Insulin Resistence As A Non Invasive Predictor of Esophageal Varices in Patients with Chronic Liver Diseases

A thesis submitted for partial fulfillment of master degree in internal medicine.

Submitted by

Amr Mohammad Ibrahim Ali Al-Sharawy

M.B. B. CH.
Ain Shams University

Under the Supervision of

Professor, Doctor/Mohsen Mostafa Maher

Professor of internal medicine
Faculty of medicine Ain Shams University

Professor, Doctor/Emad Ahmad Awad Hussein

Professor of internal medicine
Faculty of medicine Ain Shams University

Doctor/Wesam Ahmad Ibrahim Mohammed

Lecturer of internal medicine
Faculty of medicine Ain Shams University

Faculty of medicine
Ain Shams University
2011

Acknowledgement

First and foremost thanks to ALLAH, the most merciful.

I wish to express my deepest appreciation and sincere gratitude to **Prof. Dr. Mohsen Mostafa Maher**, Prof. of Internal Medicine, Faculty of Medicine, Ain Shams University, for his continuous encouragement, kind supervision, valuable instructions and sincere advice which have been the main factors to complete this work. It was a great honor to me to work under his supervision.

Words can never express my deepest gratitude, appreciation and greatest respect to **Prof. Dr. Emad Ahmad Awad Hussein**, Prof. of Internal Medicine, Faculty of Medicine, Ain Shams University, for his close supervision, continuous guidance, great help and indispensable advice in every step of this work. He has generously devoted much of his valuable time, experience and effort for planning and supervision of this work and for presenting it in an ideal form.

I am also delighted to express my supreme gratitude and everlasting appreciation to **Dr. Wesam Ahmad Ibrahim Mohammed**, Lecturer of Internal Medicine, Faculty of Medicine, Ain Shams University, for her keen supervision, great support, endless help and continuous guidance during all stages of this work.

Also, I wish to introduce my deep respect and thanks to **Prof. Dr**. **Abd AL-Baset Al-Sharawy,** Prof. of Internal Medicine, Faculty of Medicine, Ain Shams University for his great effort in discussing this work. He has generously supervised this work in a supportive and educational way.

I am endlessly grateful to **Prof. Dr.Ahmed El-Sawy** Prof. of Internal Medicine, Military Medical Academy, for his sincere advice and great effort in performing this work. His generous participation and valuable cooperation in this work are greatly appreciated.

Last, but not least, I am also delighted to express my deep gratitude and thanks to all my dear professors, my parents, my wife and my colleagues that without their help, this work could not have been completed.

Table of Contents

Table of Figures

Table of Tables

List of Abbreviations

AASLD:	American Association for the Study of Liver Disease
ALT:	Alanine Aminotransferese
APC:	Argon plasma coagulation
AST:	Aspartate Aminotransferese
BRTO:	Balloon-Occluded Retrograde Transvenous Obliteration
BUN:	Blood Urea Nitrogen
Cb:	Color blue
CHA:	Coded Harmonic Angio
CRS:	Cherry Red Spot
CT:	Computerized Tomographic
CTP	Child Tourqote Pugh
Cw:	Color white
DM:	Diabetes Mellitus
DR:	Diffuse Redness
ELISA:	Enzyme-linked immunosorbent assay
EV:	Esophageal varices
EVL :	Endoscopic variceal ligation

EVS :	Endoscopic variceal sclerotherapy
EVSL:	Endoscopic variceal scleroligation
FHVP:	Free hepatic venous pressure
GGT:	Gamma Glutamyl Transferase
GIT:	Gastrointestinal tract
GOV:	Gastroesophageal varices
GRS:	Gastrorenal shunt
GTT:	Glucose tolerance testing
GVL:	Gastric variceal ligation
GVS:	Gastric Variceal Sclerotherapy
GVs:	Gastric varices
HBs Ag:	Hepatitis B surface antigen
HCS:	Hematocystic Spots
HCV Ab:	Hepatitis C virus antibody
HCV:	Hepatitis C virus
HFCS:	High fructose corn syrup
HOMA:	Homeostatic model assessment
HVPG:	Hepatic venous pressure gradient

IGT:	Impaired glucose tolerance
IGV:	Isolated gastric varices
IR:	Insulin Resistance
ISDN:	Isosorbide dinitrate
ISMN:	Isosorbide 5-mononitrate
IVC:	Inferior vena cava
LAR:	long acting release
MDSL:	Mini-Detachable Snare Ligation
OGTT:	Oral Glucose Tolerance Test
PCOS:	Polycystic ovary syndrome
PT:	Prothrombin time
QUICKI:	Quantitative insulin sensitivity check index
ROC :	Receiver Operating Characteristic
RWM:	Red Wale Markings
S.C:	Subcutaneous
SAAG:	Serum-Ascites Albumin Concentration Gradient
SI:	Splenic index
SMS:	Somatostatin
tGLVP:	Terlipressin, Triglycyl-Lysine Vasopressin

TIPS:	Transjugular Intrahepatic Portosystemic Shunt
TNF-α:	Tumor Necrosis Factor Alfa
WHVP:	Wedged hepatic venous pressure

Introduction

Introduction

Esophageal varices (EV) are extremely dilated sub-mucosal veins in the lower esophagus. EV are most often a consequent of portal hypertension, commonly due to cirrhosis. Patients with esophageal varices have a strong tendency to develop bleeding. Esophageal varices are diagnosed with endoscopy ***(Biecker et al., 2005).***

Normal portal pressure is approximately 9 mmHg compared to an inferior vena cava pressure of 2-6 mmHg. This creates a normal pressure gradient of 3-7 mmHg. If the portal pressure rises above 12mmHg, this gradient rises to 7-10 mmHg. A gradient greater than 5 mmHg is considered portal hypertension ***(Arguedas, 2003).***

In patients with Child A HCV cirrhosis, two simple, easy-to-get tests, namely the platelet/spleen ratio and insulin resistance (IR) measured by Homeostatic model assessment (HOMA), regardless of the presence of diabetes, significantly predict the presence of esophageal varices , outweighing the contribution given by transient elastography ***(D'Amico and Morabito, 2004).***

Insulin resistance (IR) is commonly associated with hepatitis C virus (HCV) infection, and development of IR can occur early in the course of HCV infection. The exact pathogenic mechanisms responsible for this association are still unknown; however, they may be related to both HCV itself and to liver injury. IR is a major independent determinat of fibrosis in chronic HCV infection, regardless of the genotype and the severity of liver damage ***(Camma, et al., 2009).***

Both IR and beta-cell dysfunction contribute to glucose intolerance in patients with chronic HCV. In addition, IR may be the earliest abnormality in this process, which in the following years may progress to glucose intolerance and also diabetes mellitus (DM). Thus, impaired glucose tolerance (IGT) has been reported in HCV-infected patients before the onset of cirrhosis. HCV infection also is associated with an increased prevalence of diabetes mellitus. These data indicate the specific

role of HCV in the evolution of impaired insulin action and IGT, independent from the development of cirrhosis ***(Qamar, et al., 2007).***

Insulin resistance, regardless of the presence of diabetes, significantly predicts the presence of esophageal varices (EV), in subjects with HCV-related cirrhosis. In order to reduce the need for endoscopic procedures, the development of a noninvasive tool for the-prediction of presence of EV is an important issue in subjects with cirrhosis ***(Camma, et al., 2009).***

Aim of Work

Aim of Work

The aim of work was to evaluate insulin resistance (IR) as a non invasive predictor of esophageal varices in patients with chronic liver diseases.

Review