Journal of Applied Biological Sciences 3(2): 59-61, 2009
ISSN: 1307-1130, www.nobel.gen.tr

Association of HLA- B7, B8, B27 and B51 with Genetic Protection Against Hepatitis B Virus

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Received: April 13, 2009
Accepted: May 27, 2009

ABSTRACT

It is generally believed that viral clearance or chronic infection following hepatitis B virus (HBV) infection is linked to the genetic background of the host and human leukocyte antigens (HLA) play a central role. This study was conducted to determine associations between some of HLA class I genes with the outcome of hepatitis B infection. Subjects of this study were 64 individuals who were assigned into two group, case and control, based on their clinical and serologic profiles. Case group were 27 patients infected with HBV and controls were 37 subjects with HBV natural convalescent who recovered from a HBV infection. Typing of HLA class I was performed by serologic method. No significant difference was found between mean age of control and patient group while the difference in sex of two groups was significant ($P<0.05$). The most frequent detected HLA antigens were B51 (40, 1%), B27 (14.1%), B8 (12.5%) and B7 (10.9%). Significant association was found between HBV persistence and HLA-B27. HLA-B27 was associated with an increase in HBV persistence. The findings support the idea that polymorphism of HLA class I may influence the chronicity of HBV infection.

Key Words: HLA, Hepatitis B, HBV persistence

INTRODUCTION

Worldwide, chronic hepatitis B affects an estimated 350 million people and is the leading cause of cirrhosis and hepatocellular carcinoma [1, 2]. Infection with hepatitis B virus (HBV) in adulthood results in viral persistence and development of chronic hepatitis in 5 to 10% of cases [3]. Factors that determine viral persistence or clearance are not well known. Host genetic factors and environment factors such as virus genotype are widely counted as common basis for the diversity in outcomes of HBV infection [4, 6]. Among the genetic factors, HLA which involve with presentation of viral antigen to immune effecter cells has a key role in the selection and establishment of the antigen-specific T cell repertoire and a major role in the subsequent activation of those T cells during the initiation of an immune response [7-9].

It has been argued that unprecedented degree of HLA loci polymorphism within a population is required to avoid the devastating effects of infectious diseases. The main questions include which human genes are important in infection and how to find them. This study was conducted to determine possible associations between some of HLA class I genes with the outcome of HBV infection.

MATERIALS AND METHODS

Subjects of this study were the patients referred to Iran Red Crescent Society clinic in Baku, Azerbaijan Republic. All the subjects were Azerbaijani and from different part of the country. The subjects were selected from those who were positive for HBV.

Using sequential sampling method, sixty four patients were assigned into two groups (case and control) based on their clinical and serological profiles. Case patients were 27 subjects with HBV infection and controls were 37 subjects with natural convalescent of HBV recovered from an HBV infection. Subjects were considered infected with HBV if they tested positive for hepatitis B surface antigen (HBsAg) twice. Subjects were considered as control if they had (i) baseline negative HBsAg test, (ii) no history of HBV vaccination and (iii) no history of HBV treatment. In individuals with viral clearance, anti hepatitis B core antigen (anti-HBc) and anti-HBsAg was checked as needed to exclude primary HBV infection. HLA typing was performed in Department of Microbiology and Immunology in Azerbaijan Medical University, in Baku, using serologic method and based on manufacture's instruction (Eu roclone, Italy). Collected data were analyzed by SPSS software. ANOVA was used to compare means of more than two independent groups. Chi-square test was used to test the HLA differences between the patients and control groups. The level of significance in all cases was set at a two-tailed $p<0.05$.

Table 1: Demographic and HLA-typing features of patient and control groups

Variable	Control	Patient	Total	P-value
Age (Mean±SD)	37.95±12.44	32.26 ± 14.20	35.55±13.41	>0.05
Sex (Female/Male)	17/20	2/25	19/45	<0.05
HLA-B7 (Negative/Positive)	32/5	25/2	57/7	>0/05
HLA-B8 (Negative/Positive)	32/5	24/3	56/8	>0/05
HLA-B27 (Negative/Positive)	**35/2**	**20/7**	**55/9**	**<0.05**
HLA-B51 (Negative/Positive)	22/15	16/11	38/26	>0/05
Total	37	27	64	

RESULTS AND DISCUSSION

Mean age of patients and controls were 32.26 ± 14.20 and 37.95±12.44 respectively. There was no significant difference in age between control and patient groups while difference in sex was significant (Table 1). The most frequent HLA-I antigens were found to be B51 (40.1%), B27 (14.1%), B8 (12.5%) and B7 (10.9%) respectively. Viral clearance has occurred in 5.5% of controls with HLA-B27 whereas 26% of patients with HBV infection had HLA-B27 (Table 1). This difference was statistically significant ($P<0.05$). Findings of this study showed that 13.5% of subjects with viral clearance had HLA-B7 and this was 7.5% for patients. Table 1 shows the frequency of different HLA in patients and control group. The differences in frequency of HLA-I were not significant for HLA-B7, B8 and B51 ($P>0.05$).

There are a number of reasons for studying the links of MHC polymorphisms and the outcome of infection. The question is why some patients recover from infection with no sequel while others develop end-stage liver disease and hepatocellular carcinoma.

Recovery from HBV infection is mainly depends on the cellular immune responses [10]. There is strong evidence in HBV infection that host genetic factors play a major role in determining the outcome of infection [4-6]. It is notable that overall, the class I alleles have the strongest associations, suggesting that the $CD8^+$ cytotoxic T lymphocytes are important in determining viral clearance or persistence [6, 7].

In autoimmune disease with an infectious etiology, it is likely that immune responses to peptides derived from the initiating pathogen are bound and presented by particular HLA molecules to activate T lymphocytes that play a triggering or contributory role in disease pathogenesis.

The key role of HLA class I and II-encoded molecules in antigen presentation has naturally generated the hypothesis that polymorphism at these loci may explain the variation in outcomes from infectious diseases and the development of autoimmune diseases [6, 8].

In this analytical descriptive study, HLA class I genetic effects on the outcome of HBV infection was evaluated. Findings of the study demonstrated an association between HLA-B27 and HBV persistence.

A number of early studies reported strong associations for specific MHC class I with chronic HBV infection. These associations were not reproducible, as illustrated by the study of Mota in Argentina reporting an association of Bw35, with persistence, and van Hattum reporting that Bw35 was associated with self-limiting infection [11, 12]. Hwang indicated that alleles of A33, DR7, are associated with HBV chronicity among Koreans patients [13]. Karan showed that HLA-A24 and Cw1 were associated with low risk for HBV-related chronic liver disease and HLA-B13, B8, DR7, DR13 and DQ3 were associated with high risk for chronic HBV infection in the Turkish population [14]. In other study in the chronic hepatitis group, CW6, DRB5 and DQB1*05 antigens were significantly more frequent in the control group, and B8, CW7, DRB1*03 and DQB1*02 antigens were more frequent in the naturally immune group [15].

Processing of antigenic peptides presented by HLA class I molecules involves the transport associated with antigen processing (TAP) molecules. It has been suggested that polymorphisms in the TAP2 gene influenced the progression of liver disease [6].

CONCLUSION

Findings of this study support the theory that human leukocyte antigen class I-restricted cytotoxic T cells play an important role in HBV chronicity. The future study including the multi-cohort collaboration is needed to clarify these preliminary associations and identify other potential candidate genes.

REFERENCES

[1] World Health Organization. 2004. Hepatitis B vaccines. Wkly Epidemiol Rec. 79:263.

[2] Raza SA, Clifford GM, Franceschi S. 2007. Worldwide variation in the relative importance of hepatitis B and hepatitis C viruses in hepato cellular carcinoma: a systematic review. Br J Cancer. 96:1127-34.

[3] Safioleas M, Lygidakis NJ, Manti C. 2007. Hepatitis B today. Hepatogastroenterology. 54:545-8.

[4] He YL, Zhao YR, Zhang SL, Lin SM. 2006. Host susceptibility to persistent hepatitis B virus infection. World J Gastroenterol. 12:4788-93.

[5] Frodsham AJ. 2005. Host genetics and the outcome of hepatitis B viral infection. Transpl Immunol. 14:183-6.

[6] Thursz M. 2001. Genetic susceptibility in chronic viral hepatitis. Antiviral Res. 52:113-6.

[7] Thio CL, Thomas DL, Karacki P, Gao X, Marti D, Kaslow RA, Goedert JJ, Hilgartner M, Strathdee SA, Duggal P, O'Brien SJ, Astemborski J, Carrington M. 2003. Comprehensive analysis of class I and class II HLA antigens and chronic hepatitis B virus infection. J Virol. 77:12083-7.

[8] Wang FS. 2003. Current status and prospects of studies on human genetical leles associated with hepatitis B virus infection. World J Gastroenterol. 9:641-4.

[9] Karan MA, Tascioglu NE, Ozturk AO, Palanduz S, Carin M. 2002. The role of HLA antigens in chronic hepatitis B virus infection. J Pak Med Assoc. 52: 253-6.

[10] Bertoletti A, Gehring A. 2007. Immune response and tolerance during chronic hepatitis B virus infection. Hepatol Res. 3:331-8.

[11] Mota AH, Fainboim H, Terg R, Fainboim L. 1987. Association of chronic active hepatitis and HLA B35 in patients with hepatitis B virus. Tissue Antigens. 30:238-40.

[12] van Hattum J, Schreuder GM, Schalm SW. 1987. HLA antigens in patients with various courses after hepatitis B virus infection. Hepatology. 7:11-4.

[13] Hwang SH, Sohn YH, Oh HB, Hwang CY, Lee SH, Shin ES, Lee KJ. 2007. Human leukocyte antigen alleles and haplotypes associated with chronicity of hepatitis B virus infection in Koreans. Arch Pathol Lab Med. 131:117-21.

[14] Karan MA, Tascioglu NE, Ozturk AO, Palanduz S, Carin M. 2002. The role of HLA antigens in chronic hepatitis B virus infection. J Pak Med Assoc. 52:253-6.

[15] Akcam Z, Sunbul M, Durupinar B, Eroglu C, Esen S, Leblebicioglu H. 2002. Tissue types as prognostic risk factor in hepatitis B virus infection. Indian J Gastroenterol. 21:139-41.