Prevalence Of Diabetes In Chronic Liver Disease Patients: A Cross-Sectional Study

Dr Parimal Koirala[1*], Dr Binod Pantha[2] , Dr Milan Khadka[3] , Dr Lochan Karki[4] ,

Dr Prasanna Amatya[5] .

[1]Department of Internal Medicine, National Academy of Medical Sciences, Bir-Hospital, Kathmandu, Nepal

[2]Department of Internal Medicine, National Academy of Medical Sciences, Bir-Hospital, Kathmandu, Nepal

[3]Department of Internal Medicine, National Academy of Medical Sciences, Bir-Hospital, Kathmandu, Nepal

[4]Department of Internal Medicine, National Academy of Medical Sciences, Bir-Hospital, Kathmandu, Nepal

[5]Department of Cardiology, National Academy of Medical Sciences, Bir-Hospital, Kathmandu, Nepal.

[*]**Correspondence:**
Dr Parimal Koirala, Department of Medicine, NAMS. Bir Hospital, Nepal.

Email: koirala_55@hotmail.com, Phone: +977 9857040039

Abstract

Background
Diabetes Mellitus (DM) is a complex metabolic condition defined by the level of hyperglycemia giving rise to risk of micro vascular or macro vascular complications. DM is associated with reduced life expectancy and significant morbidity due to micro or macro vascular complications and impaired quality of life. Diabetes develops from an imbalance between insulin sensitivity and insulin secretion. The liver plays a key role in the whole-body response to insulin. The prevalence of diabetes is higher in patients who have certain liver diseases. There is a link between the presence of diabetes and the severity of liver injury. On analysis of various studies, it is important to remember the link between diabetes and cirrhosis, because studies with an increased proportion of cirrhotic patients are more likely to find an association between diabetes and disease severity. The liver diseases associated with diabetes include nonalcoholic fatty liver disease, chronic viral hepatitis, hemochromatosis, alcoholic liver disease, and cirrhosis.

Objectives
The objective of this study is to determine the prevalence of diabetes in patients with CLD.

Methods
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 were 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.

Results
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 was

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.

Conclusions
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

INTRODUCTION:
Chronic liver disease in the clinical context is a disease process of the liver that involves a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis.[1] DM is associated with reduced life expectancy and significant morbidity due to micro or macro vascular complications and impaired quality of life.[2] Current estimates suggest that there are 170 million people suffering from diabetes worldwide and this number is going up to 266 million by year 2030.[3] The age and sex standardized prevalence of diabetes in Nepal (known and newly diagnosed), was 19.0%. Of the total population, 30.5% (37.8% of men and 25.3% of women) had some abnormality of glucose tolerance. Though association of diabetes with cirrhosis has been recognized for more than 100 years, liver disease in diabetes remains under estimated.[5] The association of diabetes with liver disease can be in three different ways – 1) liver disease causing diabetes 2) diabetes contributing to or causing liver disease and 3) similar risk factors for both liver disease and diabetes. Glucose metabolism disorders (GMD) are frequent in liver cirrhosis.[6] Hence, the present study will be conducted in Bir Hospital, Mahabouddha, Kathmandu, to find out the magnitude of the problem of type 2 diabetes mellitus among patients with various types of chronic liver diseases.

Criteria for the diagnosis of diabetes.[7]
Estimation of HbA1c will be done in the laboratory using a method that is NGSP certified and standardized to the DCCT assay.
FPG will be done defined as no caloric intake for at least 8hrs.
*A patient will be said to have diabetes if his/her
1) Blood HbA1c level is ≥6.5% OR
2) FPG level of ≥126mg/dl OR
3) 2 hour PG is≥200mg/dl OR
4) 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 Pugh's grading of Liver Disease:
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.

Table1:Child Pugh's scoring system

Parameter	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

OBJECTIVES:

General Objectives:

- To determine the prevalence of diabetes in patients with CLD.

Specific objectives:

- To determine the prevalence of diabetes in CLD patients with different etiologies.
- To determine the prevalence of diabetes based on the severity of CLD (child pugh's)

MATERIAL AND METHODS

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)

Type of study: Cross-Sectional Observational study
Place of study: Department of Internal Medicine, Bir Hospital, Mahabouddha, Kathmandu
Study period: 1 year.
Sample size: 48
Inclusion Criteria: Patients admitted and attending outpatient department (Internal Medicine) in hospital with clinical, biochemical and sonographic evidence of CLD during the study period was included in the study after obtaining informed consent.
Presence of CLD defined by signs and symptoms of liver disease lasting for more than 6 months diagnosed according to combination of One clinical sign of hepatocellular failure + One clinical sign of portal hypertension + At least three USG findings suggestive of cirrhosis of liver. And /or UGI endoscopy evidence of portal hypertension in permissible Cases.[19]

Exclusion criteria:

1. Chronic pancreatitis,
2. Corticosteroids therapy,
3. Type 1 diabetes,
4. Other specific types of diabetes due to other causes, e.g., diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced (such as in the treatment of HIV/AIDS or after organ transplantation,)
5. Age below 18 years
6. Diabetes diagnosed prior to onset of CLD.
7. Pregnant lady.
8. Patients not willing to give consent.

RESULTS

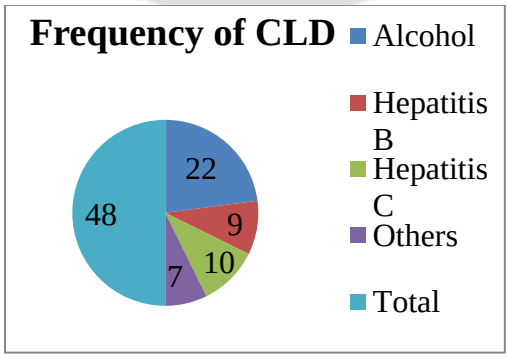


FIG1

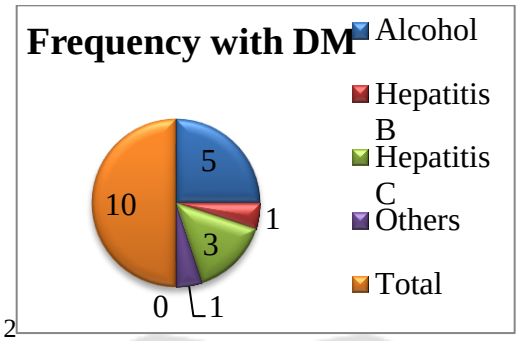


FIG 2

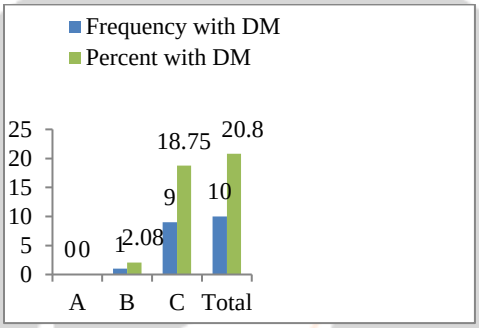
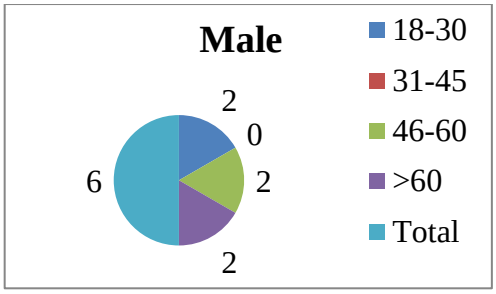


FIG3

Fig 1: Frequency of etiological distribution of CLD patients
Among 48 CLD patients, 22 (45.8%) patients were related to alcohol, 9 (18.75%) patients were related to hepatitis B, 10(20.83%) patients were related to hepatitis C and 7(14.58%) were related other causes.
Fig 2: Frequency with DM in CLD patients
Among 48 CLD patients, the prevalence of DM was in 10 patients (20.8%). The causes of DM in CLD patients were alcoholic liver cirrhosis in 5 patients (22.7%), chronic hepatitis B related liver cirrhosis in 1 patient (11.1%), and chronic hepatitis C related liver cirrhosis in 3 patients (30%) and other causes in 1 patient (14.2%).

Fig 3: Frequency of DM with Child Pugh score

Among 10 DM patients, there was no Child Pugh A score patient. 1 patient (2.08%) came under Child Pugh B score and 9 patients (18.75%) came under Child Pugh C score. The mean value and standard deviation for presence of DM in CLD patient with Child Pugh score was 2.75 and
0.484respectively.



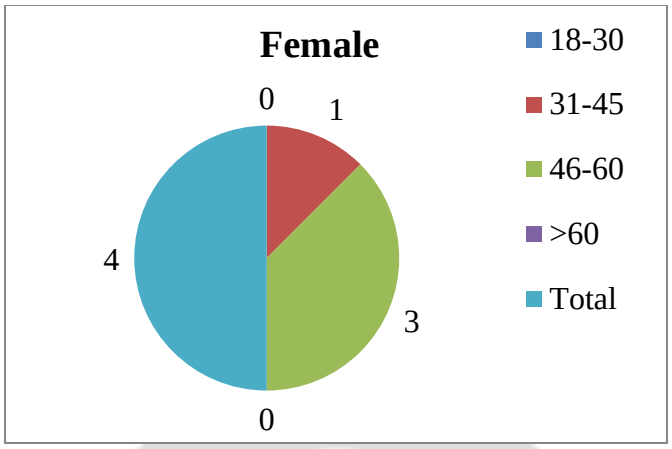


Fig 4: Frequency of DM in male and female patients according to age distribution.

Among 48 CLD patients, 24 were male and 24 were female patients. Among them DM was seen on 6 male patients and 4 female patients. Age was divided into 4 groups, i.e. 18-30, 31-45, 46-60 and above 60. Highest number (5 patients) of DM patients was found in age group of 46-60.

DISCUSSIONS

Most patients in this study were in the 46 – 60 age group. The minimum age was 18 and the maximum age was 75 with a standard deviation of ±12.717 and the mean age of 46.18. In the study conducted in Kolkata, the mean age of the study subjects was 44.30 ± 10.42 years.[8]

The result of Kolkata study showed, out of the total 136 CLD patients, 101 (74.3%) suffered from alcoholic liver disease, 19 (14.0%) had chronic hepatitis B, 9 (6.6%) had chronic hepatitis C, 4 (2.9%) had Wilson's disease, and 3 (2.2%) had autoimmune hepatitis. Out of these 136 patients, 27 (19.9%) were in Child-Pugh class A, 86 (63.2%) were in class B, and 23 (16.9%) in class C.[13]In this study, among 48 CLD patients, 22 (45.8%) patients were related to alcohol, 9 (18.75%) patients were related to hepatitis B, 10 (20.83%) patients were related to hepatitis C and 7(14.58%) were related other causes. The study done at Dharan, Nepal also supports this result. Most common etiology of the study population was alcohol related cirrhosis (86%) followed by cryptogenic cirrhosis (11%), hepatitis B (2%) and hepatitis C (1%).[11] A cross-sectional study done in Bir hospital in 2001 found that the alcohol consumption was the most common cause for liver cirrhosis accounting for 31.8% of the total cases.[12] Alcohol abuse is common worldwide, with an estimated lifetime prevalence of 18 percent among adults in the United States. The National Institutes of Health estimates that in the United States in 2009, there were more than 31,000 deaths from cirrhosis and that alcohol played a role in 48 percent of those deaths (age-adjusted death rate of 4.5 deaths per 100,000 population).[13]

Different studies have shown increased risk of diabetes in patients with chronic liver disease due to different mechanisms.[9] However, there is no such study done in Nepal till now. I have done my study on the basis of an Indian literature where the prevalence of diabetes in chronic liver disease was 14%.[8] In this study total 48 chronic liver disease patients visiting Bir Hospital, Mahaboudha, Kathmandu in time period of 1 year were included. This study showed that, the prevalence of diabetes in chronic liver disease patients is 20.8%. According to a study done by Alavian et al, About 30% - 40% of cirrhotic patients develop DM.[9] In another study, DM was found in 21.6% patients.[10] In another study, DM was reported in 21.6% of patients with CLD (53.7% in cirrhosis, 13.7% in chronic hepatitis, and 9.5% in HBV inactive carrier).[16,17,18] Clinical and experimental observations suggest that HCV may directly interfere with glucose homeostasis. The first ever document published in this regard was by Allison et al.[19] who pointed out that type 2 Diabetes Mellitus was five times more prevalent in HCV related cirrhotic patients as compared to cirrhotic patients due to other causes. Several other cross-sectional, case control and longitudinal studies also suggested that type-2 Diabetes is more prevalent in chronic hepatitis C patients especially above 40 years of age, even if other major risk factors for glucose intolerance are lacking.[20]In this study prevalence of diabetes according to etiological distribution of the CLD patients showed, alcohol 22.7%, hepatitis C 30%, hepatitis B 11.1% and others 14.2%. This study showed the significant difference among etiological distribution of the CLD patients with p value =<0.00001 with CI=95%. Different studies have shown the prevalence of diabetes is more associated with hepatitis C related CLD.[10,8]

CONCLUSIONS

This study concluded the increasing risk of developing DM in patients with chronic liver disease. The prevalence of DM in CLD patients was concluded to be 20.8%. Occurrence of DM can be enhanced by various etiological distributions such as alcoholic cirrhosis, hepatitis B, hepatitis C and others. The prevalence of DM due to hepatitis C was determined as 30%. According to child pugh score more diabetic patient came under child pugh score C which reveals that the severity of liver disease leads to higher risk of DM.

Conflict of Interest: None declared.

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