

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

Thesis

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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 Phosphatase
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.