Serum Chemerin level in type 2 diabetic patients with Diabetic Retinopathy

Thesis

Submitted for partial Fulfillment of Master Degree

In Endocrinology

By

Ahmed Mohamed Mohamed El Sabawy

M.B.B.Ch

Under Supervision of

Prof. Mohamed Reda Halawa

Professor of Internal Medicine & Endocrinology

Faculty of medicine – Ain Shams University

Prof. Abeer Ahmed Abdallah

Professor of Internal Medicine & Endocrinology

Faculty of medicine – Ain Shams University

Dr. Nesma Ali Ibrahim

Lecturer of Internal Medicine & Endocrinology

Faculty of medicine – Ain Shams University

Faculty of Medicine

Ain Shams University

2018

بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgments

My thanks are submitted first and foremost to **ALLAH** *who gave me the strength and ability to complete this work.*

I would like to express my thanks and appreciation to **Prof. Mohamed Reda Halawa,** *Professor of internal Medicine & Endocrinology, Faculty of Medicine – Ain Shams University, for his candid opinions, timely feedback and the effort he has devoted to the fulfillment of this work.*

I can't forget to thank with all appreciation, **Prof. Abeer Ahmed Abdallah,** *Assistant Professor of Internal Medicine & Endocrinology, Faculty of Medicine – Ain Shams University, for the efforts and time she has devoted to accomplish this work*

I would like to express my thanks and appreciation to **Prof. M. Hesham El Gayar,** *Professor of internal Medicine & Endocrinology, Faculty of Medicine – Ain Shams University,* **and Prof M. Hesham El Hefnawy**, *Dean of the National Institute of Diabetes and Endocrinology for their excellent discussion.*

My sincere gratitude are also due to **Dr. Nesma Ali Ibrahim,** *Lecturer of Internal Medicine, Diabetes and Endocrinology, Faculty of Medicine-Ain Shams University, for her kind help, constant encouragement and the effort she dedicated to this work.*

I can't forget to thank with all appreciation **Prof. Ibrahem Emara**, *the head of laboratory department, NIDE and* **Dr. Sally Youseif**, *lecturer of ophthalmology, NIDE for their great efforts during the study.*

I can't forget to thank **Prof Tahny Abdel Sallam**, *Laboratory department, Ain Shams University, I ask Allah to forgive her.*

Last but not least, all thanks to all members of my **Family**, *especially, my* **Parents,** *for pushing me forward in every step in the journey of my life.*

Ahmed El Sabawy

List of Contents

Subject *Page No.*

List of Abbreviations ..... **i**

List of Tables ..... **iv**

List of Figures **6**

Introduction **7**

Aim of the Work **9**

Review of Literature

Diabetic Retinopathy **10**

Chemerin **38**

Subjects and Methods **64**

Results **75**

Discussion **104**

Summary **109**

Conclusion **109**

Recommendations **114**

References **115**

Arabic Summary ..... **—**

List of Abbreviations

Abbr.	Title
AA	:Arachidonic Acid
AGE	:Advanced Glycation End-Products
AGEs	:Advanced Glycation End Products
AMPA	: Aminomethylphosphonic acid
ANOVA	:Analysis of variance
BDNF	:Brain Derived Neurotrophic Factor
BRB	:Blood Retinal Barrier
CAN	:Cardiac Autonomic Neuropathy
CCRL2	:Chemokine Receptor Like 2
CIMT	:Carotid Intima-Media Thickness
CMKLR1 ChemR23	:Chemokine-Like Receptor 1
COX2	:Cyclooxygenase 2
CVD	:Cardiovascular disease
DC	: Dendritic cell
DCCT	:Diabetes Control and Complications Trial
DM	:Diabetes Mellitus
DME	:Diabetic Macular Edema
DR	:Diabetic Retinopathy
ELISA	:Enzyme Linked Immunosorbent Assay
ERK	:Extracellular Signal-Regulated Kinases
FasL	:Fas Ligand
FFA	:Free Fatty Acid

FIELD Study	:Effects Of Long-Term Fenofibrate Therapy On Cardiovascular Events In People With Type 2 Diabetes Mellitus
GPR1	:G Protein Coupled Receptor 1
HOMA	:Homeostasis Model Assessment
HPLC	:High Performance Liquid Chromatography
HsCRP	:High Sensitive C-Reactive Protein
HTR2B	:Hydroxytryptamine Receptor 2B
ICAM-1	:Intracellular Adhesion Molecule-1
IGF-1	:Insulin-Like Growth Factor
IL	:Interleukin
IL13RA2	:Interleukin-13 Receptor Alpha2
IR	:Insulin resistance
IRP	:Interstitial Retinol-Binding Protein
kDa	:Kilodalton
Lp	:Lipoprotein
MCP-1	:Monocyte Chemoattractant Protein 1
miRNA	:MicroRNA
mRNA	:messenger RNA
NAPDH	:Nicotinamide Adenine Dinucleotide Phosphate
NGD	:Nerve Growth Factor
Nm	:Nanomol
NMDA	:N-Methyl-D-Aspartate
NO	:Nitric Oxide
NO2	:Nitrogen Dioxide
NOX	:Mono-Nitrogen Oxides

NPDR	:Non-Proliferative Diabetic Retinopathy
PDR	:Proliferative Diabetic Retinopathy
PEDF	:Pigment Epithelial-Derived Factor
PGE2	:Prostaglandin E2
PKC	:Protein Kinase C
PLA2	:Phospholipase A2
PPARγ	:Peroxisome Proliferator-Activated Receptor Gamma
RAAS	:Renin-Aldosterone-Angiotensin System
R-AGE	:Receptors of Advanced Glycation End Products
RAS	:Renin Angiotensin System
ROS	:Reactive Oxygen Species
RT- PCR	:Reverse Transcriptase Polymerase Chain Reaction
SLC16A	:Solute Linked Carrier 16A
SSC	:Squamous Cell Carcinoma
SST	:Somatostatin
TIG2	:Tazarotene-Induced Gene 2
TLR	:Toll Like Receptors
TNF	:Tumor Necrosis Factor
tPA	:Tissue Plasminogen Activator
TrkB	:Tropomyosin-related kinase B
UKPDS	:UK Prospective Diabetes Study
VCAM-1	:Vascular Cell Adhesion Molecule-1
VEGF	:Vascular Endothelial Growth Factor

List of Tables

Table No.	Title	Page No.
Table (1):	Summary of the three known chemerin receptors	**45**
Table (2):	Comparison between the 3 groups of patients regarding the demographical and clinical data	**87**
Table (3):	Comparison between the groups of patients with diabetic retinopathy, without retinopathy and control groups regarding the laboratory data	**89**
Table (4):	Comparison between the study groups and subgroups regarding the demographical and clinical data	**90**
Table (5):	Comparison between the study groups and subgroups regarding the laboratory data	**92**
Table (6):	Correlation between chemerin and different variables by using Pearson correlation co-efficient	**94**
Table (7):	Stepwise Regression Analysis Serum chemerin is the dependent variable	**95**
Table (8):	Comparison between the diabetic with retinopathy versus without retinopathy groups by using Post Hoc Test	**96**
Table (9):	Comparison between diabetic group with retinopathy versus control group by using Post Hoc Test	**97**

Table (10): Comparison between diabetic without retinopathy versus control groups by using Post Hoc Test **98**

Table (11): Comparison between PDR versus NPDR groups by using Post Hoc Test **99**

Table (12): Comparison between PDR versus diabetic without retinopathy groups by using Post Hoc Test..... **100**

Table (13): Comparison between PDR versus control groups by using Post Hoc Test **101**

Table (14): Comparison between NPDR versus diabetic without retinopathy groups by using Post Hoc Test **102**

Table (15): Comparison between NPDR versus control groups by using Post Hoc Test **103**

List of Figures

Figure No.	Title	Page No.
Figure (1):	Different sites of diabetic occurrence in retina	**22**
Figure (2):	Simplified overview of the multiple interacting pathways leading to the pathogenesis of diabetic retinopathy	**25**
Figure (3):	General pathway in the progression of diabetic microvascular complications.	**30**
Figure (4):	Tertiary structure prediction suggests an ionic linkage in the prochemerin C-terminus Superimposed models of prochemerinand chemerinF156 created by molecular modeling	**41**
Figure (5):	Structure of G-protein coupled receptor	**43**
Figure (6):	Chemerin is involved in a variety of functions in inflammation, skin, obesity, and cell differentiation	**48**
Figure (7):	The role of chemerin and CMKLR1 in adipose tissue biology	**54**
Figure (8):	The proposed mechanism of the role of chemerin in atherosclerosis	**60**
Figure (9):	The correlation between study groups regarding serum chemerin.	**92**