

Hepatitis B Virus Subgenotype D1 is Prevalent in Pakistan

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Hepatitis B Virus (HBV) is a partially double-stranded DNA virus of the Hepadnaviridae family with a genome of only 3.2 kb containing 4 partially overlapping open reading frames designated S, C, P and X. The serological heterogeneity of HBV identified the different subtypes of HBV *ayw1*, *ayw2*, *ayw3*, *ayw4*, *ayr*, *adw2*, *adw4*, *adrq+* and *adrq-*.^{1,2} Later, the molecular basis for the serological variations within subtypes has been described. Thus, variations of the S-gene product at sites 122 and 160 identify the *d/y* and *w/r* specificity, respectively³ and residue 127 is important for the *a* subdeterminants later designated *w1/w2*, *w3* and *w4*⁴ (Table 1).

Table 1: Amino acids residues specifying determinants of HBsAg.

Position	Amino acid	Specificity
122	Lys	<i>d</i>
122	Arg	<i>y</i>
127	Pro	<i>w1^a/w2</i>
127	Thr	<i>w3</i>
127	Leu/Ile	<i>w4</i>
160	Lys	<i>w</i>
160	Arg	<i>r</i>

^a*w1* reactivity also requires Arg122, Phe 134 and/or Ala 159

The genetic classification of HBV strains, based on an intergroup divergence of 8% or more of the complete genomes,⁵ and 4.1% when comparing S-gene sequences,⁶ has led to the classification of the virus into eight genotypes designated A to H, often with distinct geographical association.^{5,7}

When the worldwide molecular epidemiology of HBV, based on the variability of the S-gene was defined, genotype A was found to be common in North-Western Europe, North America and Africa.⁸ Genotypes B and C were found in Asia. Genotype D is the most widely distributed genotype and has been found universally, with its highest prevalence in the Mediterranean region and in the Near East and India. This genotype was also found in aboriginal population in Asia in all the way from Indonesia to Papua and Alaska. Genotype E is found in Africa and genotype F is found mainly in the New World. Genotype G was described from chronic HBV carriers from North America and France. Genotype H has been found in Central America, Mexico and California in the

USA and is, together with genotype F, considered the original HBV strain of the Amerindians.

Within the genotypes, a number of subgenotypes designated with Arabic numerals are now described.⁷ In general, HBV subgenotypes as well as genotypes show a distinct geographic distribution, although the information for different countries is still scarce. Thus, subgenotype A1 is predominant in South Asia and sub-Saharan Africa and subgenotype A2 is prevalent mainly in European and North-American countries.⁷ Recently, A3 was described in native population of West and Central Africa. Also for genotypes B and C, definite geographical predilections have been shown.⁷ Genotype D is the most widespread and divides into five subgenotypes,⁷ although the geographic distribution of these subgenotypes is so far less defined than those for genotypes A through C and F. Although it is a close correlation between HBsAg subtypes and HBV genotypes, several subtypes can be found within more than one genotype⁸ or vice versa, one subgenotype could encode several subtypes as for subgenotypes D2, D3 and D4.

Little is known on the distribution of genotypes and subgenotypes in Pakistan. In this volume, Dr. Baig and co-workers have typed 201 HBV strains from patients attending the Ziauddin University Hospital during 2006. The strains were typed by genotype-specific PCR, which is a simple and quick technique when many samples are analysed. Genotype D was found to be the most prevalent, followed by genotype A and recombinant A/D HBV strains. These results confirmed previous results with genotype D as the predominant HBV genotype in Pakistan, although in this study, there were also other genotypes identified.⁹ In the study by Dr. Baig, some of the genotype D strains were also sequenced and phylogenetically compared with other genotype D strains from other parts of the world. The analysis revealed that the Pakistani genotype D strains was grouped with subgenotype D1 strains from India. It was also shown that these strains expressed subtype *ayw2*. This is in accordance with previous findings showing that subgenotype D1 strains originating from Middle Asia as India, Uzbekistan, Turkey and Iran express mainly subtype *ayw2*. The finding in this study is the first showing the phylogenetic analysis of hepatitis B virus in Pakistan. More sequences are needed for identifying if there are geographical differences in the distribution of different HBV strains in Pakistan and for subgenotyping also the genotype A and the recombinant A/D strains.

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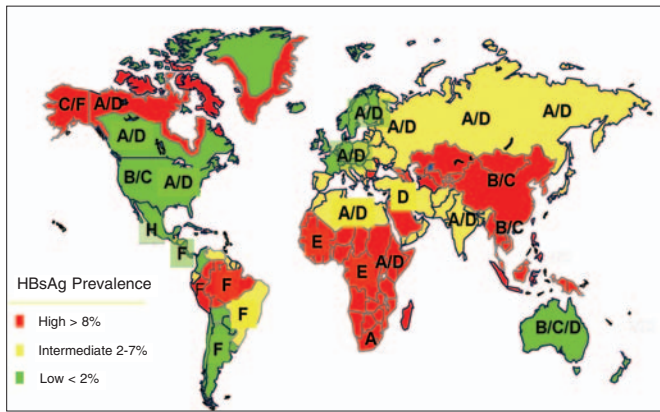


Figure 1: Geographical distribution of HBV genotypes.

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