Original Article

Prevalence of interleukin-28B single nucleotide polymorphism genotypes in patients with hepatitis C infection in Isfahan, Iran

Mohammad Minakari, Marjan Golshani, Majid Yaran[1], Behrooz Ataei[2]

Department of Infectious Diseases, [1]Acquired Immunodeficiency Research Center, [2]Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Background: Hepatitis C infection is one of the most common causes of liver-related morbidity and mortality. Due to limited efficacy and side-effects of treatment, identification of the determinants of response to treatment is an important issue. Nowadays, genotyping of interleukin (IL)-28B is one of the strongest tests used for prediction of sustained virological response. The prevalence of IL28B genotypes varies across different ethnicities. This study presents data on IL28B single nucleotide polymorphism (SNP) (rs12979860) in a group of Iranian hepatitis C virus (HCV)-infected patients in Isfahan.

Materials and Methods: One hundred patients already diagnosed for hepatitis C enrolled the study. Genomic DNA was extracted from whole blood samples. Specific primers were used to amplify IL28B gene (rs12979860). The rs129679860 SNP was genotyped by real-time polymerase chain reaction using TaqMan® probes.

Results: The mean age of patients was 33.16 years (25–42 years). Ninety-nine subjects were male and 1 was female. The frequency of HCV genotypes was as follows: Genotype 3a: 53%, genotype 1a: 42%, genotype 1b: 2%, mixed genotype (1a + 3a): 1% and 2%: Nontypable.

IL28B rs12979860 genotypes were TT in 17 patients (17%), CT in 41 patients (41%), and CC in the remaining 42 patients (42%).

Conclusion: The prevalence of C allele is much higher in our population study than in African American HCV patients (62.5% and 40% respectively), which can explain better response to treatment in our patients.

Key Words: Genotype, hepatitis C, interleukin-28B, Isfahan

Address for correspondence:
Dr. Behrooz Ataei, Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: ataei@med.mui.ac.ir
Received: 05.03.2013, **Accepted:** 08.04.2015

INTRODUCTION

Hepatitis C infection is one of the most common causes of liver-related morbidity and mortality.[1] Many hepatitis C virus (HCV) infected individuals are living worldwide and 8,000–10,000 people die because of this infection, annually. It is a major cause of cirrhosis and hepatocellular carcinoma, too. It is estimated that the occurrence of end-stage liver disease caused by HCV reaches a peak around 2020.[2,3]

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.183138

How to cite this article: Minakari M, Golshani M, Yaran M, Ataei B. Prevalence of interleukin-28B single nucleotide polymorphism genotypes in patients with hepatitis C infection in Isfahan, Iran. Adv Biomed Res 2016;5:90.

In Iran, HCV infection has a prevalence of <1%. HCV genotype 1a is the most frequent genotype (about 45%), followed by genotype 3a (more prevalent in the northwest of the country) and 1b.[4,5]

Only 40–60% of patients infected with HCV genotype 1 achieve sustained virological response (SVR) after treatment with pegylated interferon plus ribavirin, and many of them will not be cured.[6] Treatment is relatively expensive, and a large number of patients cannot afford it. Furthermore, treatment may cause many undesirable side-effects and some patients poorly tolerate the regimen because of these side-effects.[7,8] Hence, selection of patients who are more prone to respond to treatment is very important.[7,9]

Many factors such as HCV genotype, HCV RNA levels, the dose and duration of therapy, body mass index, age, insulin resistance, gender, stage of fibrosis, and co-infection with other hepatitis viruses or HIV can predict SVR.[10]

In 2009, Tanaka *et al*. found a single nucleotide polymorphism (SNP) (rs12979860) in the upstream of interleukin (IL)-28B gene which was associated strongly with difference in treatment response of HCV infection.[6] Since that time, many studies have been designed and they showed that genotyping of IL28B was one of the strongest tests for prediction of SVR and its predictive value is higher for HCV genotype 1.[11-14]

It has been found that the prevalence of IL28B genotypes vary across different ethnicities. This paper presents data on IL28B SNP (rs12979860) in a group of Iranian HCV-infected patients in Isfahan. We hope that the results will be a cornerstone for future researches.

MATERIALS AND METHODS

This is a descriptive cross-sectional study. One hundred patients already diagnosed for hepatitis C who were referred to Isfahan Infectious Research Center enrolled the study. The project was explained for them, and after they confirmed and agreed with the written informed consent, 5cc of their whole blood were obtained. Genomic DNA was extracted from whole blood samples by means of the high pure DNA template genomic kit (Roche) according to manufacturer's protocol. The rs129679860 SNP was genotyped by real-time polymerase chain reaction (RQ model, Qinagen) using TAQMAN probe method on DNA isolated from whole blood samples. Primers and probes were adopted from the study of Tillmann *et al*.[12] with the following sequences: Forward primer GCCTGTCGTGTACTGAACCA, reverse primer GCGCGGAGTGCAATTCAAC, and the probes TGGTTCGCGCCTTC (VIC) and CTGGTTCACGCCTTC (FAM), respectively.

RESULTS

Samples from 100 patients with chronic HCV infection were obtained, and genotypes of IL28 were determined. The mean age of patients was 33.16 years (25–42 years). 99 subjects were male and 1 was female.

The frequency of HCV genotypes were as follow: Genotype 3a 53%, genotype 1a 42%, genotype 1b 2%, mixed genotype 1a + 3a 1% and 2% nontypable.

Interleukin-28B rs12979860 genotypes were TT in 17 patients (17%), CT in 41 patients (41%), and CC in the remaining 42 patients (42%).

DISCUSSION

Treatment of HCV infection is frequently complicated, and discontinuation of drugs due to serious adverse events is not uncommon.

Prediction of response to treatment and evaluating the risks and benefits of such therapy would allow us to make more logical decisions about treating HCV-infected patients.[9]

As noted before, IL28B genotype is one of the strongest tests for prediction of SVR. Patients with CC genotype have a higher SVR rate than those with CT or TT genotypes.[3,15]

Furthermore, there is an association between CC genotype and spontaneous clearance of hepatitis C infection. These patients less frequently progress to chronic hepatitis C.[12]

We found that in hepatitis C infected patients in Isfahan, 42% of them had CC genotype, 41% had CT genotype and the remainder 17% had TT genotype.

Our findings were similar to the results of Khajavi *et al*. who studied on HCV patients in Mazandaran province and found that the frequency of IL28B genotypes were as follow: 41.4% C/C genotype, 41.6% C/T genotype and 17.3% T/T genotype.[16]

In 2011, Mahboobi *et al*. performed a study on patients with hepatitis C in Tehran and report that among HCV-infected patients, 52.9% have C/C, 39.7% have C/T and 7.3% have T/T genotypes.[17] Indeed, TT

genotype has a higher frequency in Isfahan than in Tehran (17% vs. 7.3%).

As mentioned previously, the frequency of IL28B gene alleles vary among different ethnicities, which can cause different treatment response rates. Previous studies showed that treatment response is higher among Iranian patients with hepatitis C infection.

In African Americans, rs12979860 genotypes were TT in 37%, CT in 48%, and CC in 16% of patients. Comparison of the above data with our findings reveals that the frequency of C allele is much higher in our patients than in African American patients which can explain the higher treatment response rate among our patients.

Financial support and sponsorship

This project was funded by Isfahan University of Medical Sciences (project number 290258).

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Thomas DL, Thio CL, Martin MP, Qi Y, Ge D, O'Huigin C, *et al.* Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. Nature 2009;461:798-801.
2. Pearlman BL. The IL-28 genotype: How it will affect the care of patients with hepatitis C virus infection. Curr Gastroenterol Rep 2011;13:78-86.
3. Fabris C, Falleti E, Cussigh A, Bitetto D, Fontanini E, Bignulin S, *et al.* IL-28B rs12979860 C/T allele distribution in patients with liver cirrhosis: Role in the course of chronic viral hepatitis and the development of HCC. J Hepatol 2011;54:716-22.
4. Alavian SM, Asl MA, Lankarani KB, Shahbabaie MA, Bahrami Ahmadi A, Kabir A. Hepatitis C infection in the general population of Iran: A systematic review. Hepat Mon 2009;9:211-23.
5. Amini S, Majd Abadi MM, Alavian SM, Joulaie M, Ahmadipour MH. Distribution of hepatitis C virus genotypes in Iran: A population-based study. Hepat Mon 2009;9:95-102.
6. Tanaka Y, Nishida N, Sugiyama M, Kurosaki M, Matsuura K, Sakamoto N, *et al.* Genome-wide association of IL28B with response to pegylated interferon-alpha and ribavirin therapy for chronic hepatitis C. Nat Genet 2009;41:1105-9.
7. Ge D, Fellay J, Thompson AJ, Simon JS, Shianna KV, Urban TJ, *et al.* Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance. Nature 2009;461:399-401.
8. Shiffman ML. Treatment of hepatitis C in 2011: What can we expect? Curr Gastroenterol Rep 2010;12:70-5.
9. Suppiah V, Moldovan M, Ahlenstiel G, Berg T, Weltman M, Abate ML, *et al.* IL28B is associated with response to chronic hepatitis C interferon-alpha and ribavirin therapy. Nat Genet 2009;41:1100-4.
10. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatitis C virus infection. J Hepatol 2011;55:245-64.
11. Rallón NI, Naggie S, Benito JM, Medrano J, Restrepo C, Goldstein D, *et al.* Association of a single nucleotide polymorphism near the interleukin-28B gene with response to hepatitis C therapy in HIV/hepatitis C virus-coinfected patients. AIDS 2010;24:F23-9.
12. Tillmann HL, Thompson AJ, Patel K, Wiese M, Tenckhoff H, Nischalke HD, *et al.* A polymorphism near IL28B is associated with spontaneous clearance of acute hepatitis C virus and jaundice. Gastroenterology 2010;139:1586-92, 1592.e1.
13. Mangia A, Thompson AJ, Santoro R, Piazzolla V, Tillmann HL, Patel K, *et al.* An IL28B polymorphism determines treatment response of hepatitis C virus genotype 2 or 3 patients who do not achieve a rapid virologic response. Gastroenterology 2010;139:821-7, 8271.
14. McCarthy JJ, Li JH, Thompson A, Suchindran S, Lao XQ, Patel K, *et al.* Replicated association between an IL28B gene variant and a sustained response to pegylated interferon and ribavirin. Gastroenterology 2010;138:2307-14.
15. Rauch A, Kutalik Z, Descombes P, Cai T, Di Iulio J, Mueller T, *et al.* Genetic variation in IL28B is associated with chronic hepatitis C and treatment failure: A genome-wide association study. Gastroenterology 2010;138:1338-45, 1345.e1.
16. Khajavi R, Rafiei A, Haghshenas MR, Hosseini-khah Z, Farazmandfar T, Sharbafi R. Association between interleukin-28B genetic variantsand hepatitis C. J Mazand Univ Med Sci 2012;22:19-27.
17. Mahboobi N, Behnava B, Alavian SM. IL28B SNP genotyping among Iranian HCV-infected patients: A preliminary report. Hepat Mon 2011;11:386-8.