Basal Core Promoter (BCP) mutations with respect to Hepatitis B Virus Genotypes and Serologic Status

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The region spanning from the nucleotide 1742 to 1849 within the 3.2kb hepatitis B virus genome has been mapped as Basal Core Promoter (BCP). This regulatory region is extremely important for correct initiation of the transcription of pre genome (pgRNA) and of other messenger RNAs during the progress of viral life cycle. Point mutations within the core promoter have been found in Asian patients with fulminant and chronic hepatitis B.

These mutations might change the binding affinity of nuclear protein and thereby alter the transcriptional activity of the HBV DNA. Most commonly occurring A1762T/G1764A double mutation within BCP have widely been reported and have functionally been shown to down regulate the expression of precore antigen (HBeAg), low viral load and sometimes also having significant association with HBeAg negative serology i.e. complete inhibition of HBeAg production. Deletion and insertion mutations have also been reported with emerging clinical manifestations. With this background in the present study we aimed to investigate the prevalence of BCP mutations and their correlation with viral genotypes and HBeAg serologic status among patients. Viral DNA was extracted from thirty HBeAg positive and fifteen HBeAg negative sera samples of patients by phenol:chloroform method. Extracted viral DNA was subjected to nested PCR amplification for the region spanning over the basal core promoter region. Generated PCR products of 320 bp size was purified with the help of PCR purification kit and subsequently sequenced. Obtained viral DNA sequences were carefully analysed for genotypes and mutations. For this purpose DNA sequences of all known genotypes of HBV were obtained from Gene bank. Analysis of genotypes and mutation was done with the help of bioinformatics softwares. Basal core promoter mutations were seen in both HBeAg positive and negative patients. However, nearly fifty percent of HBeAg negative patient (8 of 15) had these mutations, whereas only 8 of 30 (26.6%) HBeAg positive patients showed mutations in these regions. The most commonly found BCP mutations are T1753A/C and A1762T/G1764A double mutations within both HBeAg positive and negative patients. In conclusion, our results were quite in agreement with the existing scenario of the regulatory region mutation (BCP mutation) that these mutations are widely associated with HBeAg negative serology. Further these mutations are more prevalent in strains of HBV genotype D irrespective of the serologic status of the patient.