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Association between Genetic Polymorphisms and Coronary Artery Disease in Egyptian Patients

A THESIS

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By

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ABSTRACT

Lamiaa Mageed Sayed Ibrahim

"Association between Genetic Polymorphisms and Coronary Artery Disease in Egyptian Patients"

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Aim of the study: To evaluate the level of IL-18 as a pro-inflammatory cytokine and to investigate the potential associations ofthe two IL-18 promoter gene polymorphisms at positions (-607C/A) and (-137G/C), ACE (I/D) and AGT (M235T) gene polymorphisms with coronary artery disease.

Subjects: A total of one hundred and twenty Egyptian patients (Sixty with CAD and sixty without CAD) and fifty healthy control subjects were included in the study.

Methods: Genotyping of IL-18 promoter gene at (-607C/A) and (-137G/C) regions, ACE (I/D)and AGT (M235T) were analyzed by Polymerase chain reaction technique (PCR), Lipid profiles (total cholesterol, triglyceride, HDL-C) were measured by enzymatic colorimetric method. Serum IL-6 and IL-18 levels were determined using ELISA.

Results: Our data indicated that IL-18 (137 GG) was significantly associated with CAD, whereas a non- significant association was observed in IL-18 (607C/A) between cases and controls. Also, there was a significant association between ACE (DD) and AGT (TT) polymorphisms and CAD. Furthermore, a significant association between lipid profiles (TC, TG and LDL-C) and risk for CAD was occurred. Elevation of serum IL-6 and IL-18 levels was observed in CAD patients.

Conclusion: Our study suggests that an association between IL-18 (137G/C) promoter gene polymorphism, ACE (I/D) and AGT (M235T) polymorphisms and susceptibility to CAD in Egyptian patients. The present study showing a strong association between dyslipidemia as an important risk factor of atherosclerosis and CAD.A markedly high level of IL-6 and IL-18 in patients with CAD, based on which suggests that IL-6 and IL-18 may be served as susceptibility biomarkers in the pathogenesis of atherosclerosis in CAD patients.

CONTENTS

LIST OF ABBERVIATIONS

ACE	Angiotensin Converting Enzyme
ACS	Acute Coronary Syndrome
AGT	Angiotensinogen
AMI	Acute Myocardial Infarction
Ang I	Angiotensin I
Ang II	Angiotensin II
AR	Aortic Root
BP	Blood Pressure
CAC	Coronary Artery Calcium
CAD	Coronary Artery Disease
cAMP	Cyclic Adenosine Monophosphate
CHD	Coronary Heart Disease
CRP	C -Reactive Protein
CVDs	Cardiovascular Diseases
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
DN	Diabetic Nephropathy
DNA	Deoxyribonucleic Acid
ECG	Electrocardiogram
EF	Ejection Fraction
EH	Essential Hypertension
ELISA	Enzyme-Linked Immunosorbent Assay
FH	Familial Hypercholesterolemia
FS	Fractional Shortening
H4TF-1	Histone 4 Transcription Factor-1
HDL-C	High Density Lipoprotein-Cholesterol
HF	Heart Failure
HRV	Heart Rate Variability
hs- CRP	High Sensitivity C -Reactive Protein
HTN	Hypertension
ICAM-1	Intracellular Cell Adhesion Molecule-1
IDL-C	Intermediate-Density Lipoprotein Cholesterol
IFN- γ	Interferon-γ

IHD	Ischemic Heart Disease
IL-1	Interleukin-1
IL-10	Interleukin-10
IL-18	Interleukin-18
IL-6	Interleukin-6
IMT	Intima Media Thickness
LA	Left Atrium
LCA	Left Coronary Artery
LDL-C	Low Density Lipoprotein-Cholesterol
Lp-PLA-2	Lipoprotein-Associated Phospholipase A2
LVEDD	Left Ventricular End Diastolic Diameter
LVEF	Left Ventricular Ejection Fraction
LVESD	Left Ventricular End Systolic Diameter
LVH	Left Ventricular Hypertrophy
LVPWT	Left Ventricular Posterior Wall Thickening
LVSWT	Left Ventricular Systolic Wall Thickening
Mcp-1	Monocyte Chemoattractant Protein-1
MI	Myocardial Infarction
MMPs	Matrix Metalloproteinases
MPO	Myeloperoxidase
MRI	Magnetic Resonance Imaging
MRP8/14	Myeloid Related Protein 8/14 Complex
MUGA	Multigated Acquisition Scans
NLRP3	Nucleotide-Binding Domain And Leucine-RichRepeatPyrinContainingProtein-3
$NO^{\cdot}$	Nitric Oxide
ox-LDL	Oxidized LDL
PAD	Peripheral Artery Disease
PAI-1	Plasminogen Activator Inhibitor-1
PCAD	Premature Coronary Artery Disease
PCR	Polymerase Chain Reaction
PCR-RFLP	Polymerase Chain Reaction Restriction Fragment Length Polymorphism
PCR-SSP	Polymerase Chain Reaction -Specific Sequence Primer
PlGF	Placental Growth Factor
PTX3	Pentraxin-3

RAAS	Renine Angiotensine Aldosterone System
RAS	Renin–Angiotensin System
RNA	Ribonucleic Acid
ROC	Receiver Operating Characteristics
ROS	Reactive Oxygen Species
RV	Right Ventricle
RV	Right Ventricular
SAA	Serum Amyloid A
SBP	Systolic Blood pressure
sCD40L	Soluble CD40 Ligand
SD	Standard Deviation
SNPs	Single Nucleotide Polymorphisms
STEMI	Segment Elevated Myocardial Infarction
T2DM	Type 2 Diabetes Mellitus
TC	Total Cholesterol
TG	Triglyceride
TNF- α	Tumor Necrosis Factor Alpha
TnI	Troponin-I
TOE	Transoesophageal Echocardiography
UA	Unstable Angina
VCAM-1	Vascular Cell Adhesion Molecule- 1
VLDL-C	Very Low Density Lipoprotein-Cholesterol

LIST OF TABLES

Page

LIST OF FIGURES

Page