Effect of Chronic Liver Disease on Prognosis of Type II Diabetes Mellitus And Effect of Type II Diabetes Mellitus on the Liver

Thesis

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تأثير أمراض الكبد المزمنه على مرض السكر من النوع الثاني وتأثير مرض السكر من النوع الثاني على الكبد

رسالة

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مقدمه من الطبيب

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List of Abbreviations

Abb.	Meaning
ADA	: American diabetes association
AHRQ	: Agency for Healthcare Research and Quality
BCAA	: Branched chain amino acids
BMI	: Body mass index
CAD	: Coronary artery disease
CANOE	: Canadian Normoglycemia Outcome and Evaluation
CDC	: Centers for Disease Control and Prevention
CTGF	: Connective tissue growth factor
DKA	: Diabetic ketoacidosis
DNA	: Deoxyribonucleic acid
DPP	: Diabetes Prevention Program
DPP-4	: Dipeptidyl peptidase 4
DREAM	: Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication
EASD	: European Association for the Study of Diabetes
ECM	: Extracellular matrix
eGFR	: Estimated glomerular filtration rate
EV	: Esophageal varices
FDA	: Food and Drug Administration
FFAs	: Free fatty acids
FPG	: Fasting plasma glucose
GE	: Gastro-esophageal
GLP-1	: Glucagon-like peptide-1
GLP-1	: Glucagonlike peptide-1 agonists
HbA1C	: Hemoglobin A1C
HBSAg	: Hepatitis B surface antigen
HCC	: Hepatocellular carcinoma
HCV	: Hepatitis C virus
HDL	: High density lipoprotein

HE : hepatic encephalopathy
HOMA-IR : Homeostasis model assessment of insulin resistance
HPS : Hepatopulmonary syndrome
HRS : Hepatorenal syndrome
HSCs : Hepatic stellate cells
HVPG : Hepatic venous pressure gradient
IFG : Impaired fasting glucose
Ig : Immunoglobulin
IGF-1 : Insulin-like growth factor 1
IGT : Impaired glucose tolerance
IL-1 : Interleukin
IR : Insulin resistance
KCs : Kupffer cells
LDL : Low density lipoprotein
LSECs : Liver sinusoidal endothelial cells
MELD : Model for End-Stage Liver Disease
MODY : Maturity onset diabetes of youth
NAFLD : Nonalcoholic fatty liver disease
NASH : Nonalcoholic steatohepatitis
OGTT : Oral glucose tolerance test
PCOS : Polycystic ovary syndrome
PDGF : Platelet-derived growth factor
PH : Portal hypertension
PHG : Portal hypertensive gastropathy
ROS : Reactive oxygen specious
SAAG : Serum: ascites albumin gradient
SBP : Spontaneous bacterial peritonitis
SGIT-2 : Selective sodium-glucose transporter-2 inhibitors
SOCS : Suppressor of cytokine signaling
SVR : Sustained virological response
T2DM : Type 2 diabetes mellitus
TGF : Transforming growth factor
TNF- alfa : Tumer necrosis factor-alpha
TZD : Thiazolidinediones

INTRODUCTION

The spectrum of liver disease in patients with type II diabetes includes abnormal liver enzymes, nonalcoholic fatty liver disease, cirrhosis, hepatocellular carcinoma, and acute liver failure ***(Trombetta et al., 2005).***

The presence of HCV infection in patients with DM increases the proportion of DM-related chronic complications. In fact, there are some reports showing that HCV infection is associated with an increased risk of developing diabetic nephropathy ***(Pagano et al., 2005).***

There is an unexplained association of diabetes with hepatitis C, the prevalence of diabetes in cirrhosis is 12.3-57%. So, patients with diabetes have a high prevalence of liver disease and patients with liver disease have a high prevalence of diabetes ***(Trombetta et al., 2005).***

Liver disease is an important cause of death in type II diabetes. Cirrhosis was the fourth leading cause of death and accounted for 4.4% of diabetes related deaths ***(De Marco et al., 1999).***

Up to 96% of patients with cirrhosis may be glucose intolerant and 30% may be clinically diabetic ***(Hickman and Macdonald, 2007).***

In Egypt, the prevalence of DM was 25.4% among HCV patients. Chronic hepatitis C patients are three times more likely to develop DM than HCV seronegative patients ***(El-Zayadi et al., 1998).***

Cheruvattath and Balan (2007), reported that the mechanisms by which diabetes worsens the clinical course of liver cirrhosis have not been clearly established. ***Firstly***, DM accelerates liver fibrosis and inflammation giving rise to more severe liver failure. ***Secondly***, DM may potentiate the incidence of bacterial infections in cirrhotic patients which are associated with increased mortality.

It is a matter for debate whether type 2 diabetes mellitus (DM), in the absence of other risk factors contributing to metabolic syndrome (obesity and hypertriglyceridemia), could be a risk factor for the development and progression of liver disease (***El-Serag et al., 2004)***. On the other hand, the diabetes which develops as a complication of cirrhosis is known as "hepatogenous diabetes" and is not recognized by the American

Diabetes Association and the World Health Organization as a specific independent entity ***(Holstein et al., 2002)***.

The pathophysiology of hepatogenous diabetes is complex and not precisely known. Insulin resistance in peripheral tissues (adipose and muscular tissue) plays a central role in glucose metabolism disturbance ***(Hickman and Macdonald, 2007)*.**

AIM OF THE WORK

To assess the effect of chronic liver disease on type II diabetes mellitus and the effect of type II diabetes mellitus on chronic liver disease patients.

Chapter I

CHRONIC LIVER DISEASES

Definition

Chronic liver diseases describe persistent inflammation of the liver for 6 months or more after initial exposure and/or initial detection of liver disease ***(Dove and Wright, 2004)***.

Causes of Chronic Liver disease

There are 4 main causes of chronic liver diseases:

I. Viral infection

1- Hepatitis C:

Hepatitis C virus **(HCV)** is among the leading causes of chronic liver disease worldwide ***(*Chen and Morgan, 2006*).*** Egypt has the highest prevalence of **HCV** infection of any country in the world, the situation is quite worse, the overall prevalence (percentage of people) positive for antibody to **HCV** was 14.7% ***(El-Zanaty et al., 2009).***

2- Hepatitis B:

Hepatitis B virus **(HBV)** infection is a global health problem, its patterns of transmission vary greatly throughout the world. Furthermore, the consequences

of chronic **HBV** infection represent a major burden for health care systems because a large proportion of these patients go on to develop cirrhosis and hepatocellular carcinoma ***(El-Zayadi, 2007).***

The prevalence of **HBsAg** in Egypt is of intermediate endemicity (2–8%). Nearly 2-3 million Egyptians are chronic carriers of **HBV**. In Egypt **HBV** transmission is apparently a mixture of horizontal and perinatal transmission. However, the majority of HBV infection is acquired by the former route ***(El-Zayadi, 2007).***

II. Auto immune liver disease

1- Auto immune (lupoid) hepatitis:

Commonly seen in females, histologically classified by appearance of chronic active hepatitis dominated by numerous plasma cells and swollen liver cell arranged in rosette-like forms, auto antibodies to smooth muscle antigens are often present ***(Thomas et al., 2001)***.

2- Primary biliary cirrhosis:

Chronic disorders affect mainly middle-aged females. Liver biopsy shows bile duct obstruction, granulomas, ductular proliferation, fibrosis and eventual cirrhosis ***(Thomas et al., 2001)***.