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EDITORIAL

Evolution of Hepatitis B Genotype D in the Middle East and South Asia

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Hepatitis B virus (HBV) has been classified into 8 genotypes, from A to H and there are some hints that the outcome of the disease and the response to therapy might be correlated to these genomic groups (although not as serious as hepatitis C virus [HCV]).

Hepatitis B virus genotypes show a characteristic geographic distribution with a proposed association with human migration. Several scientific fields are employed for the study of human population history, including archaeology, linguistics, anthropology and, recently, genetics. Thanks to the introduction of modern technology into genetics in the past two decades, humans have been facing some very interesting findings about their history. Besides mitochondrial DNA sequence analysis, persistent viruses have opened a new window into this area, especially HBV. But why?

It is of interest that the prevalence of HBV genotypes throughout the world is clearly linked to migration. For example, the ancestors of Eskimos migrated from South East (SE) Asia to the North and passed through the Behring channel to Alaska, which partially explains why there was as high a prevalence of hepatitis B surface antigen (HBsAg) positivity in this area as in SE Asia (1).

Second, in some studies (2-5) from South America, genotypes E and A, which are the dominant types in Africans, were found in an area with genotype F/H dominancy. They derived from those with African descent who came into South America during the slave trading period a few hundred years ago. In our own research (6) in the Pacific region (which is an endemic area with genotype C dominancy) we compared HBV surface and core genes with the ones from SE Asian patients and from international databases. The gradient of nucleotide and amino acid variations from west to east in our study were most consistent with the hypothesis of migration of Polynesian people from Southern China through Melanesia and Fiji and their radiation across the Pacific to fill the Polynesian triangle in different times. We also found an interesting association that supported the immigration history of SE Asian ancestors southwards and their colonization in the Pacific islands.

D is the most prevalent and the most distributed genotype. It is found in Western populations, the Indian subcontinent, The Middle East and North of Africa. Genotype D contains 4 subgroups (D1 to D4) and 2 subtypes (ayw2 and ayw3). We have collected all the available data from India (7-18), Bangladesh (Jazayeri, unpublished), Turkey (19-33), Pakistan (34-39), and Iran (40-48). We considered the relationship between the potential genotypes in these countries and their evolution.

We considered the samples from East to West. Our unpublished data on 66 Bangladeshi isolates revealed 4 genotypes (A, B, C and D) with genotype D predominant. In India, genotype D was dominant (67%), but there were other genotypes: A

(22%), C (8 %) and recombination (3%).

In Pakistanis 62 % were genotype D, A (14%), C (6 %), other genotypes (4%) and recombination (10%). However, in Turkey, authors found genotype D as the dominant genotype (87%), 1.3% for both genotypes A and C and recombination 12%. In Iran, interestingly, no other genotype than D has been found.

Why, from west to east, is homogeneity in HBV genotypes lost?

According to archaeological and anthropological findings, the ancestors of Caucasians (Arians) firstly colonized to the North of the Caspian Sea. Because of difficulties in agriculture and climate change, they migrated in three directions: one group moved west towards Europe, another group moved south to Iran (and established the ancient Persian Empire) and the last group migrated to India.

It might be that those people who acquired the virus with the genotype D before their migration, then transmitted the virus generation by generation after their migration. This is why the dominant genotype in India, Iran and most part of the Europe is D.

Why, is there a heterogeneous pattern in the east and a homogenous pattern in the West?

It is likely that selection of HBV genotypes A to H had been occurring in different parts of the world (perhaps related to immune pressure based largely on human leukocyte antigens [HLA] types). After colonization of infected people with certain genotypes, their importation to this area from intermixing of people. Further evolution occurred, giving some of these sequences a distinctive motif, and some genetic recombination between genotypes also occurred, which led to the heterogonous pattern in parts of this area (like Bangladesh, India and Pakistan). In some areas, isolation of people in the absence of intermixing with other genotypes let to a homologous pattern (like Iran and Turkey).

Due to lack of reliable data from other genotype D-dominant countries in The Middle East and North Africa, the analysis of whole data regarding genotype D evolution in the world is not conclusive. In addition, the sample size in some studies from such countries is quite small.

Future studies are needed to carry out work on the prevalence of HBV genotypes in the neighboring countries of this region and comparing data to the European sequences which might lead to a more precise conclusion.

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