



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكرو فيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني 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



The Effect of Hepatitis C Virologic Clearance on Cardiovascular Disease Biomarker Lipoprotein associated phospholipase A2 and its relation to Serum Lipids

Thesis

Submitted for partial fulfillment of the MD Degree
in ***Internal Medicine***

By

Basant Moatz Abdelrhieem

M.B.B.Ch, M.SC

Faculty of Medicine-Ain Shams University

Supervised by

Prof. Dr. Kadry Mohamed El Saeed

Professor of Internal Medicine and Gastroenterology
Faculty of Medicine - Ain-Shams University

Ass. Prof. Dr. Eslam Safwat Mohamed

Associate Professor of Internal Medicine and Gastroenterology
Faculty of Medicine - Ain-Shams University

Dr. Rasha Samir Mohamed

Lecturer of Internal Medicine and Gastroenterology
Faculty of Medicine - Ain-Shams University

Dr. Amira Isaac Samaan

Lecturer of Internal Medicine and Gastroenterology
Faculty of Medicine - Ain-Shams University

Dr. Shereen Abdelmonem Ibrahim

Lecturer of Clinical Pathology
Faculty of Medicine - Ain-Shams University

Faculty of Medicine
Ain Shams University

2021



تأثير التخلص من فيروس (سي) على مستوى الدلالة البيولوجية لامراض القلب والاعوية الدموية الفوسفولايبيز 2 المرتبط بالليبوبروتين في الدم و علاقته بمستوى الدهون بالدم

رسالة

توطئة للحصول علي درجة الدكتوراه في امراض الباطنة العامة

مقدمة من

الطبيبة / بسنت معتز عبدالرحيم

بكالوريوس الطب والجراحة و ماجستير الباطنة العامة
كلية الطب - جامعة عين شمس

تحت اشراف

أ.د / قدرى محمد السعيد

أستاذ الباطنة العامة و الجهاز الهضمى والكبد
كلية الطب - جامعة عين شمس

أ.م.د / إسلام صفوت محمد

استاذ مساعد الباطنة العامة و الجهاز الهضمى والكبد
كلية الطب - جامعة عين شمس

د / رشا سمير محمد

مدرس الباطنة العامة والجهاز الهضمى والكبد
كلية الطب - جامعة عين شمس

د / اميرة اسحاق سمعان

مدرس الباطنة العامة والجهاز الهضمى والكبد
كلية الطب - جامعة عين شمس

د / شيرين عبدالمنعم ابراهيم

مدرس الباثولوجيا الاكلينيكية
كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

2021

Acknowledgement

“Praise to Allah, who has guided us to this; and we would never have been guided if Allah had not guided us”. First and foremost, I’d like to express gratitude to Almighty Allah, the most gracious, the most merciful for helping throughout this work.

I would like to express my sincere appreciation to **Prof. Dr. Kadry Mohamed El Saeed** and **Ass. Prof. Dr. Eslam Safwat Mohamed** for their patience, motivation, enthusiasm, and immense knowledge. I could not have imagined having better advisors and mentors for my study.

I am thankful for **Dr. Rasha Samir Mohamed** who consistently allowed this research to be my own work, but steered me in the right direction whenever she thought I needed it.

I am also grateful for the generosity, kindness and endless support of **Dr. Amira Isaac Samaan**. The door to her office was always open whenever I ran into a trouble spot or had a question about my research or writing .

I am thankful as well for **Dr. Shereen Abdelmonem Ibrahim** for providing invaluable guidance throughout this research.

Finally, I must express my profound gratitude to my parents for providing me with unfailing support and continuous encouragement throughout my years of study and the process of researching and writing this thesis. This accomplishment would not have been possible without them. Thank you.

Basant Moatz Abdelrhieem

List of Contents

Title	Page
▪ List of Abbreviations.....	I
▪ List of Tables	VII
▪ List of Figures	XIII
▪ Introduction	1
▪ Aim of the Work	5
▪ Review of Literature	
- Chapter (1): Hepatitis C Virus	6
- Chapter (2): HCV Treatment using Direct Acting Antiviral Therapy.....	23
- Chapter (3): Hepatitis C Virus and Cardiovascular Disease.....	54
▪ Patients and Methods.....	77
▪ Results.....	92
▪ Discussion	127
▪ Summary.....	140
▪ Conclusion and Recommendations	143
▪ References.....	145
▪ Arabic Summary.....	--

List of Abbreviations

Abb.	Full Term
AFP	Serum Alpha-Fetoprotein
Ag	Antigen
Ag/Ab	Antigen/Antibody
ALB	Albumin
ALT	Alanine Transaminase
ANOVA	Analysis of Variance
ANP	Atrial Naturetic Peptide
Apo	Apolipoprotein
APRI	Aminotransferase to Platelet Ratio Index
ARFI	Acoustic Radiation Force Impulse
AS	Atherosclerosis
AST	Aspartate Transaminase
AUROC	Area under the Receiver Operating Characteristic Curve
BAFF	B cell-Activating Factor
BAFFR	B cell-Activating Factor Receptor
BNP	Brain Naturetic Peptide
CAD	Coronary Artery Disease
CBC	Complete Blood Count
CD	Cluster of Differentiation
CETP	Cholesteryl Ester Transfer Protein
CHC	Chronic Hepatitis C
CI	Confidence Interval
CIA	Chemiluminescence Immunoassay
CLDN1	Claudin-1
CLDs	Cytoplasmic Lipid Droplets

List of Abbreviations (Continued)

Abb.	Full Term
CLIA	Chemiluminescent Immunoassay
CRP	C reactive Protein
CT	Computed Tomography
CV	Cardiovascular
CVD	Cardiovascular Disease
CYP	Cytochrome
DAAs	Direct-Acting Antivirals
DCV	Daclatasvir
DM	Diabetes Mellitus
DSV	Dasabuvir
EBR	Elbasvir
ECG	Electrocardiogram
EDHS	Egypt Demographic and Health Surveys
EDTA	Ethylenediaminetetraacetic acid
EGFR	Epidermal Growth Factor Receptor
eGFR	Estimated Glomerular Filtration Rate
EHIS	Egyptian Health Issue Survey
EIA	Enzyme Immunoassay
ELISA	Enzyme - Linked Immunosorbent Assay
EOT	End of Treatment
ESRD	End-Stage Renal Disease
FBG	Fasting Blood Glucose
FDA	Food and Drug Administration
FGF	Fibroblast Growth Factor
FIB4	Fibrosis-4

List of Abbreviations (Continued)

Abb.	Full Term
FRS	Framingham Risk Score
FU	Follow up
GLE	Glecaprevir
GT	Genotype
GZR	Grazoprevir
HAV	Hepatitis A Virus
Hb	Hemoglobin
HbA1c	Hemoglobin A1c
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HDL	High Density Lipoprotein
HIV	Human Immunodeficiency Virus
HOMA-IR	Homeostatic Model Assessment of Insulin Resistance
HRP	Horseradish Peroxidase
hs-CRP	High Sensitivity-C Reactive Protein
ICAM	Intercellular Adhesion Molecule
IFN	Interferon
Ig	Immunoglobulin
IL	Interleukin
INR	International Normalized Ratio
IQR	Interquartile Range
IUs	International Units
kPa	Kilopascal
LDL	Low-Density Lipoprotein

List of Abbreviations (Continued)

Abb.	Full Term
LDL-C	LDL Cholesterol
LDLR	LDL Receptor
LDV	Ledipasvir
Lp	Lipoprotein
Lp-PLA2	Lipoprotein Associated-Phospholipase A2
LV	Left Ventricle
LVPs	Lipoviroparticles
MELD	Model for End-Stage Liver Disease
MI	Myocardial Infarction
mi-RNA	Micro-RNA
mLDL	Modified LDL
mLDL-IC	Modified LDL-containing Immune Complexes
MRI	Magnetic Resonance Imaging
MS	Metabolic Syndrome
NAAT	Nucleic Acid Amplification Test
NAT	Nucleic Acid Test
NCCVH	National Committee for Control of Viral Hepatitis
Nis	Nucleotide Inhibitors
NNIs	Non-Nucleotide Inhibitors
NPV	Negative Predictive Value
NS	Non Structural
NT-proBNP	N-Terminal Prohormone of BNP
OBV	Ombitasvir
OD	Optical Density

List of Abbreviations (Continued)

Abb.	Full Term
OxFFA	Oxidized Non-Esterified Fatty Acids
OxPL	Oxidized Phospholipids
PAF-AH	Platelet Activating Factor-Acetyl Hydrolase
PAT	Parenteral Anti - schistosomiasis Treatment
PAUS	Pelvi-Abdominal Ultrasound
PCR	Polymerase Chain Reaction
PegIFN-α	Pegylated Interferon Alpha
P-gp	P-glycoprotein
PIB	Pibrentasvir
PIs	Protease Inhibitors
PLT	Platelets
PPV	Positive Predictive Value
PTV	Paritaprevir
PV	Portal Vein
PWIDs	People Who Inject Drugs
R	Ritonavir
RAS	Resistance Associated Substitutions
RBV	Ribavirin
RdRP	RNA-Dependent RNA Polymerase
RIBA	Recombinant Immunoblot Assay
RIG-1	Retinoic Acid-Inducible Gene 1
RNA	Ribonucleic Acid
ROC	Receiver Operating Characteristic
RT-qPCR	Real-Time Quantitative Polymerase Chain Reaction

List of Abbreviations (Continued)

Abb.	Full Term
SD	Standard Deviation
SE1	Standard Error of the First Group
SE2	Standard Error of the Second Group
SEd	Standard Error of the Difference between Pre and Post
SIM	Simeprevir
SOF	Sofosbuvir
SPSS	Statistical Package for the Social Sciences
SVR	Sustained Virologic Response
TMB	Tetramethylbenzidine
TNFR	TNF- α Receptor
UK	United Kingdom
USA	United States of America
UTRs	Untranslated Regions
VCAM	Vascular Cell Adhesion Molecule
VEL	Velpatasvir
VLDL	Very-Low-Density Lipoproteins
VOX	Voxilaprevir
WBC	White Blood Cell Count
WHO	World Health Organization
$\bar{X}$ 1	Mean of the First Group
$\bar{X}$ 2	Mean of the Second Group
$\bar{X}$ d	Mean's Difference between Pre and Post

List of Tables

Table No.	Title	Page
Table (1):	Approved HCV DAAs	32
Table (2):	Treatment recommendations for patients with chronic hepatitis C without cirrhosis, including treatment-naïve patients and treatment-experienced patients	33
Table (3):	Treatment recommendations for patients with chronic hepatitis C with compensated (Child-Pugh A) cirrhosis, including treatment-naïve patients and treatment-experienced patients	34
Table (4):	Baseline characteristics of the study cohort	94
Table (5):	Comparison between HCV RNA level at baseline and 12 weeks after the end of treatment, in patients who did not achieve SVR (n=4)	95
Table (6):	CBC at baseline and 12 weeks after the end of treatment, in all studied patients (n=90)	95
Table (7):	Liver function tests (LFTs) at baseline and 12 weeks after the end of treatment, in all studied patients (n=90)	97

List of Tables (Continued)

Table No.	Title	Page
Table (8):	Comparison between Lipid profile at baseline and 12 weeks after the end of treatment, in all studied patients (n=90).....	99
Table (9):	Comparison between Lipid profile at baseline and 12 weeks after the end of treatment, in patients who achieved SVR (n=86).....	102
Table (10):	Comparison between Lipid profile at baseline and 12 weeks after the end of treatment in patients who failed to achieve SVR to DAA therapy (n=4)	103
Table (11):	Comparison between serum Lp-PLA2 level at baseline and 12 weeks after the end of treatment, in all studied patients (n=90)	104
Table (12):	Comparison between serum Lp-PLA2 level at baseline and 12 weeks after the end of treatment, in patients who achieved SVR (n=86).....	105
Table (13):	Comparison between serum Lp-PLA2 level at baseline and 12 weeks after the end of treatment in patients who failed to achieve SVR (n=4).....	105