The relationship between IL-28B genotypes and viral load in HCV chronic hepatitis genotype 4 Egyptian

Thesis

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Tamer Mohammed Fakhry

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LIST OF ABBREVIATIONS

AA	:	Amino Acid
AASLD	**:**	American Association For The Study Of Liver Disease
AFP	**:**	Alpha Fetoprotein
Ag	**:**	Antigen
ALT	**:**	Alanine Aminotransferase
AP	**:**	Alkaline Phosphatatase
AST	**:**	Aspartate Aminotransferases
AT	**:**	Antithrombin
BMI	**:**	Body Mass Index
CLD	**:**	Chronic Liver Disease
D. Bil	**:**	Direct Bilirubin
DAA	**:**	Direct-Acting Antiviral Agent
DNA	**:**	De-Oxy Ribonucleic Acid
DVR	**:**	Delayed Virological Response
EDHS	**:**	Egyptian Demographic Health Survey
EIA	**:**	Enzyme Linked Immunosorbent Essay
EVR	**:**	Early Virologic Response
FDA	**:**	Food And Drug Administration
GGT	**:**	Gamma Gluteryl Transferase
HBeAg	**:**	Hepatitis B E Antigen

HBsAg	**:**	Hepatitis B Surface Antigen
HBV	**:**	Hepatitis B Virus
HCC	**:**	Hepatocellular Carcinoma
HCV	**:**	Hepatitis C Virus
Hgb	**:**	Hemoglobin
HIV	**:**	Human Immune Deficiency Virus
HRS	**:**	Hepato-Renal Syndrom
IFN α	**:**	Interferon alfa
IFN-3	**:**	Interferon-3
IgM	**:**	Immunoglobulin M
IL28B	**:**	Interleukin 28b
INF	**:**	Interferon
INR	**:**	International Normalization Ratio
ITP	**:**	Immune Thrombocytopenic Purpura
IU	**:**	International Unit
KD	**:**	Kilo Dalton
LKM	**:**	Liver/kidney microsomes
Mb	**:**	Mega base
mRNA	**:**	Messenger Ribonucleic Acid
NI	**:**	Nucleoside Analogue Inhibitor
NIHC	**:**	National Institutes of Health Consensus Development Conference

NK	**:**	Natural Killer
NNI	**:**	Non Nucleoside Inhibitor
NRTI	**:**	Neucloside Reverse Transcriptase Inhibitor
NS	**:**	Non Structural
PCR	**:**	Polymerase Chain Reaction
PEG-IFN	**:**	Pegylated Interferon
PHTN	**:**	Portal Hypertension
PLT	**:**	Platelets
PT	**:**	Prothrombin Time
PVT	**:**	Portal Vein Thrombosis
RBV	**:**	Ribavirin
RDRP	**:**	RNA Dependent RNA Polymerase
RNA	**:**	Riboneucleic Acid Of Hepatitis C Virus
RVR	**:**	Rapid Virologic Response
SBP	**:**	Spontaneous Bacterial Peritonitis
SNPs	**:**	Single nucleotide polymorphisms
STAT-C	**:**	Specially Targeted Antiviral Therapy For HCV
SVR	**:**	Sustained Virologic Response
T.bil	**:**	Total Bilirubin
TE	**:**	Transient Elastography
Te	**:**	Transient Elastography
TGF	**:**	Transforming Growth Factor

TMA	**:**	Transcription Mediated Amplification
TSH	**:**	Thyroid Stimulating Hormone
U/S	**:**	Ultra Sound
USA	**:**	United States Of America
UTR	**:**	Untranslated Regions
WBC	**:**	White Blood Cells
WHO	**:**	World Health Organization

Abstract

Background: Egypt has the highest prevalence of HCV worldwide 13.8 %. The treatment with (IFN-α) and ribavirin. As these therapies have side effects and high costs, it is important to identify patients having the best chance to respond before initiation of therapy.

Objective: The objective of the study is to determine the correlation between Hcv viral load and IL-28B genotypes before starting treatment and to find out if viral load and IL-28B genotypes could serve as a predictor of response to HCV treatment in Egyptian patients infected by HCV genotype 4.

Methods: This study was conducted on 30 patients with chronic hepatitis C genotype 4 before treatment with pegylated interferone and ribavirin.IL28 genotyping prior to treatment will be assessed and patients divided according to their genotype into 3 groups:

Group 1: CC Group 2: CT Group 3: TT

Correlation between IL28b genotyping and viral load was studied and statistically analyzed

Results:

There is significant increase of virus load in TT polymorphism group (367.02±308.99) when compared to CT (111.27±87.10) or CC (273.47±311.59) groups.

Conclusion: baseline viral load is strongly correlated with and IL-28B genotypes, baseline viral load and IL28B may help in selecting patients prior to initiation of treatment. This will help a lot in cutting costs and in prioritization of patients.

Keywords: HCV, baseline viral load, IL-28B genotypes.

INTRODUCTION

Chronic hepatitis C virus is a major health problem affects ~ 170 million individuals worldwide, Egypt has one of the highest HCV prevalences in the world. Genotype 4 comprises 93% of the total HCV infections in Egypt, and other genotypes comprise only small proportions of the infected population **(El-Zayadi et al., 1994 & Abdel-Hamid et al., 2007).**

The combination of a pegylated IFN plus ribavirin, together they significantly increases sustained virological response rates (**Zeuzem et al., 2009**). It is important in treating the chronic HCV infection to identify patient and viral characteristics that predict response to current therapies. These factors include; HCV genotype, viral load, body weight, age, liver histology, co-infection with HIV and treatment adherence and patient tolerance **(Nelson et al., 2009).**

Recent studies showed that presence of IL28b affects response of hepatitis C virus to interferon-based therapy as well. Among people with hepatitis C, individuals with the C/C gene pattern, meaning they carry 2 copies of the "C" variant or allele- are more likely to respond well to interferon Alfa plus ribavirin. People with the T/T pattern have the least favorable

response, while those carrying 1 “C” and 1 “T” allele fall somewhere in between **(Kurbanov et al., 2010).**

The rapid virologic response (RVR) is a key element in the early identification of patients who may benefit from treatment regimens; thus, RVR is now regarded as a valuable tool in the clinical management of genotype 4 HCV patients **(Kamal et al., 2007).**

There is a correlation between viral load and IL-28B genotypes in HCV chronic hepatitis genotype 4. We therefore conducted this prospective study, to determine this correlation as a pretreatment variable that could be clinically useful as predictor of RVR, which will be useful for tailoring anti-viral regimens.

AIM OF WORK

The objective of the study is to determine the correlation between Hcv viral load and IL-28B genotypes before starting treatment and to find out if viral load and IL-28B genotypes could serve as a predictor of response to HCV treatment in Egyptian patients infected by HCV genotype 4.