"Impact of gene polymorphism on Egyptian HCV patients under direct antiviral Drugs"

BY

Basma Mohamed Moawad Ali

B.SC. in Chemistry-Biochemistry, Fayoum University, 2013

A thesis submitted in partial fulfillment

Of

The requirements for the degree of

Master of Science

In

Biochemistry

Department of chemistry

Faculty of Science, Fayoum

Fayoum University

2019

IMPACT OF GENE POLYMORPHISM ON EGYPTIAN HCV PATIENTS UNDER DIRECT ANTIVIRAL DRUGS

BY

Basma Mohamed Moawad Ali

B.SC. in Chemistry-Biochemistry, Fayoum University, 2013

Prof. Dr. Soha Mohamed Hamdy

Professor of Bio chemistry,
Chemistry Department,
Faculty of Science,
Fayoum University
Signature: …….

Dr. Ahmed Ali Gomaa Afify

Professor of Tropical Medicine,
Gastroenterology Department,
Faculty of Medicine,
Fayoum University
Signature: …….

Dr. Amany mohmmed mohmmed

Assistant Professor of Biochemistry,
Chemistry Department,
Faculty of Science,
Fayoum University
Signature: …….

Vice-Dean for post graduate and research, Faculty of Science, Fayoum University
Dr. Mohamed Said Mahmoud Abu El Ghar
Signature: ……

Approval Sheet

IMPACT OF GENE POLYMORPHISM ON EGYPTIAN HCV PATIENTS UNDER DIRECT ANTIVIRAL DRUGS

BY

Basma Mohamed Moawad Ali

B.SC. in Chemistry-Biochemistry, Fayoum University, 2013

This thesis for M. SC. Degree has been

Approved by:

1- Prof. Dr. Firoz Anwar

Professor of Biochemistry,
Department of Biochemistry,
Faculty of Science,
King Abdulaziz University, Jedda.

2- Prof. Dr. Magdy Mahmoud Mohamed

Professor of Biochemistry,
Faculty of Science,
Ain Shams University.

3- Prof. Dr. Soha Mohamed Hamdy

Professor of Biochemistry,
Chemistry Department,
Faculty of Science,
Fayoum University

Date of Examination: / / 2019

Chapter six

Summary

Hepatitis C viral infection is a main health problem in Egypt with the highest prevalence rate in the world. For many years, the standard of care for treatment of chronic hepatitis C (CHC) had been a combination of pegylated interferon (Peg-IFN) and ribavirin (RBV) for 48 weeks. DAAs have now become the standard of care for treatment of chronic HCV infection, due to higher efficacy, safety and fewer side effects than interferon-based regimes.

In Egypt, the combination of Sofosbuvir (SOF) with Dataclasvir (DCV) is the broadly used direct acting antiviral drugs with excellent therapeutic profile, also The combination treatment of Ombitasvir, Paritaprevir with low dose of ritonavir (Qurevo) plus ribavirin is preferred for patients with HCV genotype 4 infections because it has high response near to 100% in some studies, in addition to it has low side effects.

The HCV treatment is affected by many factors, genetic variants have been associated with spontaneous clearance of HCV infection, response to treatment for CHC, the GWAS found that a single nucleotide polymorphism (SNP) rs2596542 located in MICA promoter region to be strongly associated with HCV related HCC. MICA is a membrane protein which was described in 1994 on the short arm of chromosome 6 among a group of genes within the human major histocompatibility complex (MHC) class I region.

The aim of the current study is to assess the predictive value of single-nucleotide polymorphisms (SNP) rs2596542 C/T located in the major histocompatibility complex class I chain-related gene A (MICA) on the

response to direct acting antivirals (DAAs) in chronic HCV infected Egyptian patients.

This study was performed on 70 subjects of Egyptian patients positive for HCV RNA in serum (by RT-q PCR assay) the patients were classified in to two groups according to the anti -viral drug used during the course of treatment. **Group I**: (33) patients were received combination therapy Sofosbuvir (Sovaldi) 400 mg/day plus declatasvir 60 mg once daily for a course of 12 successive weeks. **Group II**: (37) patients were received ombitasvir 25 mg, paritaprevir 150 mg and ritonavir100 mg/day plus Ribavirin 15mg/kg/day for 12 weeks.

After SNP rs2596542 C/T genotyping, (5) cases were excluded from this study (undetermined genotype), the remainders (65) subjects, (22) cases of them gave TT-genotype, (28) gave CT-genotype, and the rest (15) cases gave CC-genotype.

In this study, all patients were subjected to the following clinical laboratory investigations before the treatment**:-**

History taking and full clinical assessment; blood samples were taken from volunteers before treatment to investigate the following:

The blood HCV level by real time polymerase chain reaction (RT-PCR); MICA single nucleotide polymorphism of rs 2596542 evaluation was performed in all volunteer patients; liver function tests [Alanine aminotransferase (ALT), Aspartate aminotransferase activity (AST), total bilirubin, and serum albumin level]; fasting blood sugar level; glycosylated hemoglobin (Hb A1C %); complete blood picture (CBC); kidney function tests [serum creatinine]; tumor markers [Alpha Fetoprotein (AFP)]; international normalized ratio (INR); abdominal ultrasound (U/S), for liver cirrhosis. After (12 weeks) of DAAs treatment, Blood samples were

collected from the volunteers to evaluate: - the blood HCV level by real time polymerase chain reaction (RT-PCR), and biochemical parameters.

In this study, the investigation of the associations between SNP (rs2596542C/T) with the response to DAAs in chronic HCV infected Egyptian patients was examined. It is noticed that the majority of patients gave negative PCR results at the end of treatment this means high SVR was achieved after completing the administration of DAAs. The study showed that, The HCV patients treated with Sofosbuvir (Sovaldi) 400 mg/day plus declatasvir 60 mg once daily for a course of 12 successive weeks responded with 100% in both CC and TT- SNP genotypes, However CT – genotype responded with 91.67%.

And the HCV patients treated with Ombitasvir 25 mg, paritaprevir 150 mg and ritonavir 100 mg/day plus Ribavirin 15 mg/kg/day for 12 weeks, responded with 100% in CT- SNP genotype, However Both CC and TT- SNP genotypes responded with 83.33% and 91.67% respectively.

Results also showed that, there was no observed significant association between this SNP and some clinical parameters such as liver enzymes (ALT, AST), total bilirubin, serum Albumin, serum creatinine, HB, INR, HbA1c %. However, there was statistical a positive significant correlation among the platelets count and AFP in the CC – genotype ($p < 0.05$).