# **Original article:**

# Assessment of Correlation of Occurrence of Diabetes with Severity in Patients with Cirrhosis of Liver: An Observational Study

# Irfan K. J.

Assistant Professor, Department of General Medicine, M. S. Ramaiah Medical College & Hospitals, Bangalore, Karnataka, India.

Corresponding Author: Dr. Irfan K. J., Assistant Professor, Department of General Medicine, M. S. Ramaiah Medical College & Hospitals, Bangalore, Karnataka, India.

#### Abstract:

**Background:** People living with type 2 Diabetes Mellitus (DM) are more vulnerable to various forms of both short- and long-term complications, which often lead to their premature death. The prevalence of type 2 diabetes is higher in patients who have liver diseases, such as nonalcoholic fatty liver disease, chronic viral hepatitis, hemochromatosis, alcoholic liver disease, and cirrhosis. Hence; present study was conducted to assess the effect of severity of liver cirrhosis on the occurrence of diabetes.

**Materials & Methods:** The present study included assessment correlation of the occurrence of diabetes and severity of cirrhosis of liver. A total of 60 liver cirrhosis patients were included in the present study, among which, 30 were diabetic while the remaining 30 were non-diabetic. Grading of the liver cirrhosis was done in all the patients of both the study groups according to the child's classification of liver cirrhosis. All the results obtained were compiled in the Microsoft excel sheet and were analyzed by SPSS software.

**Results:** When graded on the basis of Child's classification of cirrhosis of liver, 16, 8 and 6 patients of the diabetic group had grade A, B and C of severity of liver cirrhosis. In the non-diabetic group, 15, 8 and 7 patients of the non-diabetic group had grade A, B and C of severity of liver cirrhosis. Non-significant results were obtained while comparing the effect of severity of liver cirrhosis on the occurrence of diabetes.

**Conclusion:** Occurrence of diabetes is independent of the severity of the cirrhosis of liver.

Key words: Cirrhosis, Diabetes, Severity.

## INTRODUCTION

Liver fibrosis results from the perpetuation of the normal wound healing response resulting in an abnormal continuation of fibrogenesis (connective tissue production and deposition). Fibrosis progresses at variable rates depending on the cause of liver disease, environmental and host factors. Cirrhosis is an advanced stage of liver fibrosis that is accompanied by distortion of the hepatic vasculature. It leads to shunting of the portal and arterial blood supply directly into the hepatic outflow (central veins), compromising exchange between hepatic sinusoids and the adjacent liver parenchyma, i.e., hepatocytes.<sup>1-3</sup>

Type 2 DM is characterized by insulin insensitivity as a result of insulin resistance, declining insulin production, and eventual pancreatic beta-cell failure. This leads to a decrease in glucose transport into the liver, muscle cells, and fat cells. There is an increase in the breakdown of fat with hyperglycemia. The involvement of impaired alpha-cell function has recently been recognized in the pathophysiology of type 2 DM.<sup>4,5</sup>

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People living with type 2 DM are more vulnerable to various forms of both short- and long-term complications, which often lead to their premature death. This tendency of increased morbidity and mortality is seen in patients with type 2 DM because of the commonness of this type of DM, its insidious onset and late recognition, especially in resource-poor developing countries India.<sup>6-8</sup> Hence; present study was conducted to assess the effect of severity of liver cirrhosis on the occurrence of diabetes.

#### **MATERIALS & METHODS**

The present study was commenced in the Department of General Medicine, M. S. Ramaiah Medical College & Hospitals, Bangalore, Karnataka (India) and it included assessment correlation of the occurrence of diabetes and severity of cirrhosis of liver. Written consent was obtained from all the subjects after explaining in detail the entire research protocol. A total of 60 liver cirrhosis patients were included in the present study, among which, 30 were diabetic while the remaining 30 were non-diabetic. Grading of the liver cirrhosis was done in all the patients of both the study groups according to the child's classification of liver cirrhosis.<sup>8</sup> Complete data in related to the demographic information and medical and family history of all the subjects was obtained.

#### **Exclusion Criteria**

- Subjects above 70 years of age,
- Subjects with presence of any other co-morbid condition,
- Subjects with any known drug allergy,
- Subjects with uncontrolled diabetes

All the results obtained were compiled in the Microsoft excel sheet and were analyzed by SPSS software. Chisquare test was used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

## RESULTS

A total of 30 diabetic subjects and 30 non-diabetic subjects were included in the present study. All the 60 subjects had positive history of liver cirrhosis. Mean age of the subjects of the diabetic group and the non-diabetic group was 58.3 years and 54.1 years. Positive family history of diabetes was present in 15 subjects of the diabetic group, while it was present only in the 6 subjects of the diabetic group. When graded on the basis of Child's classification of cirrhosis of liver, 16, 8 and 6 patients of the diabetic group had grade A, B and C of severity of liver cirrhosis. Non-significant results were obtained while comparing the effect of severity of liver cirrhosis on the occurrence of diabetes (P- value > 0.05).

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| Parameter                           | Diabetic group | Non-diabetic group | P- value |
|-------------------------------------|----------------|--------------------|----------|
| Number of subjects                  | 30             | 30                 | -        |
| Mean age (years)                    | 58.3           | 54.1               | 0.57     |
| Males                               | 22             | 20                 | 0.34     |
| Females                             | 8              | 10                 |          |
| Positive family history of diabetes | 15             | 6                  | 0.02*    |

Table 1: Demographic details and medical history of the subjects

\*: Significant

Table 2: Effect of severity of liver cirrhosis on the occurrence of diabetes

| Severity of liver  | Diabetic group |            | Non-diabetic group |            | Р-    |
|--------------------|----------------|------------|--------------------|------------|-------|
| cirrhosis (Child's | Number of      | Percentage | Number of          | Percentage | value |
| classification)    | subjects       |            | subjects           |            |       |
| Α                  | 16             | 53.3       | 15                 | 50         | 0.98  |
| В                  | 8              | 26.7       | 8                  | 26.7       |       |
| С                  | 6              | 20         | 7                  | 23.3       |       |

Graph 1: Effect of severity of liver cirrhosis on the occurrence of diabetic group



# DISCUSSION

The prevalence of type 2 diabetes is higher in patients who have liver diseases, such as nonalcoholic fatty liver disease, chronic viral hepatitis, hemochromatosis, alcoholic liver disease, and cirrhosis. The development of diabetes in patients with cirrhosis is well recognized, but evidence is emerging that the development of chronic liver disease

and progression to cirrhosis may occur after the diagnosis of diabetes and that diabetes plays a role in the initiation and progression of liver injury.<sup>9</sup> In the present study, a total of 30 diabetic subjects and 30 non-diabetic subjects were included in the present study. All the 60 subjects had positive history of liver cirrhosis. Mean age of the subjects of the diabetic group and the non-diabetic group was 58.3 years and 54.1 years. Petit JM et al determined the prevalence and clinical correlates of DM in a large cohort of patients with cirrhosis. A total of 1,068 patients with LC were included in this cross sectional study (CIRCE study). There were 383 patients with cirrhosis associated with hepatocellular carcinoma (HCC). DM was found in 412 (39.7 %) patients. Patients with DM were older and more likely to be overweight and male, with a family history of DM and a diagnosis of HCC. DM was not associated with a history of stroke or myocardial infarction. Cirrhosis secondary to hepatitis infection was less strongly associated with DM than with NASH or alcoholic cirrhosis. The severity of LC was not associated with DM. In multivariate analysis, the factors associated with DM were age, BMI, a family history of DM, and statin use. There was a significant interaction between HCC and cirrhosis etiology for the risk of DM. Cirrhosis secondary to hepatitis was associated with a lesser presence of DM only in patients with HCC. LC was strongly associated with DM, with around 40 % of diabetic patients. In the group of patients with LC without HCC, diabetes was not associated with the etiology of cirrhosis.<sup>10</sup>

In the present study, positive family history of diabetes was present in 15 subjects of the diabetic group, while it was present only in the 6 subjects of the diabetic group. When graded on the basis of Child's classification of cirrhosis of liver, 16, 8 and 6 patients of the diabetic group had grade A, B and C of severity of liver cirrhosis. In the non-diabetic group, 15, 8 and 7 patients of the non-diabetic group had grade A, B and C of severity of liver cirrhosis.

In the present study, non-significant results were obtained while comparing the effect of severity of liver cirrhosis on the occurrence of diabetes (P- value > 0.05). Zhang H et al determined the association of diabetes mellitus (DM) and international normalized ratio (INR) level in hepatocellular carcinoma (HCC) patients. Unconditional multivariable logistic regression analysis was used to determine the association of DM and INR level in HCC patients. Of the total, 63 (16.8%) patients were diabetic (diabetic group) and 312 (83.2%) patients were diagnosed without diabetes (non-diabetic group). Their mean age was  $56.4 \pm 11.0$  years and 312 (83.2%) patients were male. No significant difference in the relationship between INR level and fasting glucose was shown by Pearson test. Among the 63 diabetic regimens, 35 (55.6%) patients had been diagnosed with DM for more than 5 years, 23 (36.5%) received oral anti-diabetic regimens, 11 (17.5%) received insulin, and 30 (47.6%) reported relying on diet alone to control serum glucose levels. No significant differences were found for the association between DM duration/treatment and INR level, except for the age at diabetes diagnosis. The INR level was increased in HCC patients with DM and these patients should be monitored for the coagulation function in clinical practice.<sup>11</sup>

## CONCLUSION

Under the light of above obtained data, it can be concluded that occurrence of diabetes is independent of the severity of the cirrhosis of liver. However; further research is recommended.

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