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CIRRHOSIS OF LIVER AND INSULIN RESISTANCE- AN OBSERVATIONAL STUDY IN ASSAM

Biochemistry

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ABSTRACT

Background:- The prevalence rate of Diabetes Mellitus in cirrhosis of liver varies from 35 to 71%. Diabetes developing in such cases is referred to as Hepatogenous Diabetes. Studies on insulin resistance and Cirrhosis of Liver in North-East India is, however, limited. **Aims And Objectives-** 1) To estimate fasting plasma glucose and fasting Insulin levels in patients with Cirrhosis of Liver. 2) To calculate HOMA-IR in these patients. **Materials And Methods-** A hospital-based observational study on 110 non-Diabetic patients having Liver Cirrhosis was undertaken. Cases were divided according to Child Pugh classification into Grade A, B and C. Fasting plasma glucose and fasting Insulin were estimated in VITROS-5600 Autoanalyzer and HOMA-IR was determined for each case. **Results-** The mean insulin level was 5.8±2.3 in Child Pugh A, 7.5±3.5 in Child Pugh B and 22.2±11.5 in Child Pugh C. The mean HOMA-IR was 1.3±0.6 in Child Pugh A, 1.8±0.9 in Child Pugh B and 5.8±3.5 in Child Pugh C. The difference in Fasting Insulin and HOMA-IR in Child Pugh Grade A, B and C was found to be statistically significant ($p<0.05$). **Conclusion-** It can be concluded that insulin resistance is maximum in cases with Cirrhosis of Liver having highest Child Pugh grading. Follow-up studies may help in demonstrating Insulin Resistance with increasing grade of Liver Cirrhosis.

KEYWORDS

Cirrhosis of Liver, Hepatogenous Diabetes, HOMA-IR.

INTRODUCTION

Liver plays a central role in glucose homeostasis.[1] Cirrhosis of Liver has been suggested to be associated with an increased incidence of insulin resistance (IR) and Diabetes Mellitus (DM). Diabetes that develops as a complication of cirrhosis of liver is known as 'Hepatogenous diabetes' (HD). Bohan et al.[2] first described about occurrence of diabetes in cirrhosis. This was later termed as Hepatogenous diabetes by Megyesi et al.[3] The pathophysiology of Hepatogenous Diabetes is complex and poorly understood. However, it has been hypothesized that Porto-systemic shunting of insulin result in systemic hyperinsulinemia ultimately resulting in down regulation of insulin receptors and causing insulin resistance.[4] The major causes of death in cirrhotic patients with DM relate to liver disease or its complications, such as chronic liver failure, gastrointestinal hemorrhage, spontaneous bacterial peritonitis, sepsis, renal dysfunction, definite clinical implications in the form of decrease response to treatment, rapid progression to fibrosis and hepatocellular carcinoma (HCC).[5,6] HOMA can be used to determine Hepatogenous insulin resistance/diabetes in cirrhotic patients.

HOMA-IR strongly predicts the development of type 2 diabetes, independent of obesity, body fat distribution and glucose tolerance status[4,7]. Studies on insulin resistance, CLD and Cirrhosis in North-East India are, however, limited.

AIMS & OBJECTIVES:

1. To estimate fasting plasma glucose and fasting Insulin levels in patients with Cirrhosis of Liver.
2. To calculate HOMA-IR in these patients.

MATERIALS AND METHODS

A hospital-based observational study on 110 non-Diabetic patients having Cirrhosis of Liver was undertaken for a period of one year from 1st June 2021 to 31st May 2022 in the department of Biochemistry, AMCH, Dibrugarh. The relevant clinical details were noted. Patients with HbA1c ≥ 6.5, Fasting plasma glucose ≥ 126mg/dL, receiving insulin and oral hypoglycemic agents, Pregnant or Lactating women, with disorders of thyroid, hypertriglyceridemia, on steroids etc. were excluded from the study.

Fasting plasma glucose and fasting serum insulin levels were estimated in VITROS 5600 Autoanalyzer using glucose oxidase-peroxidase and immunometric immunoassay method respectively.

HOMA-IR was calculated using formula:
HOMA-IR = Fasting plasma glucose (mg/dL) x Fasting serum insulin(μU/mL)/405
Child-Turcotte-Pugh score was determined for all cases, having cirrhosis.

A total Child-Turcotte-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease), 7 to 9 is class B (significant functional compromise), and ≥10 is class C (decompensated disease).

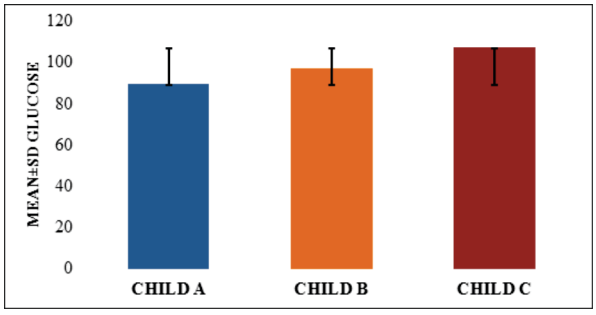
Statistical analysis was done using SPSS 25.0 and ANOVA test. Ethical approval was obtained from the committee of the Medical Ethics of the hospital. All patients provided their written informed consent in the study.

CHILD-PUGH CLASSIFICATION[8]

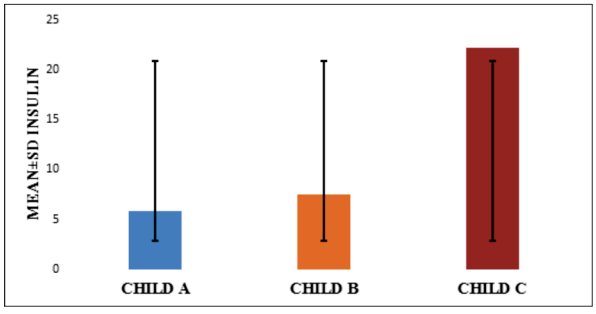
FACTOR	POINTS TOWARDS TOTAL SCORE			
	UNITS	1	2	3
Serum Bilirubin	mg/dL	<2.0	2.0-3.0	>3.0
Serum Albumin	gm/dL	>3.5	3.0-3.5	<3.0
Prothrombin time	Seconds prolonged INR	<4 <1.7	4-6 1.7-2.3	>6 >2.3
Ascites		None	Easily controlled	Poorly controlled
Hepatic Encephalopathy		None	Minimal	Advanced

RESULTS

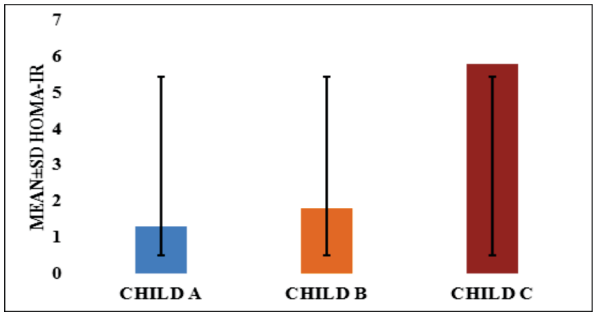
In our study, a total of 110 cases were analyzed during the study period. The Mean ± SD of glucose levels in Child Class A, B and C was found to be 89.6±19.5, 97±19.7 and 107.2±22.4 respectively, the variation of mean glucose levels along with Child Pugh score was found to be statistically significant ($p<0.05$) using One-way ANOVA.



The Mean ± SD of insulin levels in Child Class A, B and C was found to be 5.8±2.3, 7.5±3.5 and 22.5±11.5 respectively and the variation of mean Insulin levels along with Child Pugh score was found to be statistically significant ($p<0.05$) using One-way ANOVA test.



The Mean ± SD of HOMA-IR levels in Child Class A was found to be 1.3±0.6, in Child Class B it was 1.8±0.9 and in Child Class C it was found to be 5.8±3.5 and the variation of mean HOMA-IR levels along with Child Pugh score was found to be statistically significant ($p<0.05$) using One-way ANOVA test.



DISCUSSION

In our study, fasting plasma glucose and fasting insulin were highest in Child Pugh C and lowest in Child Pugh A. The difference between the 3 groups of Child Pugh grading and the various parameters was found to be statistically significant ($p< 0.05$). With the severity of liver disease in Cirrhosis, as indicated by Child Pugh Classification, fasting blood glucose and fasting Insulin levels were increased, which indicated that the severity of liver disease is closely related to the occurrence of abnormal glucose metabolism. This is similar to a study conducted by Huan Li et al.[9] in the year 2021 on Clinical study of abnormal glucose metabolism and insulin resistance in patients with liver cirrhosis where they found that the fasting insulin levels of patients with cirrhosis of Child-Pugh grade C was significantly higher than that of Child-Pugh grade B patients.

HOMA-IR was found highest in Child Pugh Class C patients with a mean of 5.8±3.5. It was seen that, as the Child Pugh grade increases, the risk of developing insulin resistance among these patients also increased and it was found to be statistically significant ($p <0.05$). This is consistent with the study conducted by Kalaichelvi S et al.[5] where they found that as the Child Pugh grade increases, insulin resistance among the patients also increased which was statistically significant (p value <0.001). Another study from Jodhpur, India by Goswami & Bhargava et al.[10] showed significant increase in insulin resistance in patients with CTP >10 and MELD >15. The study conducted by Hardeep Singh Deep et al.[11] showed that there is a significant increase in Insulin Resistance in patients with increased Child Pugh score and advanced liver disease. Similar to the present study, Gharavi et al.[12] also found that the relationship between Insulin Resistance and severity of liver cirrhosis was significant statistically ($p=0.01$)

CONCLUSION:

It can be concluded that cases of Liver cirrhosis having more severe symptoms, as indicated by Child Pugh score, have higher Insulin resistance which is represented by HOMA-IR. Although in the same group of patients, the Fasting blood glucose and Fasting Serum Insulin levels were normal.

Thus, interpreting Fasting Blood Glucose in isolation will not be sufficient in commenting elaborately on abnormalities of glucose metabolism in cirrhosis. Serum insulin levels and HOMA-IR can be recommended as investigations to be done routinely in these patients.

However, follow-up studies and randomized control trials with higher sample size and additional parameters like Leptin, C-peptide, Post Prandial Insulin, Adipo-IR could have been done for more conclusive evidence.

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