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PROGNOSTIC EFFICACY OF GLYCEMIC CONTROL IN PATIENTS WITH HBV & HCV RELATED CIRRHOSIS PRESENTING WITH CO-MORBID DIABETES MELLITUS

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Abstract:

Background: *Alterations in carbohydrate metabolism are frequent in cirrhosis, the prevalence being dependent of the stage of the disease. In 15% to 30% of patients the clinical and laboratory picture is that of overt diabetes with fasting hyperglycemia and frank glycosuria. Diabetes follows cirrhosis in approximately 50% of patients with associated diseases, but the two conditions may be simultaneously diagnosed, or cirrhosis may even follow diabetes. The association is clinically relevant and merits attention.* ***Objective:*** *To study the prognostic efficacy of glycemic control in patients with HBV & HCV related cirrhosis presenting with co- morbid diabetes mellitus.* ***Methodology:*** *This retrospective analysis was conducted using hospital records of 374 patients admitted to a tertiary care hospital with HBV & HCV related cirrhosis presenting with co-morbid diabetes mellitus from January 2018 to December 2018. No gender or age related bias was observed and all records were chosen via non-probability consecutive sampling. Data was recorded onto a structured questionnaire containing inquiries about the glycemic control history (prior to admission and during hospital stay), the viral load kinetics (at presentation and discharge), self-rated symptom severity, inferences obtained from clinical examination notes at presentation and discharge and details of all morbidity and mortality during hospitalization. The data obtained was analyzed using SPSS v.21 & Microsoft Excel 2016.* ***Results:*** *Among, the patient records obtained, 59.09% belonged to men, while the remaining 40.91% belonged to women. The mean age of the sample stood at 47.63 (SD ± 8.1). Among the subjects, poor glycemic control was common found, being particularly worse in patients with a high viral load and a longstanding history of cirrhosis. In-hospital mortality rate in the sample was 18.98%.* ***Conclusion:*** *After careful consideration, it can be concluded that eventual glycemic control has a lot of potential to be used as aprognostic indicator as is evident from our finding that mortality rate and glycemic control align well together. Further prospective research is needed to cement this prognostic association.*

Keywords: *HBV, HCV, Diabetes Mellitus, Cirrhosis and Prognosis.*

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INTRODUCTION:

The prevalence of type 2 diabetes is increasing with a new diagnosis made every 21 seconds. [1] Historically, the development of diabetes in patients with cirrhosis is well documented with overt diabetes present in up to 70% of cirrhotic subjects. [2] However, evidence is emerging that the development of chronic liver disease and progression to cirrhosis may occur after the diagnosis of type 2 diabetes and that diabetes plays a role in the initiation and progression of liver injury.

Type 2 diabetes accounts for 90% to 95% of all diagnosed cases of diabetes mellitus [3] and is responsible for the majority of the health burden attributable to diabetes. Type 2 diabetes develops from an imbalance between insulin sensitivity and insulin secretion. [4] The earliest detected abnormality in individuals who develop type 2 diabetes is impairment in the body's response to insulin. [5, 6]

This is described as insulin resistance. Risk factors associated with insulin resistance and type 2 diabetes include central obesity, positive calorie load, physical inactivity, age, and genetic predisposition. [7] The liver plays a key role in the whole-body response to insulin. In the fasting state the liver releases glucose into the circulation. After a meal, as blood glucose increases, insulin is secreted from the pancreas and acts on muscle and fat to stimulate glucose uptake and on the liver to suppress glucose output. In insulin-resistant states, more insulin is required for the same effects

The prevalence of type 2 diabetes is higher in patients who have certain liver diseases. There is a link between the presence of type 2 diabetes and the severity of liver injury. On analysis of these studies, it is important to remember the link between diabetes and cirrhosis, because studies with an increased proportion of cirrhotic patients are more likely to find an association between type 2 diabetes and disease severity. The liver diseases associated with type 2 diabetes include nonalcoholic fatty liver disease, chronic viral hepatitis, hemochromatosis, alcoholic liver disease, and cirrhosis.

The term "hepatogenous" diabetes is used to describe the association between cirrhosis and impaired glucose metabolism. Up to 96% of patients with cirrhosis have diabetes or impaired glucose tolerance. [8] Hepatogenous diabetes differs from type 2 diabetes in that there is less association with risk factors such as age, body mass index, and family history of diabetes.

Cirrhosis may contribute to the development of type 2 diabetes through numerous factors. With the development of portal hypertension, blood shunting redirects blood away from hepatocytes and results in reduced insulin clearance with peripheral hyperinsulinemia. [9] This systemic hyperinsulinemia may contribute to the development of insulin resistance through the down-regulation of insulin receptors. [11] However, cirrhosis alone does not always induce diabetes, and the cause of liver disease and environmental factors may play a role.

There is evidence from a range of liver diseases linking obesity with insulin resistance and hepatic steatosis, which in turn contribute to liver injury. In nonalcoholic fatty liver disease, a range of studies have consistently identified type 2 diabetes as an independent predictor of fibrosis, [12] faster fibrosis progression, [13] and increased mortality. [14] This relationship is maintained when analysis is restricted to non-cirrhotic patients.

Scrutiny of the impact of type 2 diabetes in HCV has identified a role for insulin resistance and type 2 diabetes in disease progression. Hyperinsulinemia, [15] hyperglycemia, [16] and insulin resistance [17] have all been associated with more severe fibrosis in HCV. Again, an important observation is that the onset of insulin resistance occurs early, before the development of cirrhosis. [18]

METHODOLOGY:

This retrospective analysis was conducted using hospital records of 374 patients admitted to a tertiary care hospital with HBV & HCV related cirrhosis presenting with co-morbid diabetes mellitus from January 2018 to December 2018. No gender or age related bias was observed and all records were chosen via non-probability consecutive sampling. Data was recorded onto a structured questionnaire containing inquiries about the glycemic control history (prior to admission and during hospital stay), the viral load kinetics (at presentation and discharge), self-rated symptom severity, inferences obtained from clinical examination notes at presentation and discharge and details of all morbidity and mortality during hospitalization. The data obtained was analyzed using SPSS v.21 & Microsoft Excel 2016.

RESULTS:

Among, the patient records obtained, 59.09% belonged to men, while the remaining 40.91% belonged to women. The mean age of the sample stood at 47.63 (SD ± 8.1). Among the subjects, poor glycemic control was common found, being particularly worse in patients with a high viral load and

a longstanding history of cirrhosis. In-hospital mortality rate in the sample was 18.98%.

AGE (YEARS)	MALES	FEMALES	TOTAL
UP to 30	*9*	*2*	*11*
31 to 40	*31*	*18*	*49*
41 to 50	*102*	*62*	*164*
51 to 60	*63*	*49*	*112*
61 & above	*16*	*22*	*38*

HBA1C	FREQUENCY	MORTALITY
6.5 to 8.4	*23*	*0*
8.5 to 10.4	*49*	*2*
10.5 to 12.4	*110*	*31 (2 tailed sig. < 0.05)*
12.5 to 14.4	*105*	*27 (2 tailed sig. < 0.05)*
14.5 & above	*87*	*11*

DISCUSSION:

Type 2 diabetes seems to be associated with an increased risk of cirrhosis complications. The Verona Diabetes Study, a population-based study on more than 7000 subjects with type 2 diabetes, found an increased risk of death from chronic liver disease and cirrhosis compared with the general population (standardized mortality ratio after 5 years of 2.52, 95% confidence interval [CI], 1.96-3.2). [19]

In addition, there was an increased risk of mortality from hepatocellular carcinoma (standardized mortality ratio after 10 years of 1.86, 95% CI, 1.43-2.38). [20] Insulin treatment of type 2 diabetes, perhaps as a marker of more severe diabetes, was associated with a particularly high risk of mortality in cirrhotic patients (relative risk 6.84) [21]

Similar observations have been made in smaller cohort studies. It has been found that in nonalcoholic fatty liver disease, patients with type 2 diabetes had an overall mortality twice that of nondiabetic subjects. After adjustment for potential confounders, including cirrhosis, the risk ratio was 22.83 (95% CI, 2.97-175.03) for liver-related mortality in those with type 2 diabetes and 3.30 (95% CI, 1.76-6.18) for overall mortality. [22]

It is also reported that the survival rates of cirrhotic patients with type 2 diabetes were significantly lower than those with normal glucose tolerance. Several studies have demonstrated an increased incidence of diabetes among patients with hepatocellular carcinoma ranging from 2- to 4-fold. [23] Type 2 diabetes seems to play an etiologic role in hepatocellular carcinoma cirrhosis independently of alcohol, viral hepatitis, or demographic features, [24] although the risk of hepatocellular carcinoma increases up to 10-fold when viral hepatitis and

hazardous alcohol consumption are combined with type 2 diabetes. [25]

CONCLUSION:

After careful consideration, it can be concluded that eventual glycemic control has a lot of potential to be used as a prognostic indicator as is evident from our finding that mortality rate and glycemic control align well together. Further prospective research is needed to cement this prognostic association.

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