

## EVALUATION OF INSULIN RESISTANCE AMONG PATIENTS OF CIRRHOSIS OF LIVER

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### ABSTRACT

**Background:** The etiopathology of hematogenous diabetes is complex and it is not precisely reported in previous studies but porto-systemic shunting of insulin reported in systemic hyperinsulinemia which leads to subsequent down regulation of insulin receptors which result in insulin resistance. **Material & Methods:** The present prospective study was conducted at the Department of general medicine of our tertiary care hospital. Patients were enrolled from the outdoor and ward by simple random sampling. Clearance from Institutional Ethics Committee was taken before the start of the study. Written informed consent was taken from each study participant. All patients with liver cirrhosis were enrolled in the present study. **Results.** Out of the 50 patients with liver cirrhosis, insulin resistance was found among 39 (78%) patients with a mean IR value of  $5.87 \pm 3.52$ . 11 (22%) patients reported no insulin resistance with a mean IR value of  $0.79 \pm 0.64$ . This difference was statistically significant ( $p$ -value  $< 0.05$ ). On the basis of the Modified child Pugh score majority of study participants 23 were in Class C ( $>10$ ) which was followed by 22 patients in Class B (7-9) and 5 patients in Class A (5-6). Out of these 2 (4%) patients of class A had IR value ( $>1.64$ ) with mean IR value of  $5.92 \pm 3.28$  ( $p$ -value  $< 0.05$ ). 2 (4%) patients of class B had IR value ( $>1.64$ ) with mean IR value of  $5.77 \pm 4.12$  ( $p$ -value  $< 0.05$ ). 20 (40%) patients of class C had IR value ( $>1.64$ ) with mean IR value of  $5.89 \pm 3.92$  ( $p$ -value  $< 0.05$ ). **Conclusion:** Insulin resistance is a better predictor of impending diabetes mellites. We further conclude that HbA1c levels and fasting plasma glucose are not sufficient in diagnosing glucose metabolism disorders in cirrhosis. We conclude that insulin resistance can be used as a prognostic marker in cirrhosis of the liver.

**Keywords:** liver cirrhosis, insulin resistance, diabetes.

### INTRODUCTION

The prevalence of non-communicable diseases is increasing compared to communicable diseases. Among the non-communicable diseases, diabetes mellitus is rapidly increasing globally and affecting all age groups (1). In 2014, WHO reports that 8.5% of adults aged 18 years or above had been diagnosed with diabetes. It was estimated that by the year 2030 diabetes will become the seventh leading cause of mortality worldwide. In 2016, WHO reports that diabetes was directly responsible for 1.6 million mortality occurred worldwide (2). In India, the prevalence of diabetes is increasing and imposing challenges on the health care infrastructure of the country (3).

Diabetes is a chronic disease in etiology and occurs when the pancreas does not produce enough amount of insulin or when there is resistance towards its action on the body (4). Chronic liver diseases are the process of long-term progressive destruction and regeneration of the liver, and with advancing disease, hepatic fibrosis (scarring) and cirrhosis frequently occur. Progression of CLD and deterioration of liver function are associated with various hepatic complications such as chronic liver failure and hepatocellular carcinoma (HCC) (5).

The etiopathology of hematogenous diabetes is complex and it is not precisely reported in previous studies but porto-systemic shunting of insulin

reported in systemic hyperinsulinemia which leads to subsequent down regulation of insulin receptors which results in insulin resistance. Previous studies reported that chronic inflammation also leads to the occurrence of insulin resistance (6). It is well known that insulin resistance at peripheral tissues (muscular tissue and adipose) plays a key role in the glucose metabolism disturbance in diabetes. The present study was conducted to evaluate the insulin resistance among patients with cirrhosis of the liver at our tertiary care center.

## MATERIALS & METHODS

The present prospective study was conducted at the Department of General Medicine of our tertiary care hospital. The study duration was January 2019 to September 2019. A sample size of 50 was calculated at a 95 % confidence interval at a 5 % acceptable margin of error by epi info software version 7.2. Patients were enrolled from outdoor and from the ward by simple random sampling. Clearance from Institutional Ethics Committee was taken before the start of the study. Written informed consent was taken from each study participant. All patients with liver cirrhosis were enrolled in the present study.

All the study participants who had previously diagnosed diabetes mellitus and patients who were in diabetes treatment, Thiazides, corticosteroids, and Phenytoin were excluded from the present study. Pregnant mothers were also excluded from the present study. All the study participants were subjected to recording demographic details as per the proforma. Diagnosis of liver cirrhosis was done by clinical examination and evaluation, biochemical tests (PTI, LFTs, TSP/DSP) were conducted and USG abdomen was performed for all the patients. Fasting glucose levels and fasting insulin levels were recorded and insulin resistance was calculated by the HOMA-IR formula. All the data was recorded on a Microsoft Excel spreadsheet and data analysis was done at 5% alpha and 95% confidence interval using SPSS v22 software. Test of significance was applied on collected and organized data and a p-value less than 0.05 was considered as a statistically significant association between study variables.

## RESULTS

In the present study, we enrolled 50 patients with liver cirrhosis outdoor and from the ward by simple random sampling. Clearance from Institutional Ethics Committee was taken before the start of the study. Written informed consent was taken from each study participant. In the present study male

(62%) to female (38%) ratio was 1.63:1. The mean age of patients was  $52 \pm 6.2$  years. Out of the 50 patients with liver cirrhosis, insulin resistance was found among 39 (78%) patients with a mean IR value of  $5.87 \pm 3.52$ . 11 (22%) patients reported no insulin resistance with a mean IR value of  $0.79 \pm 0.64$ . This difference was statistically significant (p-value < 0.05). (Table 1)

**Table 1: Distribution of study participants insulin resistance.**

Insulin resistance	No. of cases	Mean IR	P-value
<1.64	11 (22%)	$0.79 \pm 0.64$	<0.05
>1.64	39 (78%)	$5.87 \pm 3.52$	

In the present study, on the basis of Modified child Pugh score majority of study participants 23 were in Class C (>10) which was followed by 22 patients in Class B (7-9) and 5 patients in Class A (5-6). Out of these 2 (4%) patients of class A had IR value (>1.64) with mean IR value of  $5.92 \pm 3.28$  (p-value < 0.05). 2 (4%) patients of class B had IR value (>1.64) with mean IR value of  $5.77 \pm 4.12$  (p-value < 0.05). 20 (40%) patients of class C had IR value (>1.64) with mean IR value of  $5.89 \pm 3.92$  (p-value < 0.05). These all differences were statistically significant and the association was present. (Table 2)

**Table 2: Distribution according to Modified child Pugh score and insulin resistance.**

child Pugh score	Total no. of patients	No. of cases with IR value (>1.64)	Mean IR	P-value
Class A (5-6)	5	2 (4%)	$5.92 \pm 3.28$	<0.05
Class B (7-9)	22	17 (34%)	$5.77 \pm 4.12$	<0.05
Class C (>10)	23	20 (40%)	$5.89 \pm 3.92$	<0.05

## DISCUSSION

In the present study, we enrolled 50 patients with liver cirrhosis from the outdoor and the ward by simple random sampling. Clearance from

Institutional Ethics Committee was taken before the start of the study. Written informed consent was taken from each study participant. In the present study male (62%) to female (38%) ratio was 1.63:1. The mean age of patients was  $52 \pm 6.2$  years. Out of the 50 patients with liver cirrhosis, insulin resistance was found among 39 (78%) patients with a mean IR value of  $5.87 \pm 3.52$ . 11 (22%) patients reported no insulin resistance with a mean IR value of  $0.79 \pm 0.64$ . This difference was statistically significant ( $p$ -value  $< 0.05$ ). A similar result to the present study was obtained in a study conducted by Deep HS et al among 100 patients diagnosed with liver cirrhosis. They reported Insulin resistance was observed in 79 patients out of 100 patients. The  $p$ -value is  $< 0.001$  which is statistically highly significant (7).

In the present study, on the basis of Modified child Pugh score majority of study participants 23 were in Class C ( $>10$ ) which was followed by 22 patients in Class B (7-9) and 5 patients in Class A (5-6). Out of these 2 (4%) patients of class A had IR value ( $>1.64$ ) with mean IR value of  $5.92 \pm 3.28$  ( $p$ -value  $< 0.05$ ). 2 (4%) patients of class B had IR value ( $>1.64$ ) with mean IR value of  $5.77 \pm 4.12$  ( $p$ -value  $< 0.05$ ). 20 (40%) patients of class C had IR value ( $>1.64$ ) with mean IR value of  $5.89 \pm 3.92$  ( $p$ -value  $< 0.05$ ). These all differences were statistically significant and the association was present. A similar result to the present study was obtained in a study conducted by Erice E et al among patients diagnosed with liver cirrhosis. They reported Mean HOMA-2 score was  $3 \pm 1.4$ . 57% of patients had Insulin resistance. A weak correlation between the HOMA-2 score and HVPG was reported. 86% of patients had portal hypertension. HOMA-2 score was an independent predictor of portal hypertension. However, in patients with portal hypertension, the correlation between HOMA-2 score and HVPG was not found (8).

Similar results to the present study were obtained in a study conducted by Goswami A et al among patients diagnosed with liver cirrhosis. They reported prevalence of Insulin resistance among liver cirrhosis was 68.5%. Insulin resistance was seen in all hepatitis C patients followed by non-alcoholic

fatty liver disease and autoimmune hepatitis patients followed by hepatocellular carcinoma patients followed by alcoholic liver disease and hepatitis B patients. These all differences were statistically significant and the association was present (9). A similar result to the present study was obtained in a study conducted by Mukherjee S et al among patients diagnosed with liver cirrhosis. They reported 58.1% of patients had impaired glucose tolerance and 14.0% of patients had diabetes mellitus. These were significantly higher among patients aged more than 45 years ( $P < 0.05$ ). However, no association was reported with the gender of the patients. No association was reported between diabetes and severity and duration of liver cirrhosis. 20% of patients with chronic hepatitis B reported having diabetes, however, it was least reported in patients with alcoholic liver disease. However, the overall Insulin resistance status had no significant association with the etiology of liver cirrhosis (10).

## CONCLUSION

We concluded from the present study that Insulin resistance is a better predictor of impending diabetes mellitus. We further conclude that HbA1c levels and fasting plasma glucose are not sufficient in diagnosing glucose metabolism disorders in cirrhosis. We conclude that insulin resistance can be used as a prognostic marker in cirrhosis of the liver. Therefore, serum insulin levels should be recommended as routine investigation among patients with cirrhosis of the liver.

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