Pilot study to Show Prevalence of Different Types of Single Nucleotide Polymorphism in IL-28B-gene in Egyptian population

Thesis

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*May **ALLAH** accept the work of all those and reward them for it.*

Saber Abdullah Ali

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Abstract

Background Chronic hepatitis C virus (HCV) infection is a global healthcare problem, with the estimated number of people positive for anti-hepatitis C virus antibodies increasing from >122 million to >185 million between 1990 and 2005. Egypt has the highest HCV prevalence in the world. Single nucleotid polymorphism in gene IL28B correlated strongly with both hepatitis C virus spontaneous clearance and treatment-related response.

Individuals with the C/C genotype had a 3-fold greater likelihood of spontaneous HCV clearance compared to patients who had the T/C or T/T genotype. Additionally, the strong association between C/C genotype and spontaneous clearance was present in both whites and blacks. In addition, the global distribution of the protective CC allele correlated strongly with ethnic differences in spontaneous resolution of HCV, just as Ge et al. had reported for treatment-related response.

Objective the current study aimed to determine the prevalence of different types of single nucleotid polymorphism in gene IL28B in Egyptian population.

Method 60 persons were subjected to IL28b genotyping by sequencing mechanism (Taq Man® Real- Time PCR) to detect type of IL28b polymorphism and patients divided according to their genotype into 3 groups. Group 1: CC favorable Group 2: CT unfavorable Group 3: TT. Unfavorable gene.

Results In our study As regard gene polymorphism, it was CC in 10 cases (16.6%), CT in 31cases (51.6.0%) and TT in 19 cases (31.6%) with no significant difference between males and females or between urban populations and rural populations.

Conclusion From our study we found that un favorable IL28 B genotypes (C/T)and (T/T) are more frequent than favorable genotype (C/C) with Egyptian population.

INTRODUCTION

Chronic Hepatitis C virus (HCV) infection is a global healthcare problem, with the estimated number of people positive for anti-hepatitis C virus antibodies increasing from >122 million to >185 million between 1990 and 2005 **[Hanafiah KM et al., 2013**].

Central and Eastern Asia, North Africa, and the Middle East are thought to have the highest prevalence of anti-HCV antibodies (>3.5%) **[Hanafiah KM et al., 2013**]. HCV prevalence among the general population of Egypt is documented to be very high. The 2008 EDHS (Egypian Demographic and Health Survey) measured HCV prevalence to be 14.7% among a nationally representative sample of 11, 126 Egyptians aged 15–59 years old [**El-Zanaty F, Way A, 2009**]. Accordingly, Egypt has the highest HCV prevalence in the world [**Lavanchy D, 2011**].

In Egypt, prevalence of genotype-4 presents 96% of the HCV isolated from the mothers and their infants [**Abdel Hamid et al., 2007**].There is a hypothesis that the high prevalence of HCV is linked to a now-discontinued mass-treatment campaign for schistosomiasis, which is endemic in that country. Regardless of how the epidemic started, a high rate of HCV

transmission continues in Egypt, both iatrogenically and within the community and household [**Frank C et al., 2000**].

The natural course of chronic hepatitis C varies considerably from one person to another. Although almost all people infected with HCV have evidence of inflammation on liver biopsy, the rate of progression of liver scarring (fibrosis) shows significant variability among individuals. Accurate estimates of the risk over time are difficult to establish because of the limited time that tests for this virus have been available. Recent data suggest that among untreated patients, roughly one-third progress to liver cirrhosis in less than 20 years. Another third progress to cirrhosis within 30 years. The remainder of patients appear to progress so slowly that they are unlikely to develop cirrhosis within their lifetimes [**"NIH Consensus Statement on Management of Hepatitis C: 2002"**].

Factors that have been reported to influence the rate of HCV disease progression include age (increasing age associated with more rapid progression), gender (males have more rapid disease progression than females), alcohol consumption (associated with an increased rate of disease progression), HIV coinfection (associated with a markedly increased rate of disease progression), and fatty liver (the presence of fat in liver cells has been associated with an increased rate of disease progression) [**Ngo Y et al., 2006**].

Studies found that the C allele occurred more frequently in patients who spontaneously cleared HCV. Individuals with the C/C genotype had a 3-fold greater likelihood of spontaneous HCV clearance compared to patients who had the C / T or T/T genotype. Additionally, the strong association between C/C genotype and spontaneous clearance was present in both whites and blacks [**Thomas DL et al., 2009**]. In addition, the global distribution of the protective CC allele correlated strongly with ethnic differences in spontaneous resolution of HCV, just as Ge et al., had reported for treatment-related response [**Ge D et al., 2009**].

The SNPs (single nucleotide polymorphisms***)*** had the most significant predictive value for treatment outcomes in several countries **[Hayes CN et al., 2011**].The polymorphism in IL28B forms a cluster of single nucleotide polymorphisms (SNPs) that appear to delineate a genetic haplotype within a very low recombination fragment containing the IL28B gene. Among all the SNPs within this cluster, rs12979860 and rs8099917 are the strongest markers of the haplotype, and consistently predict treatment outcomes for patients receiving IFN-based (interferon -based) regimens [**Rauch A et al., 2010**].

Recently, a study examining a cohort of African Americans identified a novel interferon lambda 4 (IFNL4) gene located in an immediate proximity to the IL28B, and suggested that it was associated with HCV clearance **[Prokunina-Olsson**

L et al., 2013]. The IFNL4 SNP improved the prediction rate of IFN-based regimens in African Americans, and more recently in Caucasians and Japanese **[Clark PJ et al., 2011**] and [**Fujino H et al., 2013**].

AIM OF THE WORK

To determine the prevalence of different types of single nucleotid polymorphism in gene IL28B in Egyptian population.