Estimate of the pattern and prevalence of alterations of glucose metabolism in diabetic and non-diabetic HCV cirrhotic patients

Thesis

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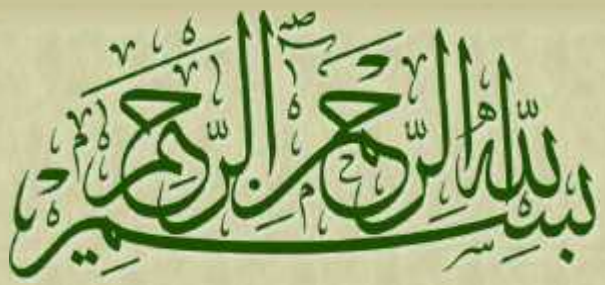

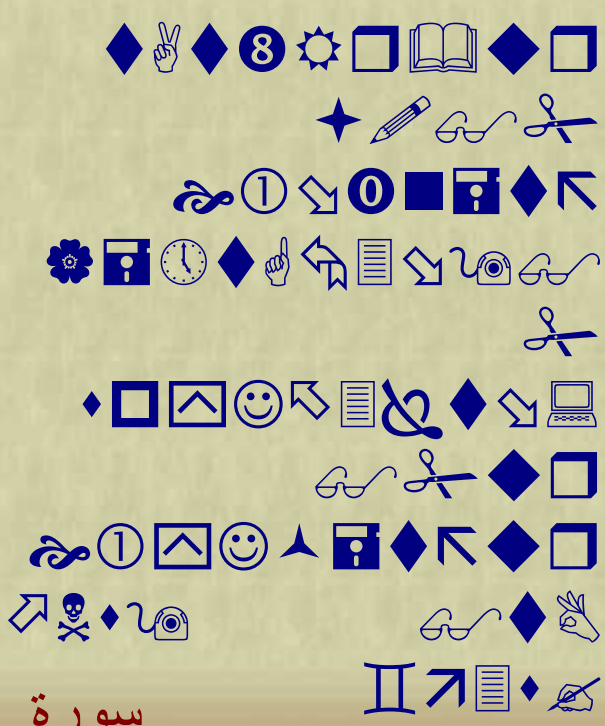

سورة

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List of Abbreviations

Abbrev.	Meaning
AVH ……..	Acute viral hepatitis
ALT…….	ALanine amino-Transferase
AST…….	ASpartate amino-transferase
AFP…….	Alpha Feto Protein.
ASB……...	Asymptomatic Bacteriuria
Akt…….	The serine/threonine kinase Akt or protein kinase B (PKB) is a downstream effector of phosphatidylinositol 3 (PI 3)-kinase. It was shown to be the mediator of growth factor-dependent cell survival in a variety of cell types.
BMI……..	Body Mass Index
BP…….	Blood Pressure
CMV……...	Cytomegalovirus.
CTL……...	Cytotoxic T Lymphocyte.
DIE……..	Diabetes In Egypt
DM……	Diabetes Mellitus
EIAs……..	Enzyme Immunoassays
ESRD…….	End Stage Renal Disease
EVR……	Early Viral Response
GADA……	Glutamic Acid Decarboxylase Antibodies
GGT……	Gamma-Glutamyl-Transpeptidase
GLP……	Glucagons-Like Peptide
GM-CSF…….	Granulocyte/Monocyte Colony Stimulating Factor
HBc…….	Hepatitis B core.
HbsAg…….	Hepatitis B surface Antigen.
HBV……	Hepatitis B Virus
HCC……...	Hepatocellular Carcinoma.
HCV ……..	Hepatitis C Virus
HDL……..	High Denisty Lipoprotein

Abbrev.	Meaning
HIV……	Human Immunodeficiency Virus
HNF-4α……	Hepatic Nuclear Factor-4α.
HRQOL……	Health-Related Quality Of Life.
HOMA IR…….	Homeostasis Model Assessment for Insulin Resistance
ICA……	Islet Cell Antibody
IDDM…….	Insulin-Dependent Diabetes Mellitus
IFG……	Impaired Fasting Glucose
IFN…….	Interferon
IGFBP-1……...	Insulin-Like Growth Factor-Binding Protein-
IGT……	Impaired Glucose Tolerance
IL……...	Interleukin
IPF-1……...	Insulin Promoter Factor-1
IR…….	Insulin Receptor.
IRES……	Internal Ribosome Entry Site
IRS…….	Insulin Receptor Substrate
IRS-1…….	Insulin Receptor Substrate-1
IRS-2…….	Insulin Receptor Substrate-2.
Ire…….	Insulin Resistance
JNC……...	Joint National Committee
LADA……...	Latent Autoimmune Diabetes of the Adult
LADY……..	Latent Autoimmune Diabetes in Youth
LFA……	Lymphocyte Function-associated Antigen
MODY…….	Maturity-Onset Diabetes in Youth.
MPG……	Membrano-Proliferative Glomerulonephritis
NAC……	N-Acetyl Cysteine
NASH……	Non-Alcoholic Steatohepatitis
NAT…….	Nucleic Acid Amplification Technology
NCR……	Non-Coding Gene
NHANES III……..	The Third National Health and Nutrition Examination Survey.
NHL…….	Non Hodgkin's Lymphoma
NIDDM……..	Non Insulin-Dependent Diabetes Mellitus

Abbrev.	Meaning
NK…….	Natural Killer
NSAIDs……..	Non Steroidal Anti-Inflammatory Drugs
OGTT……	Oral Glucose Tolerance Test
PAT……	Parenteral Antischistosomal Therapy
PCR…….	Polymerase Chain Reaction
PEG-IFN=PegIFN…….	Pegylated Interferon
PEPCK……...	Phosphoenolpyruvate Carboxykinase
PI…….	Pro-Insulin
PI3K……..	Phosphatidylinositol 3-kinase.
2hrPPG…….	Two-hour Postprandial Plasma Glucose
PTDM……	Posttransplantation Diabetes Mellitus.
RBV……	Ribavirin
ROM……..	Reactive Oxygen Metabolites
ROS……..	Reactive Oxygen Species
RT-PCR……...	Reverse Transcriptase Polymerase Chain Reaction
SBP……...	Systolic Blood Pressure
SCD4……..	stearoyl coenzyme A desaturase 4
SREBP-1……	Sterol Regulatory Element Binding Protein-1c
STAT-3……..	Signal Transducer and Activator of Transcription 3
SOC……	Suppressor of Cytokine signaling
SST…….	Sho-Saiko-To.
SVR……	Sustained Virological Response
T1DM…….	Type 1 Diabetes Mellitus=IDDM
T2DM……..	Type 2 Diabetes Mellitus= NIDDM
TGF-β……...	Transforming Growth Factor-beta
TIW……	Three Times per Week
TT……...	Triple Therapy.
WHO……..	World Health Organization
UDCA…….	UrsoDeoxyCholicAcid.

INTRODUCTION

Hepatitis C virus (HCV) is considered the most common etiology of chronic liver disease (CLD) in Egypt, where prevalence of antibodies to HCV (anti-HCV) is approximately 10-fold greater than in the United States and Europe ***(Strickland, et al., 2002).*** Egypt has the highest worldwide prevalence of HCV (10-20%) ***(Ray et al., 2000 and Kamal & Nasser, 2008).***

The majority of infected individuals (60-80%) develop chronic hepatitis C (CHC), which is associated with progressive liver fibrosis and a 3-9% risk of cirrhosis after 20 years ***(Freeman et al., 2001)***. CHC is also associated with significant morbidity and mortality, accounting for 50-76% of all liver cancer cases worldwide, and two thirds of liver transplants in the developed world ***(WHO, 2008).***

Strickland *in* ***(2006)*** reported that, in Egypt, schistosomiasis was traditionally the most important public health problem and infection with Schistosoma mansoni is the major cause of liver disease.

It is now widely recognized that CHC is associated with insulin resistance (IR) and type 2 diabetes (T2DM), so can be considered a metabolic disease. Apart from the well-described complications of diabetes, IR in CHC predicts faster progression to fibrosis and cirrhosis that may end in liver failure and hepatocellular carcinoma (HCC). More recently, it has been recognized that IR in CHC predicts a poor response to antiviral therapy ***(Douglas and George, 2009).***

A previous study of cirrhotic patients confirmed that T2DM was present in 21% of patients with cirrhosis due to CHC. Significantly, subsequent case control studies have confirmed that T2DM is associated with CHC even in the absence of cirrhosis ***(Knobler et al., 2000 and Antonelli et al., 2005)***.

Of relevance, it has been previously reported that there was no association between CHC and type 1 diabetes, and no association of hepatitis B virus infection with T2DM, suggesting a virus-specific association of HCV with T2DM ***(Douglas and George, 2009).*** It was also noted that HCV-associated T2DM mainly occurred in patients with other risk factors for diabetes, such as older age and a high body mass index ***(Mehta et al., 2003).***

Insulin resistance is present in > 90% of individuals before the onset of frank T2DM. The homeostasis model of insulin resistance (HOMA-IR) was used to diagnose IR, calculated by the following equation: **HOMA-IR = fasting glucose (mg/dL) × fasting insulin (μU/mL)/405** ***(Matthews et al., 1985).*** Typically, a HOMA-IR value > 2 is used as a significant indicator of IR ***(Douglas and George, 2009).***

Hui et al. (2003) first reported that IR is increased in patients infected with HCV, particularly genotype 1. Subsequent studies have confirmed this association for genotype 4 ***(Moucari et al., 2008)*** and possibly also genotype 2a ***(Negro, 2006).***

The mechanisms of HCV-induced IR occur through increased levels of interleukin (IL)-1, tumor necrosis factor (TNF)-α, IL-6 and leptin, and reduced levels of adiponectin ***(Bugianesi et al., 2005).***

Aim of the study

The aim of the present study is to estimate the pattern and prevalence of glucose intolerance and alterations of glucose metabolism in diabetic and non-diabetic HCV cirrhotic patients