CYTOKINES PRODUCTION AND GENETIC VARIABILITY OF HEPATITIS B VIRUS (HBV): INFLUENCE ON THE COURSE OF INFECTION IN PATIENTS WITH ACUTE AND CHRONIC HEPATITIS B

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Recently, several viral HBV factors, including viral load, HBsAg level, genotype, genome mutations and cytokine production have been reported to be associated with different risks of progression of liver disease. The aim of this study was to investigate the influence of HBV genetic variability and cytokine uptake in the association with progression of hepatitis B virus infection in individuals with acute and chronic hepatitis B. All samples(n=57) of the study were tested for the presence of HBV DNA by real-time and nested-PCR, positive samples were purified, sequenced and genotyped for phylogenetic tree construction and mutation search. The cytokines (IL-35, IL-6, IL-17A, IFN-γ) were detected by ELISA. Four genotypes were found (A, D, E and F) and the isolates obtained were mostly of genotype A, subgenotype A2. We analyzed 65 mutations in the pre-S/S gene region of these 44 were found. The C48G mutation was found only in acute individuals, this mutation may be involved in the reactivation of HBV during an immunosuppression in patients with resolved infection, which in some cases could lead to severe acute hepatitis, fulminant hepatic failure and death. The F141L mutation that may play a vital role in the pathogenesis of hepatocarcinoma as it induces cell proliferation and transformation has been found only in acute individuals and important mutations such as C105T, C7A and G145K/R that also are involved in increased risk of hapatocarcinoma have been found to be more prevalent in chronic individuals. The acute profile of infection was the one with the highest frequency of mutations, being the only one to present the mutations of the C69stop and W52stop codons. Genotype A subgenotype A2 showed the highest number of mutations and no mutation was found in genotype D. IL-6 levels (p=0.052) were higher in acute patients, this cytokine would be involved in viral elimination and protection against chronicity. In chronic patients the levels of IFN-γ and IL-17A were higher in comparison to the acute patients, these cytokines would be modulating pro-inflammatory effectors and inducing hepatocellular damage, respectively.

Keywords: hepatitis B, cytokines, viral variability, disease progression

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