بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

Fibroscan as Non Invasive Modality for Studying the Effect of Hepatic Steatosis on Viral Response to Direct – Acting Antiviral in Patients with Chronic Hepatitis C

Thesis

Submitted for Partial Fulfillment of Master Degree in **Hepatology and Gastroenterology**

By

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Abdallah Abd El Hameed Ghoneim

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List of Abbreviations

Abb.	Full term
AFP	*Serum alpha-fetoprotein*
ALT	*Alanine aminotransferase*
AST	*Aspartate transaminase*
CAP	*Controlled attenuation parameter*
CBC	*Complete blood count*
COX-2	*Cyclooxygenase-2*
DAA	*Direct Antiviral Agents*
DAAs	*Direct Acting Antiviral Drugs*
EHMs	*Extra-hepatic manifestations*
EIA	*Enzyme immunoassay*
ELISA	*Enzyme-Linked Immunosorbent Assay*
FBS	*Fasting blood sugar level*
FFA	*Free fatty acids*
FLI	*Fatty liver index*
GGT	*Gamma glutamyl transferase*
HCC	*Malignancy either primary*
HCV	*Hepatitis C virus*
HDL	*High density lipo-protien*
HSCs	*Hepatic stellate cells*
HVR	*Hyper variable regions*
IDU	*Intravenous drug use*
IgG	*Immunoglobulin G*
INR	*International normalized ratio*
IQR	*Interquartile range interval*
ISGs	*INF-stimulated genes*
KCs	*Kuppfer cells*
kPa	*kiloppascals*
LDL	*Low density lipo-protein*
LSM	*Liver stiffness measurement*
LTx	*Liver transplantation*
MIP1α-1β	*Macrophages inflammatory proteins*
NAFLD	*Non-alcoholic fatty liver disease*
NASH	*Non-alcoholic steatohepatitis*

List of Abbreviations **cont...**

Abb.	Full term
NIs	*Nucleotide inhibitors*
NNIs	*Non-nucleotide inhibitors*
NS	*Nonstructural*
NS	*Non Structural*
PCR	*Polymerase Chain Reaction*
PDFF	*Proton density fat fraction*
R155K	*Retains activity against mutated Arg155*
RIG-1	*Retinoic acid–inducible gene 1*
SR	*Success rate*
SVR	*Sustained virologic response*
TE	*Transient elastography*
TLRs	*Toll-like receptors*
VCTE	*Vibration controlled transient elastography*

ABSTRACT

Background: Hepatic steatosis in hepatitis C virus (HCV) infected patients has been shown to enhance the progression of liver fibrosis and cirrhosis. Liver biopsy was the gold standard for diagnosis of hepatic steatosis. However, liver biopsy is an invasive procedure and associated with complication (e.g., bleeding). Recently, controlled attenuation parameter (CAP) in transient elastography (TE) has been introduced to detect and quantify hepatic steatosis. CAP measures the ultrasonic attenuation in the liver tissue depending on the viscosity [fat] of the medium [liver] and the distance of propagation of the ultrasonic signals into the liver. Non alcoholic fatty liver disease (NAFLD) was defined by CAP values ≥ 216 dB/m. Direct-acting antiviral (DAA) therapy is associated with high sustained virologic response (SVR) and overcomes negative predictive factors including steatosis.

Objectives: The aim of this study to use the fibroscan as non invasive modality for study the impact of hepatic steatosis on SVR in HCV infected patients receiving DAA therapy.

Results: This study was conducted on 40 patients diagnosed as HCV with NAFLD based on positive anti-HCV antibody, positive HCV viremia, abdominal ultrasonography, serum liver enzymes, body mass index (BMI). All patients assessed by TE with CAP to detect and quantify hepatic steatosis (CAP cut off value ≥ 216 dB/m) and also assessed by non invasive scores (APRI score, FIB-4 score, HSI score). After start of antiviral treatment, patients were seen every 4 weeks until the end of therapy and 12 weeks after the end of therapy to assess SVR-12. The overall SVR-12 (n=36) was 90% and was not impacted by presence of hepatic steatosis.

Conclusion: Our study confirmed that hepatic steatosis has no impact on SVR in HCV infected patients receiving DAA therapy. TE with CAP can be used as non invasive method for assessment of hepatic steatosis.

KEYWORDS: FIBROSCAN, NON INVASIVE MODALITY, HEPATIC STEATOSIS, VIRAL RESPONSE TO DIRECT, ACTING ANTIVIRAL, CHRONIC HEPATITIS C

INTRODUCTION

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease, more than 185 million people are infected in the whole world ***(Gower et al., 2016)***. Egypt has the highest world wide prevalence (8%-12%) country wide and up to 50% in age above 50 years in certain rural areas due to specific modes of infection ***(Elghraably et al., 2017).*** The long term impact of HCV infection is highly variable, ranging from minimal effects to chronic hepatitis advanced fibrosis, cirrhosis, decompensated cirrhosis and hepatocellular carcinoma. Chronic HCV infection may also induce severe extra-hepatic complications ***(Maasoumy and Wedemeyer, 2016).***

The primary goal of HCV therapy is to cure the infection, i.e. to achieve a sustained virological response (SVR) which defined as undetectable HCV RNA 12 weeks (SVR12) or 24 weeks (SVR24) after treatment completion. Long-term follow up studies have shown that an SVR corresponds to a definitive cure of the HCV infection, with a very low chance of late relapse ***(Bruno et al., 2016).***

Direct Antiviral Agents (DAA) can be divided into 3 classes defined by the Non Structural (NS) HCV protein they target: NS3 Protease inhibitors, NS5B Polymerase inhibitors and NS5A protein inhibitors ***(Swain et al., 2015).*** The high efficacy, combined with the near perfect safety profile of DAAs, has challenged the need for regular on treatment