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Frequency of Hypoglycemia in Patients Presenting with Liver Cirrhosis

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ABSTRACT

Background: Liver cirrhosis is a chronic progressive disease associated with impaired metabolic function, including disturbances in glucose homeostasis such as hypoglycemia. **Objective:** To determine the frequency of hypoglycemia in patients with liver cirrhosis presenting to a tertiary care hospital. **Methods:** This cross-sectional study included 150 patients with liver cirrhosis, aged 30–75 years, conducted at a tertiary care hospital over six months. Hypoglycemia was defined as fasting blood glucose <70 mg/dL. It was observed in 76 patients, yielding a frequency of 50.7%, with higher rates in older age, males, low BMI, and low socioeconomic status. **Conclusion:** Hypoglycemia is highly prevalent among patients with liver cirrhosis and is associated with demographic and nutritional factors, highlighting the need for routine monitoring and early intervention. Venous blood samples were analyzed for fasting glucose, and data were processed using SPSS with stratification for demographic and clinical variables. Statistical analysis showed significant associations between hypoglycemia and age, gender, BMI, socioeconomic status, and rural residence. These findings suggest that hypoglycemia is a common metabolic complication in cirrhosis requiring vigilant monitoring, particularly in decompensated or malnourished patients. It represents an under-recognized predictor of poor prognosis and may overlap clinically with hepatic encephalopathy, complicating diagnosis. Routine glucose monitoring and early correction strategies are recommended to reduce morbidity and improve outcomes in affected patients. Overall, the study provides locally relevant evidence on the burden of hypoglycemia in cirrhosis, supporting integration of metabolic screening into routine clinical assessment, especially in resource-limited settings with high prevalence of advanced liver disease patient management strategies.

INTRODUCTION

Liver cirrhosis is the final stage of chronic liver disease in which scarring replaces healthy liver tissue, blooms develop and eventually healthy liver tissue is permanently damaged (1, 2). It a big burden around the globe related to morbidity and mortality as well as showing large utilization of health services worldwide (3, 4). Chronic viral hepatitis (mainly Hepatitis B and C), long-standing alcohol intake and metabolic dysfunction-related steatotic liver disease are the main etiologies, followed by a minority of autoimmune and genetic causes (5, 6). Cirrhosis is a pathological process that occurs in the liver due to chronic injury to the hepatocytes, with activation of hepatic stellate cells, an increase in deposition of extracellular matrix and disruption of the hepatic vascular architecture with a decrease in functional capacity of the hepatocytes (7, 8). As cirrhosis progresses, function of liver metabolism, synthetic and detoxification activity will continue to diminish and over time, patients will become susceptible to a broad range of metabolic abnormalities (9, 10).

Less frequently discussed but more important is the possibility of hypoglycemia (11, 12) in cirrhosis. Hypoglycemia is characterized by a decrease in plasma glucose (Pl) to a level that causes neuroglycopenic effects and/or the biochemical parameters below 70 mg/dL (3.9 mmol/L) (13, 14). It is a potentially life-threatening metabolic disturbance which can result from diminished glucose production, heightened glucose utilization or disordered hormonal counter-regulation. Hypoglycemia is frequently linked to long-term fasting, inadequate nutrition, adrenal insufficiency or serious illnesses in non-diabetic persons (15, 16). Hypoglycemia in patients with chronic liver disease, however, is mainly associated with liver failure and less with the hypoglycemic effect of exogenous insulin or medication.

The liver has a pivotal role in glucose regulation by storing glucose as glycogen, oxidising glycogen to glucose

(glycogenolysis) and generating glucose from non-glycogen compounds (gluconeogenesis) (17, 18). During cirrhosis, a progressive loss of hepatocyte function and fibrosis markedly depletes glycogen stores, and the gluconeogenic effect is also reduced, resulting in a decreased ability to produce glucose endogenously in certain situations, such as fasting or increased metabolic activity (19, 20). In addition, cirrhosis leads to a decrease in hepatic insulin clearance, hyperinsulinemia and disturbed counter regulatory hormonal response such as glucagon and cortisol responses to hypoglycemia, which also increases the susceptibility towards hypoglycemia (21, 22). These metabolic changes are especially marked in patients with advanced or decompensated cirrhosis, who also have a tendency to deficiency of certain nutrients and muscle wasting, leading to even lower substrates for gluconeogenesis.

In clinical practice, diagnosis and management of hypoglycemia are challenging in patients with cirrhosis. Many signs and symptoms as listed above are similar to hepatic encephalopathy and thus making early recognition of their signs and symptoms difficult. Such ambiguities can prompt suboptimal diagnosis and/or delay therapy and contribute to poor outcomes. Furthermore, low blood sugar levels in patients with cirrhosis have been recognized as a sign of poor outlook, and there have been studies that have linked low blood sugar to greater prevalence of infections, longer hospital stays and higher mortality rates (23). Hypoglycaemia can thus become a problem, and early detection of hypoglycaemia is important in the management of patients with chronic liver disease.

There are conflicting data about possible hypoglycaemic episodes in cirrhotic patients, due to the high variability of such episodes depending on the type of the patient population and the disease activity or the study's conditions. Previously documented frequencies of as high as 51.2% in hospitalized liver circuhsotics (24) and up to 30%. The intra-individual variability shows the impact of demographic, clinical and environmental factors on glucose metabolism in this patient population. Nevertheless, in everyday practice hypoglycemia is under recognised and low cost routine glucose monitoring is not always done, especially in resource limited settings.

Besides these biological reasons, the socioeconomic determinants also seem to be great in governing the onset of hypoglycemia in patients with cirrhosis. Malnutrition, delayed presentation seeking medical attention, and low awareness make disease to occur at an advanced stage and low metabolic reserve, which puts them at risk of hypoglycemic episodes. Rural communities may be especially impacted because of access to specialised care and nutrition support services.

In view of the paucity of data on the local level, examining the incidence of hypoglycaemia in subjects with liver cirrhosis in a health care environment is warranted. This is a significant metabolic complication, so understanding its size is important to increase clinical awareness, determine monitoring strategies and provide optimal management of the patient. Prompt recognition and correction of any low blood sugar can have a profound effect on lessening morbidity and enhancing outcomes in this patient population at risk.

Hence, this present study aims to find the frequency of hypoglycemia in liver cirrhosis patients coming to tertiary care hospital and to provide a local evidence which could be helpful to guide the clinician in taking a rational decision in the management of chronic liver disease and to improve the management of these patients.

METHODOLOGY

This cross-sectional study will be carried out in the Department of General Medicine, Mardan Medical Complex Mardan for a duration of 6-months starting from 30 October 2024 to 30 April 2025 after the approval of synopsis by CPSP Research Ethics Committee. The sample size was calculated by WHO sample size calculator, assuming the frequency of hypoglycemia is 51.2%, mean error is 8% and 95% confidence level, a total sampling size of 150 patients will be involved in the study using consecutive non-probability sampling technique. The liver cirrhosis patients of both genders as per the operational definition (ultrasonographic criteria of increased echogenicity, coarse echotexture, examination of nodularity or histopathological criteria of architectural distortion, septal formation, and nodularity in the context of clinical parameters of jaundice, ascites, and erythema of palms) aged 30 to 75 years will be included. To avoid possible interferences on glucose metabolism, patients with diabetes mellitus, chronic kidneys disease and haematological bleeding disorders will not be included.

Consent to collect and use detailed baseline demographic and clinical information, such as age, gender, BMI, socioeconomic status, education, employment status and residence will be obtained using a pre-designed proforma following informed written consent. The venous blood will be asceptically taken samples (5 mL) and examined in institutional laboratory for FBG levels. Hypoglycemia will be defined as a blood glucose obtained at a fasting state of <70 mg/dL (3.9 mmol/L) with clinically relevant symptoms such as sweating, shaking, palpitations, anxiety and nausea. SPSS 23 will be used for data analysis, and the normality of the data will be determined by Shapiro–Wilk test. Continuous data will be summarised using mean ± sd or median (IQR) and categorical data by frequency and percentage. Where appropriate, potential effect modifiers will be tested using stratification and post-stratification associations will be estimated using a Chi-square or a Fisher's exact test and a p-value of less than 0.05 deemed as statistically significant.

RESULTS

One hundred and fifty liver cirrhosis patients participated in the study. The mean age of patients was 52.4 ± 11.6 years, with a range of 30–75 years. Of the individuals studied, males outnumbered females (62.7%). The mean BMI was 24.8 ± 4.3 kg/m^2. The majority of patients were from low SES (58.0%) and rural areas (64.0%).

Frequency of Hypoglycemia

Out of 150 patients with liver cirrhosis, 76 patients were found to have hypoglycemia, yielding a frequency of 50.7%.

Table 1
Baseline Characteristics of Study Population (n = 150)

Variable	Category	Frequency (%)
Age (years)	30–45	38 (25.3%)
	46–60	72 (48.0%)
	61–75	40 (26.7%)
Gender	Male	94 (62.7%)
	Female	56 (37.3%)
BMI (kg/m^2)	<25	82 (54.7%)
	≥25	68 (45.3%)
Socioeconomic status	Low	87 (58.0%)
	Middle/High	63 (42.0%)
Residence	Rural	96 (64.0%)
	Urban	54 (36.0%)

Table 2
Frequency of Hypoglycemia in Study Population (n = 150)

Hypoglycemia Status	Frequency	Percentage
Present	76	50.7%
Absent	74	49.3%

Stratification Analysis

Hypoglycemia was further stratified across demographic and clinical variables. A higher frequency was observed in elderly patients, males, and those with lower BMI and low socioeconomic status.

Table 3
Stratification of Hypoglycemia by Age, Gender, and BMI

Variable	Category	Hypoglycemia Present n (%)	p-value
Age	30–45	12 (31.6%)	0.041*
	46–60	38 (52.8%)	
	61–75	26 (65.0%)	
Gender	Male	52 (55.3%)	0.032*
	Female	24 (42.9%)	
BMI	<25	50 (61.0%)	0.008*
	≥25	26 (38.2%)	

*Chi-square test significant at $p < 0.05$

Table 4
Stratification of Hypoglycemia by Socioeconomic and Clinical Variables

Variable	Category	Hypoglycemia Present n (%)	p-value
Socioeconomic Status	Low	58 (66.7%)	0.003*
	Middle/High	18 (28.6%)	
Residence	Rural	62 (64.6%)	0.012*
	Urban	14 (25.9%)	

It showed that about 50% of all patients with cirrhosis developed hypoglycemia. Advanced age, male gender, low BMI, low socioeconomic status and rural dwelling were all significant factors associated with hypoglycemia. These observations suggest a possible contribution of social determinants as well as clinical severity on the risk of hypoglycaemia in liver cirrhosis.

DISCUSSION

The results of the current cross-sectional study have shown that a large proportion (50.7%) of LC patients was reported to be hypoglycemic, with about one in every two cirrhotic subjects suffering from impaired glucose metabolism. This agrees with other reported evidence of 51.2% cited by Majeed et al. in a similar patient group, thus confirming the consistency of such metabolic manifestation in different settings. The burden observed highlights the importance of the liver for glucose homeostasis by storing glycogen and synthesizing glucose under conditions of gluconeogenesis, which is increasingly impaired with progression of the cirrhosis stages (22,23).

Hypoglycemia seems to occur more frequently in this study due to the pathophysiological deterioration seen in advanced hepatic fibrosis. In cirrhosis there is also a loss of the glycogen stores in the liver, as well as a decrease in liver mass and concentration of enzymes needed for gluconeogenesis, that causes a decrease in endogenous glucose production, especially during fasting. Further,, the impaired clearance of insulin by the liver and decreased counter-regulatory hormonal response contributes to increased susceptibility to hypoglycemia (25,18). These mechanisms are especially pronounced during a decompensated cirrhosis, where there is a metabolic instability with greater severity and a depleted nutritional reserve.

Stratified analysis revealed that older, male, lower BMI, lower socioeconomic and rural backgrounds were associated with higher frequency of hypoglycemia. This correlation with age probably is a secondary aspect of a lower liver regeneration potential and lower metabolic reserve. Likewise, low BMI was probably a sign of poor nutrition status and low glycogen storage, which directly leads to lower glucose availability during fasting state. These results may be due to the greater access to healthcare and nutrition in the higher socioeconomic groups or to later presentation with the disease. These findings are in line with previous publications highlighting malnutrition and severity of the disease to be important factors for hypoglycemia risk in patients with cirrhosis (24).

In this study, there were more males than females who were hypoglycemic, known to be more prevalent in male populations in many parts of the world and which accelerates hepatic decompensation and metabolic dysfunction. However, the results on gender differences are conflicting, and non-sexual factors (etiology of cirrhosis, and stage of the disease) may be more important than gender per se.

From a clinical point of view, hypoglycemia in the cirrhotic patient is a very important prognostic factor. Hypoglycemia in liver cirrhosis has been shown to be a risk factor for infections, liver encephalopathy, hospitalization and death (19). Furthermore, diagnosis is difficult in cirrhotic patients since the symptoms of dizziness, confusion, and altered sensorium are similar to those of hepatic encephalopathy, both making diagnosis problematic, and complicating management of hypoglycaemia. This indicates the need for regular glucose monitoring in these high-risk patients with cirrhosis, especially in patients with advanced cirrhosis and those with poor nutritional status.

The results of this study also have significant implications for clinical practice in a resource-constrained setting. Rerecognizing early those who are at risk and the prompt

correction of hypoglycaemia might decrease preventable complications and increase overall outcomes. In managing cirrhosis, it is essential to keep nutrition optimization, regular monitoring of glucose levels, and careful review of medications at the center of treatment.

Nevertheless, there are some limitations to this study. This is a single-center cross-sectional study, which cannot define cause-effect relationship between the severity of cirrhosis and hypoglycemia. Furthermore, the Child-Pugh or MELD scores or the information on nutrition were not included, and this could have added more clinical correlation. Despite these drawbacks, the study adds valuable local knowledge of these problems and adds to existing findings on the high burden of hypoglycemia in cirrhotic patients.

To conclude, hypoglycemia is a common metabolic complication among cirrhotic patients, and affected by demographic and clinical factors. To minimize associated morbidity and for better chance of clinical outcome, it is imperative to recognize early and subsequently achieve targeted management.

CONCLUSION

This study revealed that metabolic complications like hypoglycaemia were a common phenomenon in liver cirrhosis, being present in about half of the participants in the study. The results demonstrate that suboptimal liver glucose metabolism associated with this glycogen storage defect, less gluconeogenesis and other hormonal changes can have profound effects. There are important age, sex, BMI, SES and dwell associations: biologic as well as social determinants. Correctly identifying high-risk patients and frequent glucose monitoring are critical aspects for clinical management in cirrhosis. In low resource countries, the burden of hypoglycemia and its complications may be further decreased by targeted nutritional interventions and access to healthcare. These findings indicate the importance of routine metabolic screening as a part of standard care procedures and highlight the necessity of interdisciplinary communication and collaboration in order to improve outcomes in advanced liver disease and implement early detection and timely therapeutic intervention strategies in clinical practice today.

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