Diabetes Mellitus in Association with Hepatic Encephalopathy in Patients with HCV Cirrhosis: Correlation with ICU Outcome

Thesis submitted for partial fulfillment of Master Degree

in Critical Care Medicine

Investigator

Mohammed Amin Abdel Ghany

M.B.B.CH

Supervisors

Dr. Hassan Khaled, MD.

Prof. & Chief of Critical Care Medicine
Critical Care Medicine Department
Cairo University

Dr. Hazem Hossam, MD.

Lecturer of Critical Care Medicine,
Critical Care Medicine Department
Cairo University

Dr. Ashraf Abdel Khaleq, MD

Lecturer in the ICU. Department,
Theodor Bilharz
Research Institute

Cairo University

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Abstract

Background: There is growing evidence to support the concept that HCV infection is a risk factor for developing type 2DM (T2DM) & that diabetes control could affect the prognosis of hepatic encephalopathy.

Objective: To study the relation between type of DM & HCV cirrhosis & to report any relationship between the outcome of hepatic encephalopathy & the glycemic control in the period before precipitation of encephalopathy.

Methods: A thirty selected diabetic, HCV cirrhotic patients with age range from 43:70 y (Mean: 55.87) admitted to the I.C.U. for hepatic encephalopathy were prospectively enrolled in this study. Cirrhosis was evaluated according to Child classification while encephalopathy was evaluated according West Haven criteria as well as RAS score. HbA1c was used to assess the glycemic control in the period before precipitation of encephalopathy.

Results: T2DM was more prevalent than type 1 in association with HCV (83.3%T2DM & 16.7%T1DM). Diabetes control plays no role in increasing the severity of cirrhosis (Non significant P value: 0.249). The diabetic HCV cirrhotic patients admitted for hepatic encephalopathy had shorter ICU stay when DM is well controlled medically in the period before precipitation of encephalopathy (P value: 0.001). Also the mortality was decreased markedly in association with diabetes control (P value: 0.01).

Conclusion: HCV viremia had a higher risk of T2DM than T1DM. Diabetes control has no role in increasing the severity of HCV cirrhosis. In HCV cirrhotic diabetic patients well controlled DM could improve the ICU outcome (shorter ICU stay & less mortality) when admitted for hepatic encephalopathy.

Key words: HCV cirrhosis, Child classification, Hepatic encephalopathy, DM, HbA1c.

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Mohamed Amin

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List of Abbreviations

ALT	**:**	Alanin Transaminase
AST	**:**	Aspartate Transaminase
AN	**:**	Autonomic Neuropathy
BMI	**:**	Body Mass Index
CHC	**:**	Chronic Hepatits C
CIR	**:**	Cirrhotic Patients Without Diabetes
CT	**:**	Computed Tomography
CPS	**:**	Cycle Per Second
DM	**:**	Diabetes Mellitus
EEG	**:**	Electroencephalogram
GIT	**:**	Gastrointestinal Tract
HE	**:**	Hepatic Encephalopathy
HGO	**:**	Hepatic Glucose Output
HBV	**:**	Hepatitis B Virus
HCV	**:**	Hepatitis C Virus
HDV	**:**	Hepatitis D Virus

IFG	**:**	Impaired Fasting Glucose
IGT	**:**	Impaired Glucose Tolerance
IRS	**:**	Insulin Receptor Substrate
ICU	**:**	Intensive Care Unit
INR	**:**	International Normalized Ratio
MMP	**:**	Matrix Metalloproteinases
MODY	**:**	Maturity Onset Diabetes Of The Young
MELD	**:**	Model For End Stage Liver Disease
OCT	**:**	Orocecal Transit
PDGF	**:**	Platelet-Derived Growth Factor
PV	**:**	Portal Vein
PT	**:**	Prothrombin Time
RBS	**:**	Random Blood Suger
RASS	**:**	Richmond Agitation Sedation Scale
TIMPs	**:**	Tissue Inhibitors Of Metalloproteinases
TGF B1	**:**	Transforming Growth Factor B1
T1DM	**:**	Type 1 Diabetes Mellitus
T2DM	**:**	Type 2 Diabetes Mellitus

Contents

Introduction

Introduction

HCV is considered one of the most important causes of liver cirrhosis worldwide. Replication of HCV in diseased extra hepatic organs and tissues may have cytopathic effect. It, therefore, may either trigger latent autoimmunity or induce *de novo* an autoimmune disease. In addition to established liver injury there are multiple examples of extrahepatic diseases attributed to HCV infection such as thyroiditis, thrombocytopenia, lichen planus, arthritis, glomerulonephritis and diabetes mellitus ***(1).***

The pathogenesis of type 2 DM is related to insulin secretion, peripheral insensitivity to insulin and hepatic glucose production. So, the association between HCV and type 2 DM could simply reflect the underlying liver disease and the severity of HCV related liver disease was associated with a deterioration in insulin sensitivity resulting in impaired glucose homeostasis ***(2).***

Type 1 DM was not proved to be associated with HCV infection but there are seven studies on HCV infected patients proving that a risk of developing type 1 DM is present after interferon therapy due to increase in the prevalence of pancreatic auto-antibodies ***(3).***

Patients with liver cirrhosis are prone to developing cognitive dysfunction termed “hepatic encephalopathy”. The diffuse and usually reversible nature of this syndrome in chronic liver disease suggests that it is metabolic in origin. There may be factors which precipitate hepatic encephalopathy in patients with cirrhosis including constipation, GIT bleeding, high protein diet, electrolyte imbalance (e.g., hypokalemia), or drugs (e.g., sedatives). The severity of hepatic encephalopathy is not related to the severity of liver disease suggesting that other predisposing or precipitating factors may be involved ***(4)***.

Sigal et al. (5) reported that the presence of DM may be another factor in the pathogenesis of hepatic encephalopathy at least in HCV cirrhotic patients and they used in their study the Child Poughs classification to assess the severity of cirrhosis in addition to measurement of the portal hypertension ultrasonographically and they reported that poor diabetes control may be associated with more severe hepatic encephalopathy.

Aim of The Work

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To study the relation between type of DM & HCV cirrhosis & to report a relationship between the outcome of hepatic encephalopathy & the glycemic control in the period before precipitation of encephalopathy.

Review Of Literature