

# Hypoglycemia in patients presenting with Liver Cirrhosis

ATIF MAJEED<sup>1</sup>, MUHAMMAD YASIR ARAFAT<sup>2</sup>, IMRAN ALI<sup>3</sup>, ATIF MAQSOOD<sup>4</sup>

## ABSTRACT

**Background:** Due to liver cirrhosis, gastrointestinal functions of human body also disturbed and leads to the occurrence of other comorbidities. Hypoglycemia is one of the rising complications of cirrhosis. So we planned this study to find the variation in blood sugar level in patients of cirrhosis.

**Aim:** To assess the frequency of hypoglycemia in patients with liver cirrhosis

**Study design:** Cross sectional study.

**Setting & duration:** Department of Medicine, Mayo Hospital, Lahore, six months duration

**Methodology:** Eighty four cases of cirrhosis were selected through OPD. Blood sample was obtained and BSR was tested and hypoglycemia was noted. SPSS v.20 was used to analyse the data. Frequency and percentage was calculated for hypoglycemia.

**Results:** The mean age of the patients was 44.39±17.06 years. There were 61.9% males and 38.1% females. Mean duration of cirrhosis was 2.61±1.47 years. Child-Pugh grade A was noticed in 34.5%, grade B in 29.8% and grade C in 35.7%. The mean blood sugar level 88.50±37.68mg/dl. Hypoglycemia was present in 51.2% cases. Hyponatremia was present in 51.7% Child-Pugh class A, 56% in Child-Pugh class B and 46.7% in Child-Pugh class C. The difference was insignificant (P>0.05).

**Conclusion:** The frequency of hypoglycemia in cirrhotic patients was high and not negligible.

**Keywords:** Chronic liver disease, Hypoglycemia, blood sugar level

---

## INTRODUCTION

Liver plays an important part in homeostasis of glucose in blood. Dysfunction of liver in metabolism, structure or intra-cellular functioning may change the ability of liver to sustain normal glucose homeostasis. When these dysfunction changes liver glucose secretion, hypoglycemia occurs. Various drugs including alcohol might change the functioning of liver, which are essential for normal excretion of glucose through liver. Impulsive hypoglycemia is a sign to examine liver functioning and a cautious inspection of drugs and medications which cause these dysfunction or bio-chemical integrity<sup>1</sup>.

Liver cirrhosis might be one of the major cause of mortality in different areas worldwide<sup>2,3</sup>. Hepatitis C or B virus, substantial alcohol ingesting & non-alcoholic fatty liver disease, are the major risk factors of liver cirrhosis<sup>4</sup>. Cirrhosis can cause marginal hyperinsulinemia because of reduced insulin clearance. Spontaneous hypo-glycaemia in cirrhotic patients characterizes an investigative encounter because of co-existing hyperinsulinemia<sup>5</sup>.

The liver has an essential role in metabolism of carbohydrate subsequently it maintains the quantity of glucose in blood through glycogenogenesis & glycogenolysis<sup>6,7</sup>. A decreased reaction of islet β-

cells of pancreas & insulin resistance in liver are also influential factors<sup>8,9</sup>. Insulin resistance causes high risk for the failure of treatment response in cirrhotic patients and trigger evolution of cirrhosis to fibrosis<sup>10</sup>.<sup>11</sup> About 96% of cirrhotic patients may have impaired glucose level while 30% may clinically diagnosed as diabetic<sup>10,12,13</sup>.

Hypoglycemia has several factors including liver cirrhosis, because liver has main role in glucose secretion and maintenance of blood glucose levels<sup>14,15</sup>. The prevalence of hypoglycemia is reported as 58% in patients of liver cirrhosis<sup>16</sup>.

The objective of the study was to assess the frequency of hypoglycemia in patients of liver cirrhosis.

## MATERIAL AND METHODS

This cross sectional study was conducted in the Department of Medicine, Mayo Hospital, Lahore from Oct 2016 to Oct 2017. Eighty four cases were calculated with 95% confidence level, 5% margin of error and taking hypoglycemia percentage i.e., 58% in patients of cirrhosis. Simple random sampling technique was used. Patients aged 16–75 years of either gender with liver cirrhosis were included. Patients diagnosed with diabetes before cirrhosis (HbA1c>7% and patient taking antidiabetic medicine).

Eighty four patients fulfilling the selection criteria were selected through OPD. Informed consent was

---

<sup>1</sup>PGR Medicine, Services Hospital, Lahore

<sup>2</sup>MO, DHQ Hospital Sheikhupura

<sup>3</sup>MO BHU Chak 16 Tehsil Malakwal Distt. Mandibahaudin

<sup>4</sup>Assistant Professor Medicine, Aziz Fatimah Medical and Dental College, Faisalabad.

Correspondence to Dr. Atif Majeed

Email: dratifchaudhary@gmail.com Cell: 0321-4208083

obtained. Demographics were also recorded. Then blood sample will be obtained by pricking middle finger of patient. Blood drop will be obtained on glucometer and sugar level will be noted. If sugar level  $\leq 70$ mg/dl then hypoglycemia was labeled. Patients with hypoglycemia were managed as per hospital protocol. The collected information was analyzed through SPSS 21. For age, duration of cirrhosis and BSR, mean  $\pm$ SD were calculated. Frequency and percentage was calculated for sex, Child-Pugh class and hypoglycemia. Hypoglycemia was compared with Child-Pugh class and chi square test was applied. P-value  $\leq 0.05$  was considered as significant.

**RESULTS**

The mean age of the patients was  $44.39 \pm 17.06$  years. There were 61.9% males and 38.1% females. Mean duration of liver cirrhosis was  $2.61 \pm 1.47$  years. Child-Pugh grade A was noticed in 34.5%, grade B in 29.8% and grade C in 35.7%. The mean blood sugar level  $88.50 \pm 37.68$ mg/dl (Table 1) Hyponatremia was present in 51.2% cases (Fig 1).

With Child-Pugh class A, hyponatremia was present in 15 (51.7%) patients, in Child-Pugh class B, hyponatremia was present in 14 (56.0%) patients and in Child-Pugh class C, hyponatremia was present in 14 (46.7%) patients. The difference was insignificant ( $P > 0.05$ ). (Table 2)

Table 1: Characteristics of patients

n	84
Age (Years)	$44.39 \pm 17.06$
Gender (m/f)	52(61.9%) / 32(38.1%)
Duration of cirrhosis	$2.61 \pm 1.47$
Child-Pugh classification	
A	29(34.5%)
B	25(29.8%)
C	30(35.7%)
Blood sugar level	$88.50 \pm 37.68$

Fig 1: Distribution of hypoglycemia

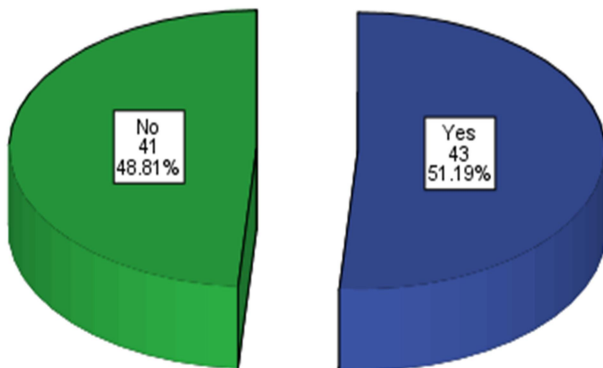


Table 2: Comparison of hypoglycemia in Child-Pugh class

Grades	Hypoglycemia	
	Yes	No
A	15 (51.7%)	14 (48.3%)
B	14 (56.0%)	11 (44.0%)
C	14 (46.7%)	16 (53.3%)
Total	43 (51.2%)	41 (48.8%)

p = 0.786 (Insignificant)

**DISCUSSION**

CLD including cirrhosis, is regarded for several metabolic changes, mainly catabolic, causing malnutrition including cachexia in few cases<sup>17,18</sup>. The obligation of liver function in management of carbohydrate homeostasis is important in considering the many physical & bio-chemical changes which happen in liver in presence of diabetes and to consider how hepatic disease can alter glucose breakdown<sup>19,20</sup>.

Usually, patients with liver cirrhosis have evident glucose intoleranc categorized as hyper-insulinemia, hyper-glucagonemia, insulin resistance & down-regulation of insulin receptors. However, hyper-insulinemia is maybe caused by declined liver regulation of insulin, hyper-glucagonemia is predominantly because of elevated pancreatic discharge<sup>21,22</sup>.

Numerous trials proposed that elevated glycemic level in blood of cirrhotic patients has high risk of further destruction of liver and high mortality rate.<sup>23</sup> In our study, we included 84 patients of liver cirrhosis, with the mean age of  $44.39 \pm 17.06$  years. There were 61.9% males and 38.1% females. Mean duration of liver cirrhosis was  $2.61 \pm 1.47$  years. Child-Pugh grade A was noticed in 34.5%, grade B in 29.8% and grade C in 35.7%. The mean blood sugar level  $88.50 \pm 37.68$ mg/dl. Hyponatremia was present in 51.2% cases. Tanveer et al., found the prevalence of hypoglycemia is 58% in patients of liver cirrhosis.<sup>16</sup> Singh et al., found the frequency of hypoglycemia in 67% patients who had liver cirrhosis<sup>24</sup>. Nouel et al., observed hypoglycemia in 50% patients with liver cirrhosis<sup>25</sup>.

In our study, hyponatremia was present in 15(51.7%) patients with Child-Pugh class A, 14(56%) patients in with Child-Pugh class B and in 14(46.7%) patients with Child-Pugh class C. The difference was insignificant ( $P > 0.05$ ). However, Singh et al., reported significant difference for hyponatremia in different grades of cirrhosis i.e. in Child-Pugh class A = 23.9%, in Child-Pugh class B = 44.8% and in Child-Pugh class C = 31.3%,  $p = 0.02$ <sup>24</sup>.

## CONCLUSION

Thus it has been concluded that hypoglycemia was present in almost half of cirrhotic patients. Now, on the basis of these results, we recommend the regular screening of blood sugar level in cirrhotic patients to prevent hypoglycemia which may cause perilous consequences.

## REFERENCES

1. Arky R. Hypoglycemia associated with liver disease and ethanol. *Endocrinology and metabolism clinics of North America* 1989;18(1):75-90.
2. Kim W, Brown RS, Terrault NA, El-Serag H. Burden of liver disease in the United States: summary of a workshop. *Hepatology* 2002;36(1):227-42.
3. Vilstrup H, Amodio P, Bajaj J, Cordoba J, Ferenci P, Mullen KD, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. *Hepatology* 2014;60(2):715-35.
4. Lazo M, Hernaez R, Eberhardt MS, Bonekamp S, Kamel I, Guallar E, et al. Prevalence of nonalcoholic fatty liver disease in the United States: the Third National Health and Nutrition Examination Survey, 1988–1994. *American journal of epidemiology* 2013;178(1):38-45.
5. Alkabbani A, Gorodeski-Baskin R, Hamaty M. A Diagnostic Dilemma of Hypoglycemia in End-Stage Liver Disease: Is It an Insulinoma? *Diabetes & Insulin Resistance Case Reports: Unusual Diagnostic Considerations & Rare Birds (Clinical)*: The Endocrine Society; 2012. p. MON-169-MON-.
6. Williams K, Shackel N, Gorrell M, McLennan S, Twigg S. Diabetes and nonalcoholic fatty liver disease: a pathogenic duo. *Endocrine reviews* 2012;34(1):84-129.
7. Krishnan B, Babu S, Walker J, Walker AB, Pappachan JM. Gastrointestinal complications of diabetes mellitus. *World journal of diabetes* 2013;4(3):51.
8. Stepanova M, Rafiq N, Younossi ZM. Components of metabolic syndrome are independent predictors of mortality in patients with chronic liver disease: a population-based study. *Gut* 2010;gut. 2010.213553.
9. Sangro B, Salem R, Kennedy A, Coldwell D, Wasan H. Radioembolization for hepatocellular carcinoma: a review of the evidence and treatment recommendations. *American journal of clinical oncology* 2011;34(4):422-31.
10. Garcia-Compean D, Jaquez-Quintana JO, Gonzalez-Gonzalez JA, Maldonado-Garza H. Liver cirrhosis and diabetes: risk factors, pathophysiology, clinical implications and management. *World journal of gastroenterology: WJG* 2009;15(3):280.
11. Dragani TA. Risk of HCC: genetic heterogeneity and complex genetics. *Journal of hepatology* 2010;52(2):252-7.
12. Zheng T, Shu G, Yang Z, Mo S, Zhao Y, Mei Z. Antidiabetic effect of total saponins from *Entada phaseoloides* (L.) Merr. in type 2 diabetic rats. *Journal of ethnopharmacology* 2012;139(3):814-21.
13. Kumar DP, Rajagopal S, Mahavadi S, Mirshahi F, Grider JR, Murthy KS, et al. Activation of transmembrane bile acid receptor TGR5 stimulates insulin secretion in pancreatic  $\beta$  cells. *Biochemical and biophysical research communications* 2012;427(3):600-5.
14. Doria C, Mandalá L, Scott VL, Gruttadauria S, Marino IR. Fulminant hepatic failure bridged to liver transplantation with a molecular adsorbent recirculating system: a single-center experience. *Digestive diseases and sciences* 2006;51(1):47-53.
15. Huang Z, Sjöholm Ak. Ethanol acutely stimulates islet blood flow, amplifies insulin secretion, and induces hypoglycemia via nitric oxide and vagally mediated mechanisms. *Endocrinology* 2008;149(1):232-6.
16. Tanveer S, Inayatullah M, Nazish Z, Nasir SA, Arshad M, Naqvi AB, et al. Hypoglycemia in liver cirrhosis. *Professional Med J* 2004;11(2):1-4.
17. Bonefeld K, Møller S. Insulin-like growth factor-I and the liver. *Liver International* 2011;31(7):911-9.
18. Nolte W, Hartmann H, Ramadori G. Glucose metabolism and liver cirrhosis. *Experimental and Clinical Endocrinology & Diabetes* 1995;103(02):63-74.
19. Levinthal GN, Tavill AS. Liver disease and diabetes mellitus. *Clinical diabetes* 1999;17(2):73.
20. Mohamed J, Nafizah AN, Zariyantey A, Budin SB. Mechanisms of Diabetes-Induced Liver Damage: The role of oxidative stress and inflammation. *Sultan Qaboos University Medical Journal* 2016;16(2):e132.
21. Shankar TP, Solomon SS, Duckworth WC, Himmelstein S, Gray S, Jerkins T, et al. Studies of glucose intolerance in cirrhosis of the liver. *The Journal of laboratory and clinical medicine* 1983;102(4):459-69.
22. Solomon S, Odunusi O, Carrigan D, Majumdar G, Kakoola D, Lenchik N, et al. TNF- $\alpha$  inhibits insulin action in liver and adipose tissue: a model of metabolic syndrome. *Hormone and metabolic research* 2010;42(02):115-21.
23. Pfortmueller CA, Wiemann C, Funk G-C, Leichtle AB, Fiedler GM, Exadaktylos AK, et al. Hypoglycemia is associated with increased mortality in patients with acute decompensated liver cirrhosis. *Journal of critical care* 2014;29(2):316. e7-e12.
24. Singh D, Memon HNA, Shaikh TZ, Shah SZA. Hypoglycemia; patients with liver cirrhosis. *Professional Med J* 2015;22(4).
25. Nouel O, Bernuau J, Rueff B, Benhamou J-P. Hypoglycemia: a common complication of septicemia in cirrhosis. *Archives of internal medicine* 1981;141(11):1477-8.