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Mutations in Hepatitis B virus polymerase gene/partial surface gene among Chronic HBV carriers as markers for anti-viral drug resistance and escape mutants

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Abstract

Resistance to anti-viral drugs is a global problem in the treatment of HBV. Around 350 million people are infected with HBV worldwide. In India there are 50 million chronic HBV carriers [1]. HBV is double stranded DNA virus, it replicates by reverse transcription process. The error rate of HBV reverse transcriptase is of $4.6x10^{-5}$/nucleotide/site/year [1]. This results in the emergence of mutations in HBV genome. There are 10 genotypes and 4 subtypes [2, 4]. The treatment and disease progression is genotype specific [3]. The objective of the study was to identify mutations in HBV pol gene and HBs gene and their impact on disease and diagnosis. Individuals positive for HBsAg by ELISA with HBV viral load more than 2000 IU/ml were recruited in the study (n=32). Blood samples were collected from 32 individuals after obtaining written informed consent. DNA was extracted from the plasma samples (Qiagen, Hilden, Germany). Conventional PCR targeting reverse transcriptase and surface gene (partial) was performed [4]. DNA sequencing (1300 bp) was performed on ABI 3730 GA platform (Applied Biosystems, USA). The sequences were analyzed for drug resistance using HBV geno2pheno drug resistance tool [1, 6] (http:// hbv. geno2pheno.org/). Mean age of the study subjects was 46.8 $\pm$ 14.1. Males (n=22) were predominant than female (n=10). The median ALT level was 45 U/L. HBe Antigen was found to be positive in 65% (n=21) and negative in 35% (n=11). Genotype D (68.7%) was most predominant followed by genotype A (18.7%) and genotype C (15.6%). The rtL180M and rtM204V lamivudine, entecavir and telbivudine refractory mutation was noticed in one individual. Compensatory mutation rt169V was found in one individual. Several minor mutations were detected in which 5 participants belonged to genotype D had substitutions in p gene hotspots including rt169, rt173, rt180, rt184, rt202, rt204, rt236, rt250. Recently, there are changes in the treatment of chronic HBV disease. However, emergence of mutations in HBV is increasingly documented. Understanding the viral mutations and their associations with clinical presentations will assist in the customized patient care.

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