Serum Level of Omentin-1 in Hepatitis C Decompensated Liver Disease with and without Diabetes Mellitus

Thesis

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*"To my dear **Father** for his help and to my beloved **Mother** and my **brothers** for their care and support*

*And to my dear **Wife** who was and still supporting me in all my hard times and to my beautiful daughter, **batool***

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List of Abbreviations

Abb.	Full term
AFP	Alpha feto protein
AKT	Tyrosine Kinase Activator
ALT	Alanine aminotransaminase
AST	Aspartate aminotransaminase
BMI	Body mass index
CBC	Complete blood count
CHC	Chronic Hepatitis C
CLD	Chronic Liver Disease
CRP	C-reactive protein
CTP	Child Turcotte Pugh
CVD	Cardiovascular disease
DAAs	Direct acting agents
DL	Decileter
DM	Diabetes mellitus
DPP-4	Dipeptidyl Peptidase-4 Inhibitors
EASL	The European Association for the Study of the Liver
EDTA	Ethylenediamine Tetra-Acetic Acid
EIA	Enzyme-linked immunoassays
ELISA	Enzyme linked immunosorbant assay
EORTC	The European Organization for Research and Treatment of Cancer
FDA	Food and Drug Administration
FPG	Fasting plasma glucose
FPS	Fasting plasma sugar
GDM	Gestational diabetes mellitus
GFR	Glomerular filtration rate
GH	Glycogenic Hepatopathy
GLP-1	Glucagon-like peptide-1
Hb	Haemoglobin
HBsAG	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma

List of Abbreviations *cont...*

Abb.	Full term
HCV Ab	Hepatitis C virus antibody
HCV	Hepatitis C virus
HD	Hepatogenous diabetes
HDL	High density lipoprotein
HE	Hepatic encephalopathy
HIV	Human immunodeficiency virus
HOMA IR	Homeostasis Model Assessment of insulin Resistance
HRS	Hepato Renal Syndrome
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IL-6	Interleukin-6
INR	International Normalized Ratio
IR	Insulin Resistance
IU	International unit
Kg	Kilogram
L	Liter
LDL	Low density lipoprotein
MELD	Model for end-stage liver disease
mg	Milligram
mL	Milliliter
NAFLD	Non-alcoholic fatty liver disease
NS5	Nonstructure viral protein 5
OGTT	Oral glucose tolerance test
PCOS	Polycystic ovary syndrome
PCR	Polymerse chain reaction
PEG-IFN	Pegylated interferon
PG	Plasma glucose
PI3K	Phosphatidylinositol 3 kinase
PLT	Platelets
PT	Prothrombin time
RIBA	Recombinant immunoblot assay
RNA	Ribonucleic acid

List of Abbreviations *cont...*

Abb.	Full term
ROC	Receiver operating characteristic
ROS	Reactive oxygen species
SBP	Spontaneous Bacterial Peritonitis
SD	Standard Deviation
SGLT 2	Sodium glucose co-transporter 2
SVR	Sustained virological response
T2DM	Type 2 diabetes mellitus
TNF	Tumor necrosis factor
TNF	Tumor necrosis factor
TZDs	Thiazolidinediones
US	Ultrasonogrphy
USA	United State of America
WBC	White blood cell
WHO	World Health Organization

Abstract

In the current study, there was no significant association between serum omentin level and age or gender in CLD patients.

BMI and body weight were found to be inversely correlated with serum omentin level. Fasting blood sugar and HbA1c were found to be negatively correlated with serum omentin level.

We reported a significant +ve correlation between serum omentin level and severity of liver disease according to Child-Pugh score.

We found no significance of HCC or serum level of creatinine on the serum level of omentin.

Keywords: Hepatogenous diabetes -Hepatitis C virus -High density lipoprotein -Impaired glucose tolerance-Interleukin-6

INTRODUCTION

The liver is a vital organ, it has a wide range of functions, including detoxification, protein synthesis, and production of biochemicals necessary for digestion. The liver is necessary for survival; there is currently no way to compensate for the absence of liver function in the long term, although new liver dialysis techniques can be used in the short term ***(Cotran et al., 2005)***.

Hepatitis C virus (HCV) is an enveloped, single stranded RNA virus of the family Flavi-viridae. It is of high revalence and endemicity in Egypt and is considered the most important cause of liver disease in Egypt. Infection with the hepatitis C virus causes inflammation of the liver and a variable grade of damage to the organ. Over several decades this inflammation and grade change can lead to cirrhosis. Among patients with chronic hepatitis C 10-20% will develop cirrhosis ***(Friedman, 2014).***

There is a number of clinically important complications which often emerge in the course of advanced liver disease, independently of the underlying liver disease. When these complications are overt, it is called decompensated liver disease ***(Rahimi and Rockey, 2011).***

Decompensated liver disease is a state of liver disease in which any of the following complications may be manifested and obvious on the patients such as bleeding varices, hepatic

encephalopathy, ascites, hepatorenal syndrome, spontaneous bacterial peritonitis or jaundice.

HCV infection as shown by many studies was demonstrated to be associated with Insulin resistance and type 2 diabetes development. Insulin resistance and type 2 diabetes during the course of HCV can indicate a more rapid progression of liver fibrosis and are considered independent predictors of impaired response to treatment. Patients with type 2 diabetes and insulin resistance are also at increased risk for HCC ***(Hung et al., 2010; Petta et al., 2008)***.

Successful treatment of HCV now is considered an important factor in reducing insulin resistance and reduction of incidence of new onset of type 2 diabetes and insulin resistance in HCV-infected patients. Antiviral treatment of HCV has been demonstrated to improve clinical outcomes and complications related to diabetes ***(Arase, 2009)***.

Omentin-1, a novel adipokine, which is highly expressed by visceral adipose tissue compared with subcutaneous adipose tissue. Omentin-1 was shown to be inversely correlated to insulin resistance and high blood glucose levels.

Recently, in vitro experiments demonstrated that treatment with recombinant omentin-1 enhances insulin-stimulated glucose uptake in human subcutaneous and omental adipocytes and thus, improving insulin sensitivity. Also, omentin-1 was shown to

trigger Akt signaling in both the absence and presence of insulin. Furthermore, omentin plasma levels and omentin gene expression in visceral adipose are decreased in obesity.

Moreover, omentin-1 was found to be elevated in patients with liver cirrhosis. And it was found to be high in patients with fatty liver disease.

However, the role of omentin-1 in the chronic hepatitis C and its metabolic consequences is not obvious yet.

This is the cause that led us to conduct the present study in which we investigated the levels of omentin-1 in sera of patients with HCV decompensated liver disease, with and without type 2 diabetes, and compared them with its levels in apparently healthy controls.