

# Prevalence of Diabetes Mellitus in Patients of Biopsy Proven Liver Cirrhosis

Diabetes Mellitus  
in Patients of  
Biopsy Proven  
Liver Cirrhosis

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## ABSTRACT

**Objective:** To determine the frequency of diabetes mellitus in patients with biopsy proven liver cirrhosis.

**Study Design:** A Descriptive, cross-sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Medicine, Bahawal Victoria Hospital, Bahawalpur, from August 2022 to February 2023.

**Materials and Methods:** Patients admitted having biopsy-proven liver cirrhosis were analyzed. Fasting blood glucose and HbA1c levels were evaluated for the presence or absence of diabetes mellitus. Diagnosis of diabetes mellitus was confirmed when there was fasting plasma glucose above 126 mg/dL and HbA1c above 6.5% on two consecutive samples taken at least 12 hours apart.

**Results:** In a total of 240 patients with biopsy proven liver cirrhosis, 138 (57.5%) were male. The mean age and BMI were 42.87±9.67 years (30 to 70 years) and 27.62±4.25 kg/m<sup>2</sup> respectively. Family history of diabetes was present in 102 (42.5%) patients. The frequency of DM was noted in 53 (22.1%) biopsy-proven LC patients. Older age (51-70) was found to have significant association with the presence of DM (34.0% vs. 18.2%, p=0.0138). Increased liver disease severity (higher child pugh class) were noted to have significant association with the presence of DM (p=0.0445).

**Conclusion:** The prevalence of diabetes mellitus was high among patients with biopsy proven liver cirrhosis. Relatively older age, and increased disease severity with linked with significantly higher prevalence of diabetes mellitus in patients with biopsy proven liver cirrhosis.

**Key Words:** Body mass index, Child pugh class, diabetes mellitus, fasting plasma glucose, liver cirrhosis.

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## INTRODUCTION

Liver cirrhosis (LC) is a condition where the liver becomes scarred and unable to function properly. It happens when the liver is harmed for a long time by different causes, such as drinking too much alcohol, having viral infections, having fat buildup in the liver, or having inherited diseases.<sup>1</sup> Regardless of the cause, 80-90% of the liver's function must be lost before liver failure ensues. The global age-standardized incidence rate of LC is 20.7 per 100,000 people.<sup>2</sup>

The reported prevalence of LC in Pakistan in one study was 44.5%, with a higher ratio among males than

females. In this report, the age group most frequently affected was 21-30 years old.<sup>3</sup>

Diabetes mellitus (DM) is a disorder of the utilization of blood glucose. The different types of DM include type 1, type 2, gestational, and prediabetes. Each type has different causes, symptoms, and treatments.<sup>4</sup> The complications of DM are serious and can affect various parts of the body. Some of the major complications of DM are vision loss, blindness, foot ulcers, an increased risk of stroke, angina, and a heart attack. Raised blood pressure, high cholesterol, smoking, and obesity are known to worsen these risks. Diabetes can also lead to kidney failure, nerve pain, tingling, numbness, or weakness.<sup>5</sup> It has been reported by "the 2nd National Diabetes Survey of Pakistan (NDSP 2016-17)" that about 26.3% of the Pakistani people over 19 years of age are suffering from DM.<sup>6</sup>

Diabetes can cause or worsen LC by increasing the accumulation of fat in the liver, causing inflammation, oxidative stress, and fibrosis. LC can also affect the metabolism of glucose and insulin sensitivity, leading to type 2 DM or worsening the existing disease. Some of the common chronic liver diseases linked to diabetes are nonalcoholic fatty liver disease (NAFLD), hepatitis C, and liver cirrhosis.<sup>7</sup> The reported prevalence of DM in LC patients is 30-60%, depending on the cause and stage of the liver disease.<sup>8</sup> Similarly, the reported

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prevalence of DM in patients with LC does vary depending on the study chosen. According to a study by Pazhanivel and Jayanthi, 17.69% of patients with cirrhosis had DM.<sup>9</sup> The prevalence rate of DM among LC patients in the study conducted by Singal and Ayoola was 19.2%, and a higher prevalence rate (23.2%) was reported by Kobashi Margain et al.<sup>10,11</sup>

Pakistan is facing an enormous economic burden of morbidity and mortality associated with DM and LC, which have a limited health care system and resources. After failing to find any existing reliable statistics, we sought to estimate the frequency of DM in LC patients in our population. The objective of this study was to determine the frequency of diabetes mellitus in patients with biopsy proven liver cirrhosis. Our findings are expected to help the clinicians in anticipating and managing the problem in a timely manner to reduce the related morbidity and mortality.

## MATERIALS AND METHODS

This descriptive, cross-sectional study was conducted at the department of Medicine, Bahawal-Victoria Hospital, Bahawalpur, from August 2022 to February 2023. Non-probability, purposive sampling technique was adopted. A total of 240 patients of either gender aged 30-70 years having biopsy-proven LC were analyzed. Patients having known history DM and chronic kidney disease (CKD) were excluded. This study was commenced after getting approval from the "Institutional Ethical Review Board". All patients were briefed and asked for informed and written consents for participation in this study. A fasting blood sample of 5 ml venous blood of each patient was dispatched to the Central Diagnostic Laboratory of department of Pathology, Quaid-e-Azam Medical College, Bahawalpur for measurement of fasting blood glucose and HbA1c evaluation in the fasting state for confirmation about the presence or absence of DM. Diagnosis of DM was confirmed when there was fasting serum sugar above 126 mg/dL and HbA1c above 6.5% on two consecutive occasions with 12 hours apart. The data of the patients like age, gender, CLD cause, CLD duration, Child pugh class, place of living, body mass index (BMI) and family history of DM were recorded on a proforma designed for this study.

The data were entered and analyzed by using "Statistical Package for Social Sciences (SPSS)", version 26.0.

**Table No. 2: Stratification of Study Variables with respect to Presence of Diabetes Mellitus**

Study Variables		Diabetes Mellitus		P-value
		Yes (n=53)	No (n=187)	
Age (years)	30-50	35 (66.0%)	153 (81.8%)	0.0138
	51-70	18 (34.0%)	34 (18.2%)	
Gender	Male	32 (60.4%)	106 (67.5%)	0.6312
	Female	21 (39.6%)	81 (32.5%)	
BMI (kg/m <sup>2</sup> )	≤30	34 (64.2%)	114 (61.0%)	0.6735
	>30	19 (35.8%)	73 (39.0%)	
Residence	Rural	20 (37.7%)	94 (50.3%)	0.1068

Mean and standard deviation were calculated for age, CLD duration, weight, height, and BMI. We calculated frequencies & percentages for gender, Child Pugh Class (A, B, C), CLD cause (hepatitis-B, hepatitis-C, others), place of living (rural, urban), family history of DM (yes, no) and DM (present, absent). Chi-square test was employed to compare the categorical data. P-value ≤ 0.05 was considered significant.

## RESULTS

In a total of 240 patients with biopsy proven liver cirrhosis, 138 (57.5%) were male. The mean age and BMI were 42.87±9.67 years (30 to 70 years) and 27.62±4.25 kg/m<sup>2</sup> respectively. Family history of diabetes was present in 102 (42.5%) patients. Demographic and clinical characteristics of all patients are given in table-1.

**Table No. 1: Demographic and Clinical Characteristics (n=240)**

Characteristics	Frequency (%)	
Age (years)	30-50	188 (78.3%)
	51-70	52 (21.7%)
Gender	Male	138 (57.5%)
	Female	102 (42.5%)
BMI (kg/m <sup>2</sup> )	≤30	148 (61.7%)
	>30	92 (38.3%)
Residence	Rural	114 (47.5%)
	Urban	126 (52.5%)
Family History of Diabetes	102 (42.5%)	
Child Pugh Class	A	88 (36.7%)
	B	124 (51.7%)
	C	26 (10.8%)
Cause of Cirrhosis	Hepatitis-B	45 (18.8%)
	Hepatitis-C	62 (25.8%)
	Others	13 (5.4%)

The frequency of DM was noted in 53 (22.1%) biopsy-proven LC patients. Older age (51-70) was found to have significant association with the presence of DM (34.0% vs. 18.2%, p=0.0138). Increased liver disease severity (higher child pugh class) were noted to have significant association with the presence of DM (p=0.0445). The details about the comparison of study variables with respect to the presence of DM are shown in table-2.

	Urban	33 (62.3%)	93 (49.7%)	
Family History of Diabetes		25 (47.2%)	77 (41.2%)	0.4359
Child Pugh Class	A	12 (22.6%)	76 (40.6%)	0.0445
	B	33 (62.3%)	91 (48.7%)	
	C	8 (15.1%)	18 (9.6%)	
Cause of Cirrhosis	Hepatitis-B	13 (24.5%)	32 (17.1%)	0.2421
	Hepatitis-C	10 (18.9%)	52 (27.8%)	
	Others	2 (3.8%)	11 (5.9%)	

## DISCUSSION

Blood sugar levels are mainly regulated by the liver, which also breaks down insulin. The liver has a strong involvement to how chronic liver diseases start, progress, and affect the body. Hepatogenous DM is the name given to the DM associated with LC. Insulin resistance and beta-cell dysfunction have been postulated towards the pathophysiology of HD. There are clear signs and causes that make hepatogenous DM different from T2DM. Hepatogenous DM is likely in LC patients who have no history of DM or metabolic syndrome in themselves or their family. Currently, the scientific organizations remain skeptic over recognizing hepatogenous DM as a unique pathological entity and a consequence of CLD.<sup>12</sup>

The criteria for diagnosing DM in patients of LC differs in available studies and it may be a source of variations in reported prevalence of DM. When diagnosis of DM was based solely on clinical history (onset of DM after diagnosis of LC), the reported prevalence rates are found to be lower than our study.

In this study, the frequency of DM in biopsy proven LC was found to be 22.1%. Wang et al reported a 15.9% prevalence rate of DM in patients with LC and a prevalence rates of 29.2% has been reported by Ramachandran et al.<sup>13,14</sup> In the study conducted by Vasepalli et al, a prevalence rate of 21% was reported.<sup>12</sup> In another study, a prevalence rate of 57% was reported by Holstein et al when OGTT was used to establish diagnosis of DM.<sup>15</sup> Since the reported prevalence rates in the above-mentioned studies are higher, this highlights the importance of doing an OGTT to establish the diagnosis of DM in LC patients. The requirement for performing the OGTT is important because fasting blood glucose and HbA1c levels have been found erroneously low in reports from patients with LC. It has been reported that LC patients can have normal fasting FBG and HbA1c levels but their OGTT are deranged. It has been suggested that such patients are likely to be suffering from hepatogenous DM.<sup>16</sup> This may have an impact on the reported prevalence of our study. In reports where oral glucose tolerance test (OGTT) was used to diagnose DM, prevalence of hepatogenous DM was found to be generally higher than our study.<sup>15</sup>

The prevalence of DM in adult patients having LC was 31%, as reported in a systematic review of more than 50 studies. The prevalence of DM in LC patients has

been reported from 33.2 to 38.4% by the same systematic review.<sup>17</sup> In that review, highest cases of DM were found in patients with cryptogenic cirrhosis (51%) and NAFLD (56%). The patients of HCV related liver cirrhosis were having a 32.2% prevalence of DM and those with HBV cirrhosis had a 22.2% prevalence of DM. The prevalence of DM in LC is also likely to be affected by the severity of liver disease. In a prospective study, a group of researchers followed 100 patients who had compensated LC and normal blood sugar levels at the start of the study. They tested their blood sugar again after one year and four years using OGTT. They found that 4.4% of the patients had diabetes after one year and 21.2% had diabetes after four years.

In this study, we noted that the frequency of DM was significantly rising with increase in the disease severity of LC. Some researchers also looked at how many patients had DM based on their current CP class. They found that DM was more common in patients with worse LC. Out of the patients with mild LC (class A), 20.5% had DM. Out of the patients with moderate LC (class B), 56% had DM. And out of the patients with severe LC (class C), 61% had DM.<sup>18</sup> A report found that hepatogenous DM was very common among the patients in their study. More than half of the patients (57%) had HD. Most of the patients in the study (56%) had moderate or severe LC, as measured by the CP class. The higher the class, the worse the LC is.<sup>15</sup> Our study has also emphasized that patients with child pugh class C were more likely to have DM than child pugh class A and B.

Being a study from a single center and conducted on a relatively moderate sample size, our findings need further verifications in large multicentric trials. Healthcare practitioners need to be very vigilant in early detection and tracking of DM in LC patients.

## CONCLUSION

The prevalence of diabetes mellitus was high among patients with biopsy proven liver cirrhosis. Relatively older age, and increased disease severity with linked with significantly higher prevalence of diabetes mellitus in patients with biopsy proven liver cirrhosis.

### Author's Contribution:

Concept & Design of Study: Wajih-ur Rehman  
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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