

**Study of the Effect of Directly Acting
Antiviral Drugs (DAA) on Hepatic Fibrosis
Using APRI Score and FIB4 Score in Chronic
Hepatitis c Patients (HCV)**

Thesis

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By

Islam Badr Ezzeldin Mohamed

M.B.B.Ch

Under supervision of

Prof. Dr. Enas Mahmoud Foda

Professor of Internal Medicine

Faculty of Medicine, Ain Shams University

Prof. Dr Amir Helmy Samy

Professor of Internal Medicine

Faculty of Medicine Ain Shams University

Ass.Prof.Shereen Abou Bakr Abd ElRahman

Assistant Professor of Internal Medicine

Faculty of Medicine Ain Shams University

Faculty of Medicine

Ain Shams University

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Islam Badr

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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List of Abbreviations

Abb.	Full term
<i>Ala</i>	<i>Alanine.</i>
<i>ALT</i>	<i>Alanine aminotransferase.</i>
<i>APO-E</i>	<i>Apolipoprotein E.</i>
<i>APRI</i>	<i>AST to platelet ratio index.</i>
<i>ARG</i>	<i>Arginine.</i>
<i>ASP</i>	<i>Aspartate.</i>
<i>AST</i>	<i>Aspartate aminotransferase.</i>
<i>AUROC</i>	<i>Area under receiver operating curve.</i>
<i>CB1</i>	<i>Cannabinoid receptor 1.</i>
<i>CDC</i>	<i>Centre for disease control and prevention.</i>
<i>CHC</i>	<i>Chronic hepatitis c.</i>
<i>CLDN-1</i>	<i>Claudin-1.</i>
<i>cLDs</i>	<i>Cytoplasmic lipid droplets.</i>
<i>CT</i>	<i>Computed tomography.</i>
<i>CYP-A</i>	<i>Cyclophilin-A.</i>
<i>DAA</i>	<i>Directly acting antiviral drugs.</i>
<i>DAMPs</i>	<i>Damage associated molecular patterns.</i>
<i>DGAT</i>	<i>Diacyl glycerol acetyl transferase.</i>
<i>DNA</i>	<i>Deoxyribonucleic acid.</i>
<i>ECM</i>	<i>Extracellular matrix.</i>
<i>EDHS</i>	<i>Egyptian demographic health survey.</i>
<i>EGFR</i>	<i>Epidermal growth factor receptor.</i>
<i>EHIS</i>	<i>Egyptian health issue survey.</i>
<i>ER</i>	<i>Endoplasmic reticulum.</i>
<i>FIB-4</i>	<i>Fibrosis-4 score.</i>
<i>GALT</i>	<i>Gut associated lymphoid tissue.</i>
<i>GT</i>	<i>Genotype.</i>

List of Abbreviations cont...

Abb.	Full term
<i>HBV</i>	<i>Hepatitis B virus.</i>
<i>HCC</i>	<i>Hepatocellular carcinoma.</i>
<i>HCV</i>	<i>Hepatitis c virus.</i>
<i>HIV</i>	<i>Human immune deficiency virus.</i>
<i>HSC</i>	<i>Hepatic stellate cells.</i>
<i>IFN</i>	<i>Interferone.</i>
<i>IR</i>	<i>Insulin resistance.</i>
<i>JAK</i>	<i>Janus activation kinase.</i>
<i>Kpa</i>	<i>Kilo pascal.</i>
<i>LDL</i>	<i>Low density lipoprotein.</i>
<i>Leu</i>	<i>Leucin.</i>
<i>LPS</i>	<i>Lipopolysaccharide.</i>
<i>LSECS</i>	<i>Liver sinusoidal endothelial cells.</i>
<i>LVP</i>	<i>Lipoviroparticles.</i>
<i>MAV</i>	<i>Mitochondrial antiviral signaling.</i>
<i>MET</i>	<i>Methionine.</i>
<i>MLNs</i>	<i>Mesenteric lymph nodes.</i>
<i>MMP</i>	<i>Matrix metalloproteinase.</i>
<i>MRI</i>	<i>Magnetic resonance image.</i>
<i>NANBH</i>	<i>Non A non B hepatitis.</i>
<i>NF-KB</i>	<i>Nuclear factor K-light chain enhancer activated B cell.</i>
<i>NS</i>	<i>Non-structural.</i>
<i>OCLN</i>	<i>Occludin.</i>
<i>PAMPs</i>	<i>Pathogen associated molecular patterns.</i>
<i>PDGF</i>	<i>Platelet driven growth factor.</i>
<i>PI</i>	<i>Protease Inhibitor.</i>
<i>PPAR</i>	<i>Peroxisome proliferator activated receptor.</i>

List of Abbreviations cont...

Abb.	Full term
<i>RIG-1</i>	<i>Retinoic acid inducible gene-1.</i>
<i>RNA</i>	<i>Ribonucleic acid.</i>
<i>ROS</i>	<i>Reactive oxygen species.</i>
<i>SAFE</i>	<i>Sequential algorithm for fibrosis evaluation.</i>
<i>TE</i>	<i>Transient elastography.</i>
<i>TGF-B</i>	<i>Transforming growth factor beta.</i>
<i>TH1</i>	<i>T helper 1 cell.</i>
<i>TIMP</i>	<i>Tissue metalloproteinase.</i>
<i>TNF</i>	<i>Tumor necrosis factor.</i>
<i>TRIF</i>	<i>TIR domain containing adaptor inducing IFN- beta.</i>
<i>U/S</i>	<i>Ultrasound.</i>
<i>UTRs</i>	<i>Untranslated regions.</i>
<i>VLDL</i>	<i>Very low density lipoprotein.</i>

INTRODUCTION

Hepatitis C virus (HCV) genotype (GT) 4 represents 12%-15% (15-18 million) of total global HCV infection. It is prevalent in Northern and Equatorial Africa and the Middle East, and is also present in some countries in Europe. GT-4 (and subtype 4a in particular) dominates the HCV epidemic in Egypt. HCV can progress to cirrhosis after decades. It can also lead to liver cell failure or hepatocellular carcinoma (HCC) (approximately 2% to 4% yearly). Several factors influence the progression of the disease, the most important of which is the extent of intrahepatic inflammation elicited by HCV (*Abdelghaffar et al., 2015*).

The accurate evaluation of liver fibrosis in chronic hepatitis C is mandatory to appraise therapeutic indications and prognosis, because complications mainly occur in patients in advanced stages of their disease. Noninvasive tests to assess hepatic fibrosis have been developed, such the AST-to-platelet ratio index (APRI). The FIB-4 index has an area under the receiver operating characteristic (ROC) curve of 0.76. A threshold value of 1.45 has a negative predictive value for the exclusion of extended fibrosis of 90%. A threshold value of 3.25 has a positive predictive value for the diagnosis of extended fibrosis of 65% (*White et al., 2008*).

DAA (Directly Acting antiviral) is effective for treatment of chronic hepatitis c virus infection, reducing the morbidity

and mortality related to the disease progression (*Gaetano et al., 2014*). Improvement in liver function within 6 months compared to untreated patients (*Graham et al., 2016*).

In this study we are demonstrating the effect of DAA on hepatic fibrosis in patients with chronic hepatitis c virus infection using APRI and FIB-4 scores as non invasive methods which are highly indicative of the degree of hepatic fibrosis.

AIM OF THE WORK

To evaluate the effect of DAA agent on the degree of hepatic fibrosis in chronic hepatitis C infection (with or without cirrhosis) after treatment using APRI (ALT to Platelet reference index) and FIB-4 score in patients who received DAA.