Hypoglycaemia in Liver Cirrhosis

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Introduction
Liver plays a vital role in blood glucose regulation\(^1\), hence it is well known that abnormalities of carbohydrate metabolism are found in Chronic Liver Disease (CLD), like liver cirrhosis, chronic hepatitis, hypocellular carcinoma. Disturbance of carbohydrate metabolism in CLD were directly correlated with degree of hepatocellular dysfunction. Liver is remarkably flexible in its role in glucose homeostasis and is the major source of net endogenous glucose production. Systemic glucose level depends on the balance between glucose influx into the circulation (i.e., Exogeneous glucose delivery, endogenous glucose production) and glucose efflux out of circulation (i.e., ongoing brain glucose utilization, variable glucose utilization by other tissues).

Aim of Study
To find out the prevalence of hypo glycemia among patients admitted with liver cirrhosis.

Materials and Method
Study Design
Observational study for a period of one year for 120 patients admitted in a tertiary care center.

Inclusion Criteria
All patients admitted with liver cirrhosis.

Exclusion Criteria
Known cases of diabetes mellites already on anti-diabetic treatment.
Patient admitted with complications other than encephalopathy.
Patient is on diabetogenic drugs.
All patients have undergone detailed clinical examination followed by the following investigations.
RBE, RUE, FBS, PPBS, RFT, LFT, SERUM ELECTROLYTES, LIPID PROFILE, VIRAL MARKERS, HBA1C, Prothrombin time, Ultra Sound Abdomen, ECG, X-Ray, Chest.
Serial blood sample was taken for analysis of blood sugar level. According to International Hypoglycaemia study group (IHSG)\(^2\), a glucose value of 70 mg/dL or less is considered as mild hypoglycaemia (level 1) and a glucose level of less than 54 mg/dL indicates clinically significant serious hypoglycaemia (level 2) and severe hypoglycaemia denotes severe cognitive impairment requiring external assistance for recovery (Level 3, ADA).

Data analysis was done with SPSS software version 17.0
Observation and Analysis

Age Distribution

| Age in Years | Frequency | Percentage |
|--------------|-----------|------------|
| < 30         | 2         | 2          |
| 31 – 40      | 11        | 9          |
| 41 – 50      | 32        | 27         |
| 51 – 60      | 44        | 36         |
| > 60         | 31        | 26         |

The mean age is 53.28 ± 9.64

Sex Distribution

| Gender     | Number | Percentage |
|------------|--------|------------|
| Male       | 117    | 97%        |
| Female     | 3      | 3%         |

75% of the patients are alcoholics while the rest are non-alcoholics.
Serum Bilirubin was elevated in 91% of cases.

| Glucose Level       | CHILD-PUGH |   |   | Total | P Value |
|---------------------|------------|---|---|-------|---------|
|                     | A          | B | C |       |         |
| Significant Hypoglycaemia | 0      | 35 | 36 | 71    | 0.441   |
| Mild Hypoglycaemia    | 0         | 1 | 2 | 3     |         |
| Normal Glucose        | 2         | 23| 21| 46    |         |
| Total                 | 2         | 59| 59| 120   |         |

The duration of cirrhosis is less than 2 years in 50%, 2–5 years in 35% and more than 5 years in 15%.
Hypoalbuminemia was present in 74%.

Serum Glucose

| Serum Glucose               | Number | Percentage |
|-----------------------------|--------|------------|
| Significant Hypoglycaemia < 54 mg/dL | 71    | 59%        |
| Mild Hypoglycaemia 55 – 70 mg/dL    | 3      | 3%         |
| Normal glucose > 70 mg/dL          | 46     | 38%        |

Severity of Cirrhosis

In this study, more patients with severe hypoglycaemia belonged to Child Class C.

|                  | Hepatic Encephal-| No Hepatic Encephal-| Total | P Value |
|------------------|------------------|----------------------|-------|---------|
|                  | -Opathy          | -Opathy (NHE)        |       |         |
| Significant Hypoglycaemia | 55    | 16       | 71    | 0.001   |
| Mild Hypoglycaemia      | 1     | 2        | 3     |         |
| Normal Glucose         | 15    | 31       | 46    |         |
| TOTAL                  | 71    | 49       | 120   |         |

The given table shows the correlation between Hypoglycaemia and Hepatic Encephalopathy.
55 out of 71 cases with hepatic encephalopathy had significant hypoglycaemia compared to only 16 out of 49 without hepatic encephalopathy.

Those proportion of patients with hypoglycaemia was more in those with hepatic encephalopathy than those in those without hepatic encephalopathy.
Discussion
Hypoglycaemia is more common in liver cirrhosis. Factors leading to hypoglycaemia are decreased gluconeogenesis, decreased hepatic glycogen content, hepatic resistance to glucagon, poor oral intake, hyperinsulinemia secondary to photo systemic shunting, diminished glucagon responsiveness, decreased capacity to synthesize glycogen due to excessive parenchyma destruction and conditions like sepsis.
In addition, both hyperinsulinemia and hyper glucagonemia may be present due to decreased hepatic clearance of these hormones resulting from portal – systemic shunting. Patient with cirrhosis also may have an elevated serum lactate levels, reflecting the decreased capacity of the liver to utilize lactate for gluconeogenesis. Hypoglycaemia although more common in acute fulminant hepatitis, also may be seen with liver cirrhosis.
In this study out of 120 patients analysis 36% belong to the age group between 51 – 60 years, 26% were age greater than 60 years, the mean age is 53.28 ± 9.64, as per Krishna C Sajja et al\(^3\) was 52 ± 1. 97% of the cases were males and 3% were females, this finding is on par with Dam Fialla A et al\(^4\) the incidence of cirrhosis is high in men than among women. The greater incidence in males may be due to the increase in the risk factor – alcoholism.\(^5\) 75% of the cases in this were alcoholics and 25% were non – alcoholics. The duration of cirrhosis is less than 2 years in 60% of the cases. Serum bilirubin is elevated in 76% of the cases and hypo albuminemia is seen in 44% of the cases.
In this study, 59% of cases had a significant hypoglycaemia i.e., Serum glucose less than 54, 3% had mild hypoglycaemia i.e., 55-70 and 38% cases had a normal serum glucose level. Significant hypoglycaemia is more common in patients with hepatic encephalopathy. The results of this study are consistent with most of the other studies.\(^10\)\(^11\)\(^12\)\(^13\) Most patients with severe hypoglycaemia belong to children class C.
Hence it is concluded that most of the patients with liver cirrhosis have the presence of hypoglycaemia which can be treated easily but if neglected can be vulnerable.

References
1. Kruzynska Y.T. Carbohydrate Metabolism: Textbook of Clinical Hepatology Oxford University Press. 2\(^{nd}\) Ed. 1999; 257.
2. International Hypoglycaemia Study Group: Glucose Concentrations of less than 3.0mmol/L (54mg/dL) should be reported in clinical trials: A joint position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2017; 40: 155-157

3. Krishna C Sajja et al, Mohan D P, Rockey D C Age and Ethnicity in Cirrhosis Journal of Investigative Medicine: The Official Publication of the American Federation for Clinical Research 2014; 62(7): 920-929.

4. Fialla Annette Dam, Ove B. Schaffalitzky De Muckadell and Annmaie Touborg Lassen. “Incidence, Etiology and Mortality of Cirrhosis: A Population Based Cohort Study”, Scandinavian Journal of Gastroenterology 47.6 (2012): 702-709.

5. Arky RA. Hypoglycemia associated with liver disease and ethanol. Endocrinol Metab Clin North Am.1989; 18(1):75-90.

6. Huang Z, Sjöholm A. Ethanol Acutely Stimulates Islet Blood Flow, Amplifies Insulin Secretion, and Induces Hypoglycemia via Nitric Oxide and Vagally Mediated Mechanisms. Endocrinology.2008; 149(1):232-36

7. Cryer PE, Fisher JN, Shamoon H. Hypoglycemia. Diabetes Care.1994; 17:734-755

8. Service FJ. Hypoglycemia. Med Clin North Am 1995; 79:1-8.

9. Guven M, F Bayram, K Guven, and F Kelestimur. Evaluation of patients admitted with hypoglycaemia to a teaching hospital in Central Anatolia. Postgrad Med J. 2000; 76(893):150-52

10. 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.

11. Singh D, Memon HNA, Shaikh TZ, Shah SZA. Hypoglycemia; patients with liver cirrhosis. Professional Med J 2015;22(4)

12. 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.

13. Fischer KF, Lees JA, Newman JH. Hypoglycemia in hospitalized patients. N Engl J Med.1986; 315:1245- 50.