The Relation between Glycated Haemoglobin and Fatty Liver in Non Diabetic Patient

Thesis

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God send peace upon soul of my mother

Hanaa Ahmed Hassan

I dedicate this work to the soul of my **mother**, my **father** my **husband** and my **son**.


بسم الله الرحمن الرحيم
"قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ
مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ
الْحَكِيمُ"
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Contents

List of Abbreviations

Abb.	Meaning
A1C	Glycated haemoglobin
AAR	AST/ALT ratio
AASLD	American Association for the Study of Liver Diseases
ACEIs	Angiotensin converting enzyme inhibitors
ALT	Alanine aminotransferase
AMPK	AMP dependent protein kinase
Apaf-1	Apoptotic-protein activation factor-1
apo B	Apolipoprotein B
APRI	AST-to-platelet ratio index
ARBs	Angiotensin receptors blockers
ART	Anti-retroviral therapy
AST	Aspartate aminotransferase
AUROC	Area-under-the-receiver-operating-characteristic curves
BMI	Body mass index
BP	Blood pressure
BSG	British Society of Gastroenterology
CC	Cryptogenic cirrhosis
CHD	Coronary heart disease
CI	Confidence interval
CK-18	Cytokeratin-18
CRP	C reactive protein
CT	Computed tomography
CVD	Cardiovascular disease

Abb.	Meaning
FFA	Free fatty acids
FLI	Fatty liver index
FRAX tool	The Fracture Risk Assessment Tool
GGT	Gamma-glutamyl transferase
GLP-1	Glucagon-like peptide-1
GSH-Px	Glutathione peroxidase
HA	Hyaluronic acid
HbA1C	Glycated haemoglobin
HBc-Ab	Hepatitis B core antibody
HBs.Ag	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HCV-Ab	Hepatitis C virus antibody
HDL	High density lipoprotein
HIV	Human immunodeficency virus
HMG-COA	3-hydroxy-3-methyl-glutaryl-CoA reductase
IKB	Inhibitory KB
IKK	Inhibitory –KB Kinase
IL	Interleukin
IR	Insulin resistance
LAP	Lipid accumulation product
LB	Liver biopsy
LCTs	Liver chemistry tests
LDL	Low-density lipoprotein
LFC	Liver fat content
LFTs	Liver functions tests

Abb.	Meaning
LKB1-mediated AMPK	LKB1 gene mediate activation of hepatic AMP-protein kinase
LPS	Lipopolysaccharides
MAPK	Mitogen activated protein kinase
MRI	Magnetic resonance imaging
MRS	Magnetic Resonance Spectroscopy
MTP	Microsomal triglyceride transfer protein
NAFL	Nonalcoholic fatty liver
NAFLD	Non-alcoholic fatty liver disease
NAS	NAFLD Activity Score
NASH	Non-alcoholic steatohepatitis
NEFAs	Nonsterified fatty acids
NF-KB	Nuclear factor -KB
NFS	NAFLD fibrosis score
OR	Odd ratio
OSA	Obstructive sleep apnoea
PAI-1	Plasminogen activator inhibitor-1
PPAR	Peroxisome proliferator-activated receptor gamma
PUFAs	Polyunsaturated fatty acids
RAS	Renin–angiotensin system
RCT	Randomised control trial
ROS	Reactive oxygen species
SNP	Single nucleotide polymorphism
SREBP	Sterol regulatory element binding protein
T2DM	Type 2 diabetes mellitus

Abb.	Meaning
TG	Triglycerides
TGF B	Transforming growth factor-beta
TNF α	Tumor necrosis factoralpha
TPN	Total parental nutrition
TRX	Thioredoxin
TZDs	Thiazolidinediones
UDCA	Ursodeoxy cholic acid
US	Ultrasonography
VAI	Visceral adiposity index
VLDL	Very low density lipoprotein
WAT	White adipose tissue
WC	Waist circumference

List of Tables

List of Figures

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is an increasingly common cause of chronic liver disease world-wide. It comprises a disease spectrum ranging from benign hepatic steatosis to non-alcoholic steatohepatitis with inflammation (NASH) and liver cirrhosis. Although simple steatosis appears to be benign, NASH can progress to cirrhosis with its resultant complications, including hepatocellular carcinoma (HCC). It is increasingly recognised that NASH accounts for a significant proportion of "cryptogenic" or "idiopathic" cirrhosis **(Tan, 2010).**

Nonalcoholic fatty liver disease (NAFLD) has gained recognition worldwide as a common chronic liver disease and as a cofactor in other diseases. The subclinical nature of the disease has lead to increased efforts to achieve its diagnosis and to prevent its potential progression to nonalcoholic steatohepatitis (NASH), liver cirrhosis and hepatocellular carcinoma **(Powell et al., 2006).**

Non alcoholic fatty liver disease is characterised by fatty infiltration of the liver, mostly in the form of triglycerides, which exceed 5% of liver weight **(Angulo et al., 2007).**

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the Western world (it

affects 30% of the general adult population) **(Musso et al., 2010).**

The NAFLD is an umbrella term for a group of diseases defined by a hepatic fat infiltration >5% hepatocyte, in the absence of excessive alcohol intake, defined by two standard drinks (20 g ethanol) daily for men and one standard drink (10 g ethanol) daily for women **(Durazzo et al., 2012).**

The NAFLD encompasses a histological spectrum ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), defined by steatosis, hepatocellular damage, and lobular inflammation in the individuals without significant alcohol consumption and negative viral, congenital, and autoimmune liver disease markers **(Farrell et al., 2005).**

While steatosis does not carry the risk of progressive liver disease, patients with NASH are at risk of developing cirrhosis (20–30% of patients) **(Farrell and Larter, 2006).**

NASH may progress to decompensated liver disease and result in liver failure. Furthermore, NASH confers an increased risk of cardiovascular disease (CVD) and diabetes both directly and through its association with other cardiometabolic abnormalities, including obesity and metabolic syndrome **(Ghouri et al., 2010).**