]. Globally, more than 415 million people, aged 20-79 years, were affected by DM and the figure is expected to rise up to 642 million in 2040. There has been a tremendous increase in the prevalence of diabetes mellitus (DM) in developing countries, where 75 percent of diabetic patients reside in countries with low and intermediate incomes. At the same time, diabetes mellitus has an impact on the working age in countries with low and intermediate incomes [2].

There is currently a lack of clarity on the precise pathophysiological process by which diabetes can cause changes in liver biomarkers. The accumulation of fat in the liver, which is a feature of nonalcoholic fatty liver disease (NAFLD), is the first plausible explanation for why diabetes mellitus (DM) causes abnormalities in liver function. Inflammation of the liver, which changes the function of the liver and induces a change in liver biomarkers, is vulnerable to persons who have metabolic syndromes such as diabetes mellitus [3]. This is the other probable assumption. Screening for liver illness, monitoring the progression of a known liver disease, and monitoring the effects of potentially hepatotoxic medicines are all examples of clinical applications for liver function tests, often known as LFTs. Among the LFTs that are utilized the most frequently are the serum aminotransferases, alkaline phosphatase (ALP), bilirubin, total protein (TP), albumin, and prothrombin time. As a marker of hepatocyte injury, the measurement of serum aminotransferases, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), functions as a helpful tool. While bilirubin, gamma-glutamyl transpeptidase (GGT), and alanine aminotransferase (ALP) serve as indicators of cholestasis and biliary function, thrombin time, albumin, and prothrombin amount are indicators of liver synthetic function [4]. In the context of clinical practice, chronic liver disease refers to a disease process that affects the liver and is characterized by the gradual destruction and regeneration of the liver parenchyma, ultimately resulting in fibrosis and cirrhosis [5]. A lower life expectancy and a significant morbidity due to micro or macro vascular problems, as well as a diminished quality of life, are both related with diabetes [6]. According to the most recent estimates, there are around 170 million people around the world who are afflicted with diabetes, and this figure is expected to increase to 266 million by the year 2030 [7]. The prevalence of diabetes in Nepal, both those who were already diagnosed with the condition and those who had just been diagnosed, was 19.0%. In the whole population, there were 30.5% of people who had some abnormalities of glucose tolerance. This included 37.8% of men and 25.3% of women. Despite the fact that the connection between diabetes and cirrhosis has been known for more than a century, the extent of liver damage in diabetics is still not fully understood [8]. It is possible for diabetes to be associated with liver illness in three distinct ways: 1) liver disease can cause diabetes; 2) liver disease can cause diabetes; and 3) Diabetes is a condition that either contributes to or causes liver disease, and there are also risk factors that are comparable for both diabetes and liver disease. Cirrhosis of the liver is associated with a high incidence of glucose metabolism disorders (GMD) [9]. The condition known as "hematogenous diabetes (HD)" [10,11] is a form of diabetes that manifests itself as a consequence of cirrhosis of the liver. There is an estimated incidence of impaired glucose tolerance (IGT) in patients with cirrhosis of the liver that ranges from around 60 to 80 percent, while the prevalence of overt diabetes is approximately 7 to 15 percent [12,13]. People who develop diabetes as a consequence of cirrhosis of the liver are distinct from individuals who have typical type 2 diabetes mellitus in that they have a lower prevalence of diabetes in their families and a lower risk of both macro- and micro-angiopathic complications [14]. A point prevalence research found that the prevalence of micro and peripheral macro-angiopathy and coronary heart disease in cirrhosis patients with diabetes mellitus was equivalent to that of controls, and it was significantly lower than the prevalence that was reported in patients with type 2 diabetes mellitus who were randomly selected [15]. There are numerous reports in the medical literature that indicate that decreased glucose tolerance and diabetes mellitus usually aggravate chronic viral hepatitis and cirrhosis. There has been a direct correlation established between the infection caused by the hepatitis B virus and the development of glucose metabolism abnormalities that are the result of pancreatic islet cell injury [16]. A recent study that was conducted in the United States as part of the third National Health and Nutrition Examination Survey (NHANES-III) documented that individuals who tested positive for HCV and were over the age of 40 had a threefold increased risk of developing type 2 diabetes in comparison to individuals who tested negative for HCV [17]. The amount of published material that discusses the prevalence of type 2 diabetes mellitus in chronic liver disorders (CLD) in the Indian context is quite limited. The liver's role in diabetes mellitus has been the

subject of extensive research. On the other hand, the incidence of diabetes mellitus in CLD patients who were not previously diagnosed with diabetes has not been adequately emphasized. The purpose of the study is to ascertain the prevalence of diabetes in patients who have chronic obstructive pulmonary disease (CLD), as well as to ascertain the prevalence of diabetes in CLD patients who have a variety of etiologies, and to ascertain the prevalence of diabetes based on the severity of CLD (child Pugh's).

2. MATERIALS & METHOD

The study was carried out once the proposal was accepted by the ethical committee of NAMS (National Academy of Medical Sciences) and IRB (Institutional Review Board) Cross-Sectional Observational study done at Department of Internal Medicine, Bir Hospital, Mahabodhi, Kathmandu for the period of 1 year. This is a cross-sectional study. The study analyzed 48 patients with liver diseases. All the patients with cirrhosis of either gender fulfilling the inclusion criteria were enrolled in the study. Ethical approval was obtained. Laboratory parameters like, platelet count, fasting and post-prandial sugar, HbA1C, ultrasonography of abdomen, and upper gastro-intestinal tract endoscopy, prothrombin time, serum bilirubin, albumin was measured. Child Pugh Scores was calculated by adding the scores of the five factors (serum bilirubin, serum albumin, prothrombin time, grade of ascites and hepatic encephalopathy). Data entry was done in SPSS version 20 and statistical analysis was done with Chi Square test. A patient will be said to have diabetes if his/her, Blood HbA1c level is ≥6.5% OR FPG level of ≥126mg/dl OR, hour PG is≥200mg/dl OR With classic symptoms of hyperglycemia or hyperglycemic crisis RPG is≥200mg/dl, In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing. Child-Turcotte score included two continuous variables (bilirubin and albumin) and three discrete variables (ascites, encephalopathy, and nutritional status) which were empirically selected because they were felt to have their own influence on the prognosis in this context.

Table 01: Child Pugh's scoring system

	1 point	2 points	3 points
Encephalopathy	None	Grade 1-2	Grade 3-4
Ascites	Absent	Slight	Moderate
Total bilirubin (mg/dl)	<2.0	2.0-3.0	>3.0
Serum albumin (g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time (sec)	<4	4-6	>6
INR	<1.7	1.7-2.3	>2.3

Child Pugh's Scoring Classes:

Class A: 5-6 points, Class B: 7-9 points, Class C: 10-15 points

3. RESULTS & DISCUSSION

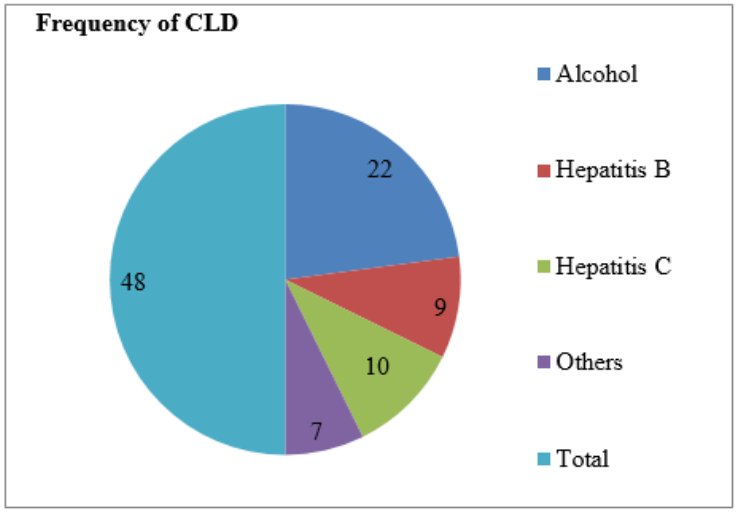

Figure 01: Frequency of etiological distribution of CLD patients

Regarding the 48 patients who were diagnosed with chronic liver disease, 22 patients (45.8%) were associated to alcohol, 9 patients (18.75%) were related to hepatitis B, 10 patients (20.83%) were related to hepatitis C, and 7 patients (14.58%) were related to other causes.

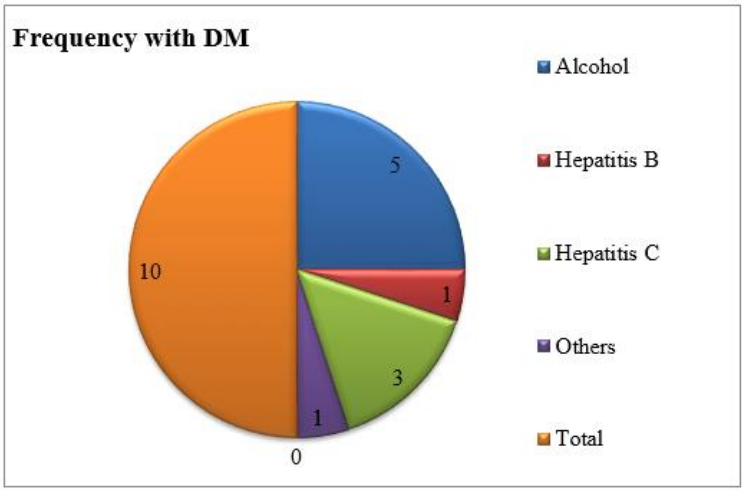

Figure 02: Frequency with DM in CLD patients

There were ten individuals out of a total of forty-eight patients with CLD who had diabetes, which represents a prevalence rate of twenty-eight percent. The causes of diabetes mellitus in patients with chronic liver disease were chronic hepatitis B related liver cirrhosis in one patient (11.1%), chronic hepatitis C related liver cirrhosis in three patients (30%), and other reasons in one patient (14.2%). Alcoholic liver cirrhosis was the source of diabetes in patients with chronic liver disease.

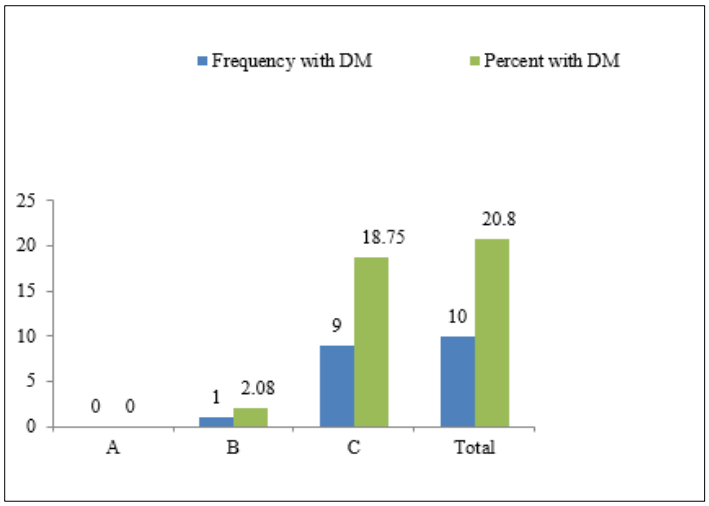

Figure 03: Frequency of DM with Child Pugh score

There was not a single patient with a Child Pugh A score among the ten diabetic patients. There was one patient who received a Child Pugh B score, which was 2.08 percent, and nine patients, which was 18.75 percent, received a Child Pugh C score. Within the population of CLD patients with a Child Pugh score, the mean value and standard deviation for the occurrence of diabetes were 2.75 and 0.484, respectively.

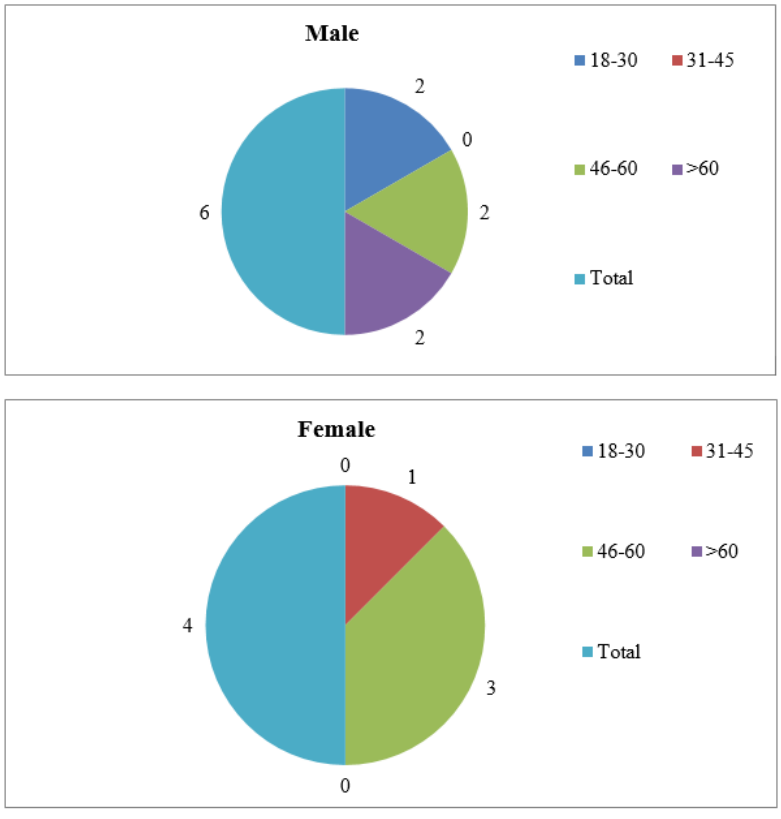

Figure 04: Frequency of DM in male and female patients according to age distribution.

24 of the 48 patients diagnosed with CLD were male, and 24 of the patients were female. Diabetes mellitus was seen in a total of eight individuals, six of them were male and four of whom were female. Eighteen to thirty, thirty-one to forty-five, forty-six to sixty, and sixty and above were the four age

categories that were considered. The age group of 46-60 years old had the highest number of diabetic patients, which was five patients.

DISCUSSION

Through non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), cirrhosis, and finally hepatocellular carcinoma [18], diabetes mellitus (DM) alone has the potential to be a cause of liver disease. The development of diabetes, on the other hand, is extremely common in patients who have chronic liver illnesses [19,20]. For the purpose of gaining an understanding of the prevalence of diabetes mellitus (DM) among the individuals of the current study who were diagnosed with chronic liver disease due to a variety of causes but were not previously diagnosed with diabetes. The majority of the patients for this study were between the ages of 46 and 60. With a mean age of 46.18 years old and a standard deviation of ±12.717 years, the minimum age set was 18 years old, and the maximum age set was 75 years old. A study was conducted in Kolkata, and the average age of the participants was 44.30 years, with a standard deviation of 10.42 years [21]. According to the findings of a study conducted in Kolkata, out of a total of 136 patients with chronic liver disease, 101 (74.3%) were affected by alcoholic liver disease, 19 (14.0%) affected by chronic hepatitis B, 9 (6.6%) affected by chronic hepatitis C, 4 (2.9%) affected by Wilson's disease, and 3 (2.2%) affected by autoimmune hepatitis. Class A patients made up 27 (19.9%) of these 136 patients, while class B patients made up 86 (63.2%) of the total, and class C patients made up 23 (16.9%) of the total [22]. The results of this study showed that out of 48 patients with chronic liver disease (CLD), 22 patients (45.8%) were associated to alcohol, 9 patients (18.75%) were related to hepatitis B, 10 patients (20.83%) were related to hepatitis C, and 7 patients (14.58%) were related to other causes. This result is also supported by the research that was conducted in Dharan, Nepal. On the other hand, cryptogenic cirrhosis (11%), hepatitis B (2%) and hepatitis C (1%) were the second and third most common causes of cirrhosis in the study population, respectively [23]. Alcohol intake was shown to be the most common cause of liver cirrhosis, accounting for 31.8% of the total cases, according to a cross-sectional study that was conducted in Bir hospital in the year 2001 [24]. According to estimates, the lifetime prevalence of alcohol misuse among individuals in the United States is as high as 18 percent. Alcohol addiction is widespread across the globe. Alcohol was a contributing factor in 48 percent of the deaths that occurred in the United States in 2009 due to cirrhosis, according to figures provided by the National Institutes of Health [25]. There were more than 31,000 deaths that occurred as a result of cirrhosis in the United States. A number of studies have demonstrated that people who have chronic liver illness are at a greater risk of developing diabetes due to a variety of distinct causes [26]. On the other hand, Nepal has not attempted to conduct such a study as of yet. My research was based on an Indian literature that stated that the prevalence of diabetes in chronic liver disease was 14% [27]. I used this information to draw my conclusions. Participants in this study included a total of 48 patients with chronic liver disease who had visited Bir Hospital in Mahabodhi, Kathmandu, over the course of one year. Based on the findings of this study, the percentage of patients with chronic liver disease who have diabetes is twenty-eight percent. One study [22] found that between thirty percent and forty percent of people with cirrhosis develop diabetes. One further study [28] indicated that diabetes was present in 21.6% of the individuals. Another study found that diabetes was present in 21.6% of patients with chronic liver disease (CLD) (53.7% of patients with cirrhosis, 13.7% of patients with chronic hepatitis, and 9.5% of all HBV inactive carriers) [29,30]. HCV may directly interfere with glucose homeostasis, according to clinical and experimental observations suggested by the virus. Type 2 diabetes mellitus was shown to be five times more prevalent in HCV-related cirrhotic patients compared to cirrhotic patients due to other reasons, according to the very first paper ever published in this respect, which was referred to as [29]. Even if there are no other major risk factors for glucose intolerance, a number of additional research, including cross-sectional, case control, and longitudinal investigations, have also revealed that type-2 diabetes is

more prevalent in chronic hepatitis C patients, particularly those who are over the age of 40 [31]. An author from Iran stated that out of the total of 185 CLD patients who participated in the study, 11.3% of them had IGT and/or IFG, and 21.6% of them had overt diabetes [32]. According to the findings of another study [33] conducted in Mexico, the prevalence of type 2 diabetes among CLD patients was nearly as high as 23 percent. Previously, [34] had provided evidence that a significant number of people with CLD had both impaired glucose tolerance and diabetes. The occurrence of diabetes was separate from the Child-Pugh score, according to the findings of a study [35]. According to the findings of a study, however, there is a substantial correlation between diabetes and a higher Child-Pugh score [36]. Prior to this, an author [37] had previously found that there was a positive link between the severity of hepatic impairment and the prevalence of diabetes and/or inhibitory glucose tolerance. Alcohol, non-alcoholic fatty liver disease (NAFLD), hepatitis C virus (HCV), hemochromatosis, and autoimmune hepatitis are more frequently associated with diabetes [38]. The etiology of liver disease has a significant role in the development of type 2 diabetes. Hepatitis C virus (HCV) infection was associated with diabetes in 21% of patients, while hepatitis B virus (HBV) infection was associated with 12% of patients [39]. 4.2% of patients in the diabetic cohort tested positive for HCV, whereas just 1.6% of patients in the control group did. According to their findings, there is a significant connection between HCV infection and diabetes. In a different investigation, type 2 diabetes was discovered in fifty percent of patients who had cirrhosis caused by HCV, in contrast to nine percent of patients who had liver disease that was not caused by HCV [40]. According to a study conducted in Karachi, Pakistan, [41] found that the incidence of diabetes was nearly identical in patients with liver illness caused by both HBV and HCV. Based on the etiological distribution of the CLD patients, this study found that alcohol was responsible for 22.7% of cases of diabetes, hepatitis C was responsible for 30% of cases, hepatitis B was responsible for 11.1% of cases, and other causes took up 14.2% of cases. With a p value of less than 0.00001 and a confidence interval of 95%, this study demonstrated that there was a significant difference between the etiological distributions of the CLD patients. Several studies have demonstrated that the prevalence of diabetes is more closely linked to chronic liver disease (CLD) that is related to hepatitis C [42].

4. CONCLUSIONS

According to the findings of this study, people who have chronic liver illness have a higher risk of acquiring diabetes syndrome. In total, there were 48 patients that participated in the study. In ten of the CLD patients, or twenty-eight percent, diabetes was present. There were three patients (30%) who had chronic hepatitis C linked liver cirrhosis, and the prevalence of diabetes mellitus (DM) in patients with chronic liver disease (CLD) was highest in those patients. The results were statistically significant, with a p value of less than 0.00001. This finding was not statistically significant with a p value of 0.53, despite the fact that child Pugh score C had the highest frequency for the incidence of diabetes, which was 9 (18.75%), compared to child Pugh scores A and B. The chronic hepatitis C-related liver cirrhosis group had the greatest prevalence of diabetes among the patients. A higher likelihood of developing diabetes is associated with an increase in the severity of liver disease. In individuals with chronic liver disease, the prevalence of diabetes was determined to be 20.8%. In addition to alcoholic cirrhosis, hepatitis B, and hepatitis C, there are a number of other etiological distributions that can contribute to an increased risk of developing diabetes. According to the findings, thirty percent of people have diabetes because of hepatitis C. According to the kid Pugh score, a greater number of diabetic patients appeared to have a child Pugh score of C. This indicates that the severity of liver illness is associated with an increased risk of diabetes.

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