بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

MONA MAGHRABY

Assessment of Genetic Polymorphism as Risk Factor of End Stage Renal Disease in Egyptian Patients

A Thesis

Submitted for the degree of Master of Science As a partial fulfillment of the requirements for the degree of Master of Science in Biochemistry

By

Esraa Adel Ramadan Ghazaly

Bachelor in Science, Biochemistry (2013)
Mansoura University

Under the supervision of

Prof. Dr. Dina M. Seoudi
Professor of Biochemistry
Faculty of Science
Ain Shams University

Dr. Afaf M. El-Saeed
Consultant of Biochemistry and Molecular Biology
Genetic Unit, Children Hospital
Mansoura University

Dr. Mostafa Abd-El Salam Mohamed

Associate Professor of Medicine and Nephrology
Faculty of Medicine
Mansoura University

2020

Declaration

This thesis has not been submitted

to this or any other university.

Esraa Adel Ramadan Ghazaly

Dedication

I dedicate this work to

My Great Family

My Great Dad

My Kind Mum

My Beloved Husband

My Loyal Sisters& Brothers

Thank you for all what you have done for me.

Yours,

Esraa Adel

2020

Biography

Name: **Esraa Adel Ramadan Mohamed Ghazaly**

Date and place of birth: **15/9/1992, Mansoura, Egypt**

Date of Graduation: **2013**

Degree Awarded: **Bachelor in Science, Biochemistry**

Grade: **Excellent**

Department: **Chemistry (Biochemistry Division)**

Faculty: **Faculty of Science**

University: **Mansoura University**

Date of Registration: **2016**

Date of Appointment: **2020**

ACKNOWLEDGEMENT

In the name of Allah, Most Gracious, Most Merciful All praise and glory to Almighty Allah who gave me courage and patience to carry out this work. Peace and blessing of Allah be upon last Prophet Muhammad (Peace Be upon Him).

I would like to express my deepest appreciation, gratefulness & sincere thanks to ***Professor Dr. Dina Mohamed Seoudi,*** *Professor of Biochemistry, Faculty of Science, Ain Shams University for her kind supervision, help, encouragement, guidance and advice. I would like also to thank her very much for her critical reading of the thesis, which helped to improve it.*

My deepest heartfelt gratefulness and appreciation to ***Professor Dr. Afaf Mohamed EL-Saeed,*** *Consultant of Biochemistry and Molecular Biology, Genetic Unit, Children Hospital, Faculty of Medicine, Mansoura University, for suggesting the point of this thesis and for her kind supervision, continuous support and valuable guidance. I am very lucky to have this great opportunity to be one of her students. No words are sufficient to express heartfelt deep thanks to her.*

I am deeply indebted to ***Dr. Mostafa Abd-El Salam Mohamed****, Associate Professor of Medicine and Nephrology, Faculty of Medicine, Mansoura University for his kind supervision, continuous support, valuable guidance and generous help in all the theoretical aspects also for his encouragement, patience and for his great effort with me along completing this thesis.*

My deep appreciation and thanks goes to ***all members*** *of Genetic Unit, Children Hospital, Mansoura University for their smiley faces, patience and kind assistance, and to* ***everyone, doctors, nurses and patients*** *in Renal Dialysis Units of Mansoura Hospital, Egypt for their help in samples collection, collecting patient's clinical data, and patient's history records as well.*

Yours,

Esraa Adel

Contents

Abstract

Background: Kidney disease is a serious public health problem worldwide. It is the fifth cause of death in Egypt. It causes approximately 3.98 % of all Egyptian deaths.

Objective: This study aims to deduce the association between *Leptin* (*-2548G/A*) and *uncoupling protein-2 45 bp I/D* genes, individually and synergistically, in the progression of renal disease.

Methods: a hundred patients with end-stage renal diseases (ESRD), forty patients with chronic kidney disease (CKD), and fifty healthy controls were enrolled. Detection of the influence of these genes was assayed by polymerase chain reaction (PCR). Correlations of single nucleotide polymorphisms (SNP) genotypes with the clinical status of patients and progression of kidney disease were statistically analyzed.

Results: The association of SNP of *UCP-2 I/D* and *leptin-2548G/A* in renal disease progression were investigated. The results revealed that genotypes of Leptin were associated with lower disease susceptibility (95 % CI = (0.08-0.63), *P = 0.01*) with risk value equal 0.22 <1 AND G/A genotype is significantly lower in cases of CKD than ESRD, so it might be protective against the development of ESRD while the *UCP-2 I/D* genotype showed no protective effect against the disease *(P = 0.27*). On the other hand, there was no significant correlation between the *UCP-2* gene and the progression of renal disease.

Conclusions: This study showed that*, Leptin −2548G/A* gene may be a promising sensitive marker for early detection of end-stage renal disease in Egyptian patients. G/A genotype might be protective against the development of CKD to ESRD..

Keywords: Leptin, uncoupling protein-2, chronic kidney disease, gene polymorphism, polymerase chain reaction.

List of Abbreviations

Abbreviations	Meaning
ACE-1	Angiotensin converting enzyme-1
ADPKD	Autosomal dominant polycystic kidney disease
AGT	Angiotensin
AGTR1	Angiotensin II type-1 receptor
AKI	Acute kidney injury
AKIN	Acute kidney injury network
ALT	Alanine transaminase
ANOVA	Analysis of variance
ARPKD	Autosomal recessive polycystic kidney disease
AST	Aspartate transaminase
ATP	Adenosine triphosphate
BCG	Bromo cresol green
Bp	Base pair
BUN	Blood urea nitrogen
CI	confidence interval
CKD	Chronic kidney disease
CRF	Chronic renal failure
CT	Computed tomography
D	Deletion
Da	Dalton
DBP	Diastolic blood pressure
DKD	Diabetic kidney disease
DM	Diabetes mellitus
DNA	Deoxy ribonucleic acid
ecNOS	Endothelial nitric oxide synthase

EDTA	Ethylenediaminetetraacetic acid
ESRD	End-stage renal disease
FBG	Fasting blood glucose
FSGS	Focal and segmental glomerulosclerosis
GFR	Glomerular filtration rate
GN	Glomerulonephritis
GNB3	β3 subunit of heterotrimeric G-protein
GOD	Glucose oxidase
GOT	Glutamate oxaloacetate
HCL	Hydro chloric acid
HTN	Hypertension
H_2O_2	Hydrogen peroxidase
HWE	Hardy-Weinberg equilibrium
I	Insertion
IL-6	Interleukin-6
IMM	Inner mitochondrial membrane
IMS	Intermembrane space
In	Inch
LDH	Lactate dehydrogenase
MDRD	Modification of diet in renal disease
MDH	Malate dehydrogenase
mRNA	Messenger ribonucleic acid
NADH	Nicotinamide Adenine Dinucleotide dehydrogenase
NO	Nitric oxide
OMM	Outer mitochondrial membrane
OR	Odds ratio
PCR	Polymerase chain reaction

PKD	Polycystic kidney disease
POD	Peroxidase
QTL	Quantitative trait loci
RAS	Renin–Angiotensin system
RFLP	Restriction Fragment Length Polymorphism
RIFLE	Risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function
ROS	Reactive oxygen species
SBP	Systolic blood pressure
SLE	Systemic lupus erythematosus
SNP	Single nucleotide polymorphism
SPSS	Statistical package for social science
TBA	Thiobarbituric acid
TBE	Tis-borate-EDTA buffer
T2DM	Type 2 diabetes mellitus
TH1	T-helper lymphocyte type 1
TH2	T-helper lymphocyte type 2
TPE	Tris Phosphate-EDTA buffer
UCP-2	Uncoupling protein-2
UTR	UnTranslated region
UV	Ultra violet
VUR	Vesicoureteral reflux
WHO	World health organization