Value of Serum Omentin as a Coronary Artery Disease Risk Factor

Protocol of Thesis

Submitted for Partial Fulfillment of Master Degree in Clinical and Chemical Pathology

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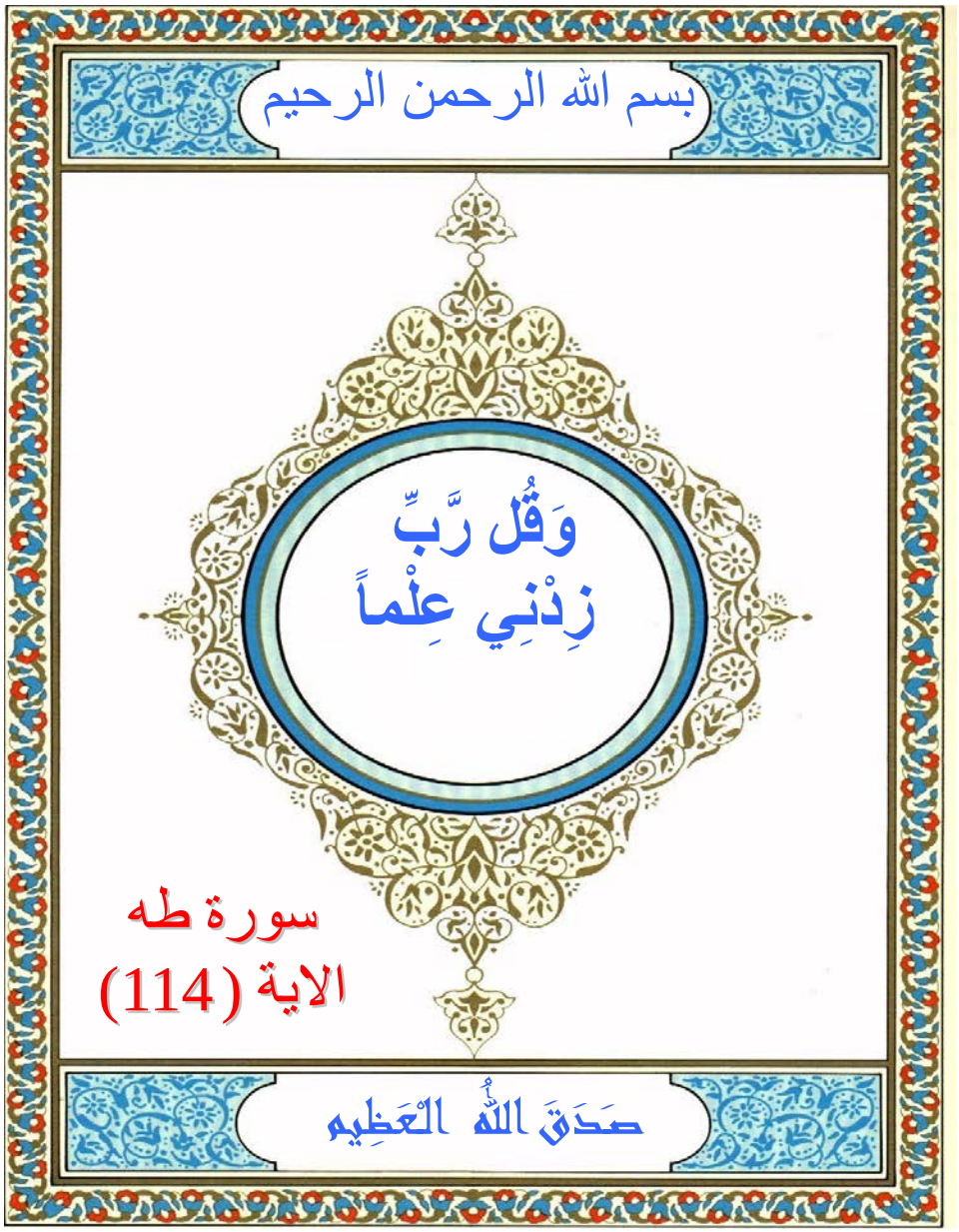
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LIST OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

List Of Abbreviations

Abb.	Full Term
Ab	Antibody
ACS	Acute coronary syndrome
Ag	Antigen
Akt	Protein kinase B
ALB	Albumin
AMI	Acute myocardial infarction
AMPK	AMP-activated protein kinase
BMI	Body mass index
CAD	Coronary artery disease
CBC	Complete blood count
CD40L	CD40 ligand
cGMP	Cyclic guanosine monophosphate
CIMT	Carotid intima media thickness
CK	Creatine kinase
CK-MB	Creatine kinase-MB fraction
CMRI	Cardiac magnetic resonance imaging
CO	Carbon monoxide
COX-2	Cyclooxygenase-2
CRP	C- reactive protein
CT	Computed tomography

CTn	Cardioc troponin
cTn C	Cardiac troponin C
cTn I	Cardiac troponin I
cTn T	Cardiac troponin T
CVD	CVD
DsDNA	Double stranded DNA
ECG	Electrocardiogram
ECM	Extracellular matrix
EDHF	Endothelial–derived hyperpolarizing factor
EIA	Enzyme immunoassay
eNOs	Endothelial nitric oxide synthase
ESC|ACC	European Society of Cardiology and the American College of Cardiology
EtBr	Ethidium bromide
FFA	Free fatty acid
Flt1	Vascular endothelial growth factor receptor
GLUT4	Glucose transporter 4
H202	Hydrogen peroxide
HDL-C	High density lipoprotein cholesterol
H-FABP	Heart –type fatty acid binding protein
HOMA	Homostasis model assessment
HPLC	High performance liquid chromatography
Hs CRP	High sensitivity CRP
IFG	Impaired fasting glucose

IgM	Immunoglobulin M
IGT	Impaired glucose tolerance
IHD	Ischemic heart disease
IL-6	Interleukin-6
IR	Insulin resistance
IRS	Insulin resistance substrate
JNK	C-jun N-terminal kinase
KD	Kawasaki disease
KDa	Kilodalton
LDL	Low density lipoprotein cholesterol
L-NMMA	NG-monomethyl-L-arginine
LV	Left ventricular
MCP-1	Monocyte chemoattractant protein-1
MetS	Metablic syndrome
MHC	Major histocampatibility complex
MMP	Matrix metalloproteinase
MPO	Myeloperoxidase
MSCT	Multislice computed tomography
MtCK	Mitochondrial creatine kinase
NAFLD	Non alcoholic fatty liver disease
NCEP-ATPIII	National cholesterol program and adult Treatment panel III
NO	Nitric oxide

NSTEMI	Non-STsegment elevation myocardial infarction
OX-LDL	Oxidized-LDL
PAPP-A	Pregnancy associated plasma protein
PCOD	Polycystic ovarian disease
PCR	Polymerase chain reaction
PCyC	Plasma cystatin C
PGI-2	Prostacyclin
PI3K	Phosphoinositide 3 kinase
PLGF	Placental like growth factor
RT-PCR	Real time-PCR
SAA	Serum amyloid A
sCD40L	Soluble CD40 ligand
SMCs	Stromal muscle cells
SR	Scavenger receptors
STE	ST segment elevation
SVCs	Stromal vascular cells
T2DM	Type 2 diabetes mellitus
TBXA2	Thromboxane A2
TC	Total cholesterol
TG	Triglycerides
Th1	T-helper1
Th2	T-helper2
TNF	Tumour necrotic factor

UA	Unstable angina
VCAM	Vascular cell adhesion molecule
WHO	World health organization

INTRODUCTION

Coronary Artery Disease (CAD) remains the leading cause of mortality in the United States and is predicted to be the leading contributor to morbidity and mortality worldwide over the next several decades *(Flint et al., 2010).* Moreover, about 80% of all cardiovascular-related deaths occur in low and middle income countries at a younger age in comparison to high income countries *(Gersh et al., 2010).*

Several biomarkers seemed to be more strongly related to CAD within the last years, such as CRP, MMP-9, fibrinogen, factor VIII and leukocyte count, all of which may be thought of as potential markers of plaque destabilization or an acute-phase reaction. Some components of the metabolic syndrome, such as HDL cholesterol, triglycerides and fasting insulin also seemed to be more strongly related to CAD. Other markers, some of which may be related to an ongoing atherosclerotic process were associated with early CAD events, including LDL, total cholesterol, D-dimer and vWF, whereas homocysteine was more strongly associated with later events *(Rossouw et al., 2008).*

Pericardial adipose tissue (PAT) is an ectopic fat depot associated with measures of adiposity and metabolic risk factors and a predictor of CAD events. It is an important local source of free fatty acids and a number of proatherogenic, proinflammatory, prothrombotic hormones and cytokines,

including leptin, monocyte chemotactic protein-1, interleukin-6 and tumor necrosis factor-α *(Liu et al., 2010).*

Omentin is a novel fat depot-specific adipokine that was identified in the year 2003 from a visceral omental adipose tissue cDNA library. The omentin gene is located in the 1q22-q23 chromosomal region *(Yoo et al., 2011).* There are two highly homologous isoforms of omentin, omentin-1 and omentin-2. The former is the major circulating form in human plasma. Serum omentin-1 levels have been shown to correlate negatively with body mass index (BMI), waist circumference, fasting insulin and positively with high-density lipoprotein cholesterol (HDL-c) levels *(Shang et al., 2011).*

Some researches suggested that low levels of omentin are closely linked to the presene of CAD *(Shibata et al., 2011).*

AIM OF WORK

The aim of this work is to investigate the relationship between circulating omentin levels and coronary artery disease.

Chapter (I)

CORONARY ARTERY DISEASE

A) Introduction:

Coronary artery disease is the most common cause of heart attacks, which occurs when blood flow to the myocardium is interrupted **(Antman et al., 2007)**.The clinical presentations of ischemic heart

disease include stable angina pectoris, silent ischemia, unstable angina, myocardial infarction (MI), heart failure, and sudden death **(Findlay and Cunningham,2005)**.

B) Epidemiology:

Coronary artery disease (CAD) is increasing in prevalence and is predicted to become the dominant cause of mortality worldwide ***(Cannon et al., 2004).*** Mortality from cardiovascular disease is predicted to reach 23.4 million in 2030 ***(Cassar et al., 2009)***. Moreover, in the developing world, cardiovascular disease tends to affect people at a younger age and thus could negatively affect the workforce and economic productivity. The morbidity, mortality and socioeconomic importance of CAD make its diagnosis and management fundamental for all practicing physicians ***(Leeder et al., 2009)***.

C) Biochemical Regulation of Coronary Blood Flow:

1) Nitric Oxide:

The principal regulator of endothelial vasodilator function through NO is vascular shear. Shear is the frictional force exerted on the vascular wall secondary to the flow of blood. These forces open calcium channels on endothelial cells, thus promoting the calcium-dependent activation of endothelial NO synthase (eNOS), which, in turn, induces the release of NO. NO then diffuses to the underlying vascular smooth muscle, where it activates soluble guanylate cyclase, causing an increase in cyclic guanosine monophosphate (cGMP) and smooth muscle relaxation ***(Saniz et al, 2004)***. Constitutive NO synthase (NOS) can be competitively inhibited by guanidine-substituted analogues of L-arginine, such as N^G-monomethyl-L-arginine (L-NMMA). It is not surprising that