RELATIONSHIP BETWEEN HEPATIC/VISCERAL FAT AND INSULIN RESISTANCE IN NON-DIABETIC AND TYPE 2 DIABETIC SUBJECTS

Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

صدق الله العظيم

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List of Abbreviations

µIU/ml	:	Microinternational unit /milliliter
Ab	:	Antibody
Ag	:	Antigen
ALT	:	Alanine aminotransferase
AMPK	:	adenosine monophosphate mediated protein kinase
Apo B	:	Apolipoprotein B
AST	:	Aspartate aminotransferase
BAT	:	Brown adipose tissue
BMI	:	body mass index
cm2	:	Square centimeter
cm3	:	Cubic centimeter
CRP	:	C-reactive protein (CRP)
CT	:	Computed Tomography
CV	:	Central vein
DAG	:	Dyacylglycerol
DNL	:	De novo lipogenesis
ELISA	:	Enzyme linked immunosorbent assay
ERS	:	Endoplasmic reticulum stress
FFA	:	Free fatty acids
GLP-1	:	Glucagonlike Peptide 1
GLUT-4	:	Glucose transporter type 4
HAIR-AN	:	Hyperandrogenism, Insulin resistance, and Acanthosisnigricans Syndrome
HBcVAb	:	Hepatitis B core Antibody
HBsAg	:	Hepatitis B surface Antigen
HCC	:	Hepatocellular carcinoma
HDL	:	High density lipoprotien
HOMA-IR	:	Homeostatic model assesment for insulin resistance
HU	:	Hounsfield units
IFG	:	Impaired Fasting Glucose
IGF-1	:	Insulinlike growth Factor–1
IGFBP-1	:	Insulinlike growth Factor binding protein–1
IgG	:	Immunoglobulin G

List of Abbreviations

IgM	:	Immunoglobulin M
IGT	:	Impaired Glucose Tolerance
IR	:	Insulin Resistance
IRS1	:	insulin receptor substrate
kg/m2	:	Kilogram/Square milimetre
kg/wk	:	Kilogram /week
Kv	:	Kilovolt
L	:	Lumber
LDL	:	dense low-density lipoprotein
Log	:	Logarithm
LSR	:	Liver-to-spleen attenuation ratio
Lt	:	Left
mAs	:	Milliampere - seconds
mcg/min	:	Microgram/minute
MCP	:	monocyte chemoattractant protein
MDCT	:	Multidetector CT
mg	:	Milligrams
mg/d	:	Milligrams/day
mg/kg/d	:	Milligrams/kilogram /day
MHz	:	Millihertz
mL	:	Milliliter
mm	:	Millimeter
mm/s	:	Millimeter/seconds
mmol/kg/m3	:	Millimol/kilogram/cubic meter
mmol/L	:	Millimol/Liter
MR	:	Mallory's hyaline
MRI	:	Magnetic resonance imaging
MTP	:	Microsomal triglyceride transfer protein
NAFLD	:	Nonalcoholic fatty liver disease
NAS	:	Non-Alcocholic Fatty Liver Disease Activity Score
NASH	:	Nonalcoholic steatohepatitis
NF- kb	:	nuclear factor-kb
NPV	:	Negative predictive value

List of Abbreviations

OGTT	:	Oral glucose tolerance test
PAI-1	:	plasminogen activator inhibitor–1
PCOS	:	Polycystic ovary syndrome
PDX-1	:	pancreatix duodenal homeoboc-1
PNPLA3	:	polymorphism of palatin-like phospholipase domain-containing 3 gene
PPARγ	:	peroxisome proliferator-activated receptor gamma
PPV	:	Positive predictive value
PT	:	Prothrombin Time
ROC	:	Receiver operator characterizing curve
ROS	:	Reactive oxygen species
Rt	:	Right
SAT	:	Subcutaneous adipose tissue
SHBG	:	Sex hormone binding globulin
SREBP-1c	:	sterol regulatory element binding protein -1c
T2DM	:	Type 2diabetes mellitus
TG	:	Triglyceride
TLR	:	Toll-like receptors
TNF α	:	Tumor necrosis factor alpha
UDCA	:	Ursodeoxycholic Acid
US	:	Ultrasonography
VAT	:	Visceral adipose tissue
VFA	:	Visceral fat area
VLDL	:	Very low density lipoprotien
WAT	:	White adipose tissue
WHO	:	World Health Organization

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Introduction

Non-alcoholic fatty liver disease (NAFLD) has been considered a benign disease often associated with central obesity and insulin resistance and in general with factors of the metabolic syndrome .NAFLD is a chronic condition, ranging from benign steatosis, (*i.e.*, hepatic triglyceride accumulation >5.5% using computed tomography or >5% corresponding to 50 mg/g by wet weight), to more significant liver injury including lobular inflammation, hepatocyte ballooning, fibrosis and cirrhosis, *i.e.*, non-alcoholic steato-hepatitis (NASH) ***(Browning JD, 2004).***

Insulin resistance is a characteristic feature of NAFLD , even when subjects are not obese . On the other hand NAFLD is highly prevalent among patients with type 2 diabetes (up to 70%) that show increased hepatic triglyceride accumulation independently of BMI **(Gastaldelli A, 2007).**

Insulin resistant subjects with NAFLD show reduced insulin sensitivity not only at the level of the muscle but also at the level of the liver and adipose tissue. In insulin-resistant conditions, the adipose tissue becomes resistant to the antilipolytic effect of insulin and the release of fatty acids is increased . Insulin resistance is accompanied by increased insulin levels that, in the presence of increased lipolysis

and/or increased fat intake, promote hepatic triglyceride synthesis ***(Fabbrini , 2009).***

Previous studies indicate that hepatic fat and not visceral fat was associated with insulin resistance. When subjects with different intrahepatic triglyceride content were matched on similar visceral fat, they showed increased hepatic and peripheral insulin resistance and increased very low density lipoprotein-triglyceride secretion rate but no difference was observed between subjects matched for intrahepatic triglyceride but different visceral fat **(Bhatia LS, 2012).**

Aim of work

We will study relationship between hepatic /visceral fat and insulin resistance in non-diabetic and type 2diabetic subjects.

Nonalcoholic Fatty Liver Disease

Introduction

Non-alcoholic fatty liver disease (NAFLD) is becoming an important public health concern due to the rising incidence of obesity in both children and adults**(Chalasani N et al.,2012).** NAFLD represents a spectrum of disease, ranging from simple steatosis to steatohepatitis (the presence of fat in liver parenchyma with inflammation, hepatocyte ballooning and lobular inflammation) through to fibrosis and cirrhosis**(Dowman JK,2010).**

Simple steatosis rarely progresses to advanced disease whereas in approximately 20% of patients with non-alcoholic steatohepatitis (NASH), it progresses to fibrosis and cirrhosis over a 15 year time period**(Angulo P,2010).** It is strongly associated with insulin resistance and other metabolic risk factors such as diabetes mellitus, central abdominal obesity and dyslipidaemia **(Roberts CK,2013).** NAFLD can be primary or secondary depending on the cause (Table 1) **(Adams LA ,2005).**