

Frequency of hypoglycaemia and its impact on outcomes in patients with liver cirrhosis: A comprehensive study

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ABSTRACT

Objective: The study aimed to determine the incidence of hypoglycaemia among patients with liver cirrhosis, and to assess its impact on clinical outcomes such as mortality and in-hospital related complications.

Material and Methods: This study was a hospital-based prospective observational study. After obtaining ethical approval, it was carried out over a 4-month period in the Department of Internal Medicine at Jinnah Postgraduate Medical Centre (JPMC) in Karachi, Pakistan. Consecutive sampling was used to enroll 196 patients aged 18 to 65 years with a confirmed diagnosis of liver cirrhosis. Random blood glucose was tested at admission, and hypoglycaemia was defined as a blood glucose level <70 mg/dL. Other clinical variables were defined according to standardized criteria. SPSS 25 software was used for statistical analysis, and $p \leq 0.05$ was set as for statistical significance.

Results: The median age was 40.0 (IQR: 27.0–54.3) years, while mean blood glucose was 96.7 (SD: 25.4) mg/dL. Hypoglycaemia occurred in 72 (36.7%), shock in 55 (28.1%), and mortality in 39 (19.9%) patients. There were no differences between the number of patients who experienced shock in the hypo-glycaemic group (20/72, 27.8%) and the number of patients who did not experience shock (35/124, 28.2%) (Fisher's exact test $p=1.000$). Hypoglycaemia was not statistically significantly associated with gender, diabetes, hypertension or smoking status (all $p > 0.05$).

Conclusion: To sum up, hypoglycaemia is a common metabolic abnormality in patients with liver cirrhosis, but it cannot independently predict short-term adverse in-hospital outcomes.

Keywords: Hepatic, Hypoglycaemia, Liver cirrhosis, Liver failure, Mortality, Shock.

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INTRODUCTION

As the end-stage phase of chronic liver disease, liver cirrhosis is defined by core characteristics including progressive fibrosis, formation of regenerative nodules, and distortion of the liver's normal structure. One of the liver's core physiological functions is to maintain the body's blood glucose homeostasis via three key pathways: glycogen storage, glycogenolysis, and gluconeogenesis [1].

When liver function sustains progressive damage, these glucose metabolism pathways become impaired in sequence, triggering glucose regulation disorders such as hypoglycaemia [2]. Hypoglycaemia is an easily overlooked but critical complication in patients with liver cirrhosis. Previous studies have identified its triggers including depleted hepatic

glycogen reserves, impaired gluconeogenesis, insufficient oral intake, muscle wasting, and abnormal counterregulatory hormonal responses [3].

It also acts as a marker of severe hepatocyte damage and insufficient metabolic reserve, often indicating a poor prognosis [4]. Earlier clinical studies found that hospitalized patients with liver cirrhosis who experience hypoglycemic episodes have a significantly higher short-term mortality rate than those who do not develop hypoglycaemia; hypoglycaemia is an independent predictor of in-hospital death, infectious complications, and bacteraemia among the liver cirrhosis patient population [5].

Additional studies using continuous glucose monitoring have further confirmed that frequent hypoglycemic events in patients with chronic liver disease are associated with elevated risks of liver disease-related complications and disease progression [6]. For patients with liver cirrhosis who also have diabetes, the presence of complex metabolic disorders pushes their risks of severe hypoglycaemia and chances of mortality even higher [7]. However, the true incidence of hypoglycaemia in liver cirrhosis patients remains widely underreported,

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and this issue is particularly prominent in resource-limited regions [8].

Variations in disease severity, nutritional status, and monitoring practices across different studies lead to widely varying prevalence estimates. In addition, there is insufficient evidence to confirm the impact of hypoglycaemia on clinical outcomes including mortality, length of hospital stays, and complications [9]. Most existing data are derived from small cohorts or heterogeneous populations, so rigorously designed studies are urgently needed to clarify the relevant associations [10].

The majority of existing data on hypoglycaemia-related outcomes in liver cirrhosis comes from cohorts in other healthcare systems with different nutritional habits, liver disease profiles and metabolic properties. Patients with cirrhosis in Pakistan might be different in terms of late presentation, nutritional status, access to medical care, prevalence of diabetes mellitus, and management; all of which might affect the incidence and clinical importance of hypoglycaemia. Thus, there is a need for locally generated evidence to understand the burden of hypoglycaemia and association with short-term clinical outcomes among liver cirrhosis patients in Pakistan. The present study was conducted specifically to fill the aforementioned gaps, with core objectives to determine the incidence of hypoglycaemia among patients with liver cirrhosis, and to assess its impact on clinical outcomes such as mortality and in-hospital related complications.

MATERIAL AND METHODS

This was hospital-based prospective observational study that was conducted at the Department of Internal Medicine, Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan, over a period of four months, from 01 January 2026 to 30 April 2026, after obtaining the required approvals from the College of Physicians and Surgeons Pakistan (CPSP) and the Institutional Review Board (IRB) of JPMC. Ethical approval from the JPMC IRB was granted on 31 December 2025, under approval number F.2-81/2025-GENL/792/JPMC. Consecutive patients with liver cirrhosis were enrolled at admission and followed prospectively throughout their in-hospital stay for assessment of short-term outcomes including shock and mortality.

This study used the WHO sample size calculator to estimate the required sample size. It adopted the 48% incidence of hypoglycaemia among patients with liver cirrhosis, reported in a previous study by Khan *et al.*,¹¹ as the baseline parameter, set a 95%

confidence level and a 7% allowable margin of error, and finally confirmed the required sample size was 196. Participants were recruited via consecutive sampling. Inclusion criteria were of patients aged 18–65 years, regardless of gender, diagnosed with compensated or stable decompensated liver cirrhosis with a disease course of ≥ 6 months; who met at least 3 imaging features of liver cirrhosis on abdominal ultrasound; and who sought care at the emergency department or internal medicine ward with liver cirrhosis-related chief complaints including ascites, variceal bleeding, jaundice, and hepatic encephalopathy. Exclusion criteria were the patients that have complicated heart failure, advanced renal insufficiency, active infection, or malignant tumors; patients with severe decompensated liver cirrhosis requiring ICU admission; and individuals who refused to participate in the study. All participants signed written informed consent prior to data collection.

Demographic and clinical information was collected via a pre-established unified data form, and random blood glucose was measured at admission using a calibrated blood glucose meter. Hypoglycaemia was defined as random blood glucose level <70 mg/dl on admission. Diabetes mellitus was determined by a previous diagnosis of diabetes, the presence of glucose lowering medication, or a documented HbA1c level $\geq 6.5\%$. Hypertension was defined as prior history of hypertension or being on anti-hypertensive drugs. Smoking status was divided into current or former smokers, based on self-reported smoking history. Shock according to mean arterial pressure (MAP) criteria: $\text{MAP} = [\text{systolic blood pressure} + (2 \times \text{diastolic blood pressure})]/3$; $\text{MAP} < 65$ mmHg was deemed to be shock. Random blood glucose was measured in the first hour after admission to hospital, using a calibrated point of care glucose meter, prior to intravenous dextrose if clinically possible. The measurement was not pre-fasting since patient presentations were through emergency services. Where possible, details of recent insulin, oral hypoglycaemic and glucose administration before admission were recorded. All patients were managed per the standard protocols of our hospital, with a maximum follow-up period covering their in-hospital stay of up to 1 week. The primary outcomes were shock and death; both outcomes were paired with standardized definitions, and the formula for calculating mean arterial pressure used to define shock was also explicitly disclosed.

The Statistical Package for the Social Sciences (SPSS) version 25.0 was used to analyse the data. The quantitative variables, age, duration of cirrhosis,

blood glucose level, and length of hospital stay were measured and the distribution of each variable was tested with Shapiro–Wilk test. Quantitative variables were expressed in a tabular summary as either Mean (SD) or Median (IQR), depending on whether the variable was normally distributed or not, respectively. Blood glucose level, therefore, was reported as Mean (SD) and age, duration of cirrhosis and length of hospital stay were reported as Median (IQR). Categorical variables such as gender, residence, hypertension, diabetes mellitus, smoking status, hypoglycaemia, shock and mortality were summarized as frequencies and percentages, n (%). Fisher's exact test was used to assess the associations with hypoglycaemia and shock and mortality. Association of hypoglycaemia with gender, diabetes mellitus, hypertension and smoking status was determined by using chi-square test with Yates continuity correction. All the tests were two-sided and a p-value of ≤ 0.05 was regarded as statistically significant.

RESULTS

All enrolled 196 participants were included in the final analysis. (Table-I) Demographic and clinical data at baseline are summarised as quantitative variables

presented according to their distribution, and as frequencies and percentages for categorical variables. Follow-up data were collected on clinical outcomes (hypoglycaemia, shock and in-hospital mortality). The association between hypoglycaemia and shock is presented in Table-II. The distribution of shock was nearly identical between patients with and without hypoglycaemia. Statistical testing demonstrated no significant association between hypoglycaemia and the occurrence of shock.

The association of hypoglycaemia with in-hospital death is summarised in Table-III. Mortality rates were evenly distributed between the two groups (hypoglycaemic and non-hypoglycaemic). Hypoglycaemia was not associated with an increased chance of death in hospital. Observed data were therefore in no way supportive of a relationship between hypoglycaemia status and death in hospital. Table-IV shows the relationship of hypoglycaemia with demographic and clinical features. No statistically significant differences were found between the groups in terms of the proportion of hypoglycaemia, with diabetes mellitus, hypertension, and smoking status groups all having a similar proportion.

Table-I: Baseline demographic and clinical characteristics of patients with liver cirrhosis (n=196)

Variable	Value
Age (years), Median (IQR)	40.0 (27.0–54.3)
Duration of cirrhosis (months), Median (IQR)	60.5 (31.0–92.0)
Blood glucose (mg/dL), Mean (SD)	96.7 (25.4)
Hospital stay (days), Median (IQR)	4.0 (2.0–6.0)
Male, n (%)	119 (60.7)
Female, n (%)	77 (39.3)
Urban residence, n (%)	104 (53.1)
Rural residence, n (%)	92 (46.9)
Hypertension, n (%)	66 (33.7)
Diabetes mellitus, n (%)	78 (39.8)
Smoking, n (%)	68 (34.7)
Hypoglycaemia, n (%)	72 (36.7)
Shock, n (%)	55 (28.1)
Mortality, n (%)	39 (19.9)

Note: Normality of quantitative variables was assessed using the Shapiro–Wilk test. Normally distributed quantitative variables are presented as Mean (SD), non-normally distributed quantitative variables as Median (IQR), and categorical variables as n (%).

Table-II: Association between hypoglycaemia and shock among patients with liver cirrhosis (n=196).

Hypoglycaemia	Shock present, n (%)	Shock absent, n (%)	Total, n	p-value*
Yes	20 (27.8)	52 (72.2)	72	
No	35 (28.2)	89 (71.8)	124	
Total	55 (28.1)	141 (71.9)	196	1.000

*Fisher's exact test. A p-value ≤ 0.05 was considered statistically significant.

Table-III. Association between hypoglycaemia and in-hospital mortality among patients with liver cirrhosis (n=196)

Hypoglycaemia	Mortality present, n (%)	Mortality absent, n (%)	Total, n	p-value*
Yes	13 (18.1)	59 (81.9)	72	
No	26 (21.0)	98 (79.0)	124	
Total	39 (19.9)	157 (80.1)	196	0.712

*Fisher's exact test. A p-value ≤ 0.05 was considered statistically significant.

Table-IV. Stratification of hypoglycaemia according to demographic and clinical characteristics (n=196)

Variable	Hypoglycaemia present, n (%)	Hypoglycaemia absent, n (%)	p-value*
Gender			0.398
Male (n=119)	47 (39.5)	72 (60.5)	
Female (n=77)	25 (32.5)	52 (67.5)	
Diabetes mellitus			0.963
Yes (n=78)	28 (35.9)	50 (64.1)	
No (n=118)	44 (37.3)	74 (62.7)	
Hypertension			1.000
Yes (n=66)	24 (36.4)	42 (63.6)	
No (n=130)	48 (36.9)	82 (63.1)	
Smoking			0.433
Yes (n=68)	28 (41.2)	40 (58.8)	
No (n=128)	44 (34.4)	84 (65.6)	

*Chi-square test with Yates continuity correction. A p-value ≤ 0.05 was considered statistically significant.

DISCUSSION

The objectives of this study were to determine the prevalence of hypoglycaemia and to investigate the association with short-term clinical outcomes in patients with liver cirrhosis. Within this group the incidence of hypoglycaemia was 72 (36.7%) patients, shock was 55 (28.1%) patients and in-hospital mortality were 39 (19.9%) patients. Likewise, no association was found between demographics and clinical parameters and hypoglycaemia, such as smoking status, diabetes mellitus, gender, or hypertension. These results suggest that in this study population, a single admission glucose level was not linked to short-term adverse events in liver cirrhosis patients [11].

Severe hypoglycaemic episodes have been shown to be very common in high-risk subgroups, including liver cirrhosis in the presence of diabetes mellitus by Yen *et al* [12]. This is clinically significant for the current group where almost one in four patients also had a diagnosis of diabetes. But our study did not show a strong link between hypoglycaemia and short-term outcomes, which might be due to variations in the characteristics of the patients, disease severity and methods used. Del Cioppo *et al*. [13] proposed that the strong parameters of hepatic decompensation—not just single metabolic abnormalities—are better predictors of mortality. Besides, Waqar *et al*. [14] emphasized that the clinical and disease course of liver cirrhosis is diverse in Pakistan, and such diversity can result in differences in the prognosis of liver cirrhosis among various populations.

Earlier studies have revealed that metabolic disorders often occur simultaneously with advanced liver disease. Azam *et al*. [15] found that hyponatremia was common in hospitalized patients with cirrhosis and proposed that several systemic abnormalities could affect clinical outcomes and mask the effect of individual metabolic abnormalities. Measurement of

hypoglycaemia in this context could be one of the components of metabolic dysfunction, and not the only factor determining prognosis. In addition, Morales-Galacia *et al*. [16] noted that liver disease is a systemic metabolic disorder in which the impaired glucose regulation is an important physiological consequence. Thus, the results of this study are consistent with the hypothesis that the prognostic relevance of hypoglycaemia should not be evaluated solely with the effects of the other indicators of severity.

The results are also in line with the knowledge that prognosis in liver cirrhosis depends upon several factors which interact with each other. D'Amico *et al*. [17] suggested a multidimensional approach to evaluate decompensated cirrhosis with a focus on severity and multiple clinical complications that are important for outcome. In a similar way, Akhtar *et al*. [18] showed that prognosis in chronic liver disease patients is dependent on a range of precipitating factors, such as complications as hepatic encephalopathy and not a single metabolic abnormality. These findings lend support to the possibility that hypoglycaemia may represent a measure of metabolic disturbance, but on its own may not be predictive of short-term outcomes, without accounting for additional clinical parameters [19].

The high frequency of hypoglycaemia in the present study was confirmed by Sohail *et al*. [19] who reported that hypoglycaemia was a common complication in patients with chronic liver disease. Furthermore, Soon and Torbenson [20] have studied hepatic glycogen metabolism and found biological evidence for the incidence of glucose regulation abnormalities in cirrhosis. Hypoglycaemia is common in patients with severe liver disease, and may be due to impaired glycogen storage and decreased gluconeogenic capacity.

In this study, the authors deliver local evidence of the burden of hypoglycaemia and the association between short-term outcomes and hypoglycaemia in patients with liver cirrhosis in a tertiary care setting. The biggest advantage of this study is the systematic evaluation of hypoglycaemia, shock and in-hospital mortality in 196 patients. Moreover, the assessment of relevant clinical features, such as diabetes mellitus, hypertension and smoking group, makes the observations more relevant to the clinical practice.

LIMITATIONS

There are a few limitations to be considered. The single centre observational design restricts generalizability of the study to other health care settings and cannot allow for causal inference. In addition, key confounding factors such as liver severity scores (Child-Pugh and MELD), nutrition status, infection status and medication exposures were not adequately adjusted for in analyses. In particular, there were no standardized cirrhosis severity scoring systems to enable the assessment of whether there was an independent prognostic value for hypoglycaemia when the severity of underlying liver disease was considered. Moreover, the measurement of glucose was made only once, not every moment, and that might have led to under-diagnosing transient or recurrent hypoglycaemic events. Standardized liver severity scores (Child-Pugh and MELD scores) and infection parameters, nutritional status, history of medication and continuous glucose monitoring should be incorporated into future multicentre prospective studies with larger and more diverse patient cohorts to better define its independent prognostic influence of hypoglycaemia. From a clinical point of view, early recognition and surveillance of hypoglycaemia are continued to be important, especially in people with advanced liver disease or other metabolic risk factors.

CONCLUSION

In this study, liver cirrhotic patients had a common metabolic abnormality, hypoglycaemia, which was not significantly associated with in-hospital mortality or shock. The results of these findings indicate that a single glucose level at admission could be a predictor of poor short-term outcomes with only limited power. However, the prognostic value of hypoglycaemia needs to be assessed in more extensive studies which account for the severity of cirrhosis by using Child-Pugh and MELD scores, as well as continuous

monitoring of glucose variability, in prospective studies.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Aamir: Drafting the manuscript, acquisition, analysis, and interpretation of data. Critical review, literature search. Statistical review, critical review and discussion, final approval, responsible for every aspect of the research.

Zeeshan Ali: Conception, data collection, formal Analysis, investigation, and resources, final approval, responsible for every aspect of the research

Shayan Rehmani: Result analysis, review, final approval, responsible for every aspect of the research

Sameeullah: Drafting, designing the study content, review, writing, and editing, final approval, responsible for every aspect of the research

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