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Association of Polymorphism of RS2275913 and Chronic HBV and HCV Infection with Liver Cirrhosis in Uzbek Population

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Abstract Chronic viral hepatitis B, C - inflammatory liver disease due to infection of hepatitis B virus (HBV) or C (HCV), capable of progressing to cirrhosis of the liver. The present study investigated the distribution of allele frequencies and genotypes of the IL-17 A G-197 A gene in patients with HBV-liver cirrhosis (LC) and HCV-LC. **Methods:** Genotyping of polymorphic regions of immune response genes was carried out by polymerase chain reaction with allele-specific primers (NPF Litech, Moscow) and electrophoretic detection of reaction products in agarose gel. **Results:** Of the results we obtained, the adverse marker for the development of HBV-LC is the A allele of 25.0% in the group of patients and 14.74% in the control, respectively. Analysis of the obtained data in the study sample showed no significant differences in the incidence of allelic variants and their genotypic combinations in the polymorphism of RS2275913 among patients with HCV-LC. **Conclusions:** The findings suggest that in the study sample, RS2275913 is significant only for chronic HBV infection with LC in the Uzbek population.

Keywords Chronic viral hepatitis, Liver cirrhosis, Gene allele, Patients

1. Introduction

Approximately 350 million people worldwide are infected with hepatitis B virus (HBV). Chronic hepatitis B develops in approximately 5% of patients with jaundice form of acute hepatitis. HCV infection is responsible for 70% of chronic viral hepatitis cases, 40% for cirrhosis of the liver, and 60% for hepatocellular carcinoma in the world. Chronic hepatitis C virus (HCV) infection usually induces immune-reactive inflammation, leading to continuous damage to liver tissue and progression of liver fibrosis to cirrhosis or hepatocellular carcinoma. Chronic HBV infection is a common cause of liver cirrhosis and hepatocellular carcinoma. Chronic HBV infection is a common cause of liver cirrhosis and hepatocellular carcinoma (HCC) [1]. HBV is an infectious disease that can be transmitted vertically from mothers to their babies or horizontally by infected blood, blood product transfusion, and body secretion [2,3,4]. The course and outcome of the disease mainly depend on the features of the virus itself and the host's immune responses. Different responses to hepatitis B virus depend on several parameters, including genetic, epigenetic and immunological factors [5]. Recent studies have shown that cytokines play a key role in inflammatory responses and the progression of liver disease. The interleukin-17 (IL-17) family is a new cytokine group that consists of six members, including IL-17A, IL-17B, IL-17C, IL-17D, IL-17E (IL-19) and IL-17f [6]. IL-17 is produced by Th17 cells and stimulates monocytes, Kupfer cells, biliary epithelial cells and stellate liver cells and makes them secret pro-inflammatory cytokines and chemokines [7]. Unadjusted IL-17 products may increase pro-inflammatory cytokine expressions and chronic inflammation. Recently, the important role of IL-17 and their products in the chronization of liver diseases associated with HBV has been reported [8]. IL-17A and IL-17F have almost the same amino acid sequence homology (50%) and their coding genes located on chromosome 6P12.3-Q13. In addition, they are similar in biological functions [9]. Several studies have demonstrated that genetic variation is responsible for differences between cytokine production. Genetic variation in cytokine and cytokine receptor genes may be responsible

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for differences between diseases [10,11,12]. The most studied with respect to IL-17 polymorphisms are SNP RS2275913 from the promoter of the IL-17A gene, which can be associated with the expression of mRNA and IL-17F SNP RS763780 on the starting codon of the IL-17F gene [13,14]. There are currently few studies on the possible role of IL17 gene polymorphisms and susceptibility to chronic hepatitis B virus infection with outcome in cirrhosis.

The Purpose of the study, investigated the association between RS2275913 polymorphism and to chronic HBV infection with LC and in HCV-LC patients in the Uzbek population.

2. Materials and Methods

The material for DNA extraction was venous blood from the ulnar vein with a volume of 3-5 ml (Beckton-Dickinson vacutiners were used for blood sampling) with an anticoagulant /preservative of 15% trikali EDTA (Ethendianin-tetraacetic acid). Blood for further treatment could be stored for up to 24 hours at a temperature not higher than + 4℃. To obtain genomic DNA, a two-step method of lysis of blood cells was used. Further purification of leukocyte lysates is based on S. Miller et al. (1988) in a modification proposed by Stanford University Laboratory. Genotyping of polymorphic regions of immune response genes was carried out by polymerase chain reaction (PCR) with allele-specific primers (NPF Litech, Moscow) and electrophoretic detection of reaction products in agarose gel. Polymorphism IL-17A G-197A (RS2275913) tested, SNPs are previously confirmed. The distribution of genotypes at the studied polymorphic loci was studied using logistic regression analysis and testing for compliance with the Hardy-Weinberg equilibrium using the Fisher exact test. They took into account the correspondence of patients and persons of the control group by sex and age. Differences at $p < 0.05$ were considered statistically significant.

3. Result

As can be seen from the results we obtained (Table 1), an unfavorable marker for the development of HBV-LC is allele A (25.0% in the group of patients and 14.74% in the control, respectively; OR = 1,929; 95% CI: 1.011 >1.929> 3.679; $\chi2$=4.057 (p=0.043996)) and heterozygous GA genotype (40,00% in the group of patients and 23,16% in the control; OR = 2,212; 95% CI: 1.002 >2.212> 4.884; $\chi2$=3.948 (p=0.046933)).

In turn, the G allele and the GG genotype were recorded as significant favorable markers. Comparative analysis of the GG genotype revealed significant differences between patients with controls (55,0% and 73,7% according; OR = 0,437; 95% CI: 0.202 >0.437> 0.945; $\chi2$=4.527 (p=0.033364)).

Further, we investigated the association between RS2275913 polymorphism and to chronic HCV infection with LC in the Uzbek population.

As can be seen from the data in Table 2, the analysis of the obtained data in the study sample did not reveal significant differences in the incidence of allelic variants and their genotypic combinations in the polymorphism of RS2275913 among patients with HCV-CP.

4. Conclusions

Thus, the findings suggest that in the study sample, the RS2275913 is significant only for chronic HBV infection with CPU in the Uzbek population, however, given the limited number of HCV study samples with LC, there is a possibility that when expanding the sample, the study marker will have any trends in reliability.

Table 1. Distribution of allele frequencies and genotypes of the IL-17A G-197A gene in patients with HBV-LC

Genotype	patients, n=40	patientы, %	Genotype	control, n=95	control, %	$\chi2$	OR (95% CI)
G	60	75,00	G	162	85,26	4.057 (p=0.043996)	0.272 >0.519> 0.989
A	20	25,00	A	28	14,74		1.011 >1.929> 3.679
GG	22	55,00	GG	70	73,68	4.527 (p=0.033364)	0.202 >0.437> 0.945
GA	16	40,00	GA	22	23,16	3.948 (p=0.046933)	1.002 >2.212> 4.884
AA	2	5,00	AA	3	3,16	0.268 (p=0.604802)	0.259 >1.614> 10.048

Note: $\chi2$ - Pearson reliability indicator; OR - relative risk;

Table 2. Distribution of allele frequencies and genotypes of the IL-17A G-197A gene in HCV-LC patients

Genotype	patients, n=32	patients, %	Genotype	control, n=95	control, %	$\chi2$	OR (95% CI)
G	50	78,13	G	162	85,26	1.767 (p=0.183694)	0.302 >0.617> 1.263
A	14	21,88	A	28	14,74		0.792 >1.62> 3.314
GG	19	59,38	GG	70	73,68	2.337 (p=0.126299)	0.225 >0.522> 1.21
GA	12	37,50	GA	22	23,16	2.512 (p=0.113015)	0.843 >1.991> 4.704
AA	1	3,13	AA	3	3,16	0 (p=1)	0.099 >0.989> 9.862

Note: $\chi2$ - Pearson reliability indicator; OR - relative risk;

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