



HBV Genotype - A Brief Review



Ruksana Raihan¹, Mamun Al Mahtab^{2*} and Sheikh Mohammad Fazle Akbar³

¹Faculty of Medicine, AIMST University, Malaysia

²Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Bangladesh

³Department of Medical Sciences, Toshiba General Hospital, Japan

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***Corresponding author:** Mamun Al Mahtab, Associate Professor, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, Email: shwapnil@agni.com

Abstract

Background: Hepatitis B virus (HBV) infection is one of the major cause of liver cirrhosis (LC) and hepatocellular carcinoma (HCC) worldwide. HBV genotypes play an important role in the outcome of chronic HBV infection.

Purpose: To review the role of HBV genotypes in the development of HBV related LC and HCC. Data Sources: Review of published literature on HBV genotypes.

Results: HBV genotypes are likely to play an important role in determining the progression, severity and treatment of HBV-induced liver disease.

Opinion

About 2 billion people of the world have been infected with hepatitis B (HBV) at some point of their life and out of these 2 billion HBV-infected subjects, around 240-370 million people become chronically infected. Presence of hepatitis B surface antigen (HBsAg) in blood for more than 6 months is regarded as chronic hepatitis B (CHB). Out of millions of CHB infected subjects, about 15-40% develop CHB related complications like liver cirrhosis (LC) and/or hepatocellular (HCC). About one million people die every year from LC and HCC [1].

The mechanisms underlying development of CHB and its complications like LC and HCC are yet to be explored properly. As HBV is a non-cytopathic virus, it has been assumed that an interaction of host with HBV induces liver damages and HBV-related complications like LC and HCC. Several viral factors appear to strongly influence outcome in HBV infection including HBV genotype, DNA levels over time, and specific HBV viral mutations. Since HBV in immune-competent persons is not ordinarily pathogenic, it is the host's immune response to the virus that determines the extent of liver inflammation and fibrosis. However, because the virus's polymerase has reverse transcriptase properties, HBV DNA integrates randomly into the host's liver cell DNA throughout the course of infection. Thus, the virus may be an independent contributor for the development of HCC. The purpose of this article is to review the data available

on the association of specific HBV genotypes and sub genotypes with clinical outcome of HBV.

HBV Genotypes and Global Distributions

HBV is the prototype member of a family of viruses called hepadnaviruses [2]. HBV is classified into ten genotypes (A-J). HBV genotypes differ by at least 8%. HBV genotypes show a distinct geographic and ethnic distribution. Genotype A is the most distributed all over the world and the leading genotype in Europe, North America, Africa and India, whereas B and C are more dominant in East and Southeast Asia [3,4]. Genotype D is common in the Middle East and Mediterranean region and India, and genotype E is usually found in sub-Saharan Africa [5,6] along with some other continents [7]. Outside, Genotype F and H are rarely found outside the Central and South America [8,9] and Genotype G is circulating among the people of USA, Mexico, France and Germany [10]. Genotype G is normally present as a co-infection with other HBV genotypes, most commonly with genotype A. The genotypes I has been detected in Laos, Vietnam and China [11,12], while the newest genotype; J was identified in the Ryukyu Islands in Japan [13]. The most commonly found genotypes in Asia are B and C except for India where the genotype A and D are most prevalent. The prominent genotypes in India are A and D whereas in Asia the commonest genotypes are B and C [14,15].

HBV Genotypes and Clinical Outcome

A greater understanding of the relationship between HBV genotypes, progression of hepatitis B disease, and clinical outcomes has developed over time. Many studies have been published regarding the relationship between HBV genotype and serious sequelae of HBV including LC and HCC. Studies in East Asia are conducted mostly among persons infected with HBV genotypes B and C. Genotype A1 has been associated with very high rates of HCC in sub-Saharan Africa. Another study from Spain showed that genotype A (presumably A2) infection was associated significantly with sustained biochemical remission, HBV DNA clearance, and HBsAg clearance in patients with CHB than patients infected with genotype D [16]. Multiple cross-sectional studies have shown that patients with genotype C experience HBeAg seroconversion at an older age and are more likely to be HBeAg positive at any given age than HBV genotype B. Some other studies showed that genotype C-associated HCC occurred at younger age (<50 years) and in comparison, genotype B HCC was found primarily in persons older than 60 years. The higher risk of development of HCC by genotype C may be related to delayed spontaneous HBeAg seroconversion and longer duration of high HBV replication. Early seroconversion of HBeAg appears to be associated with a more favourable clinical outcome than late or absent seroconversion. In most cross-sectional studies, HBV genotype C is associated with an increased risk of liver inflammation, flares of hepatitis, liver fibrosis, and cirrhosis. The BCP mutation was found to be independently associated with presence of HCC and occurred more frequently in HBV genotype C [17-23]. Persons infected with genotype D usually develops anti-HBe from HBeAg in adolescence or early adulthood. In an acute liver failure study in the United States, genotype D was found to be an independent risk factor for fulminant hepatitis [24]. A study by Thukar et al from India reported that genotype D was associated with more severe liver disease and HCC in younger patients than genotype A [25]. Overall, these results suggest seroconversion to HBeAg differ among HBV genotypes and that late or absent seroconversion could be related to progression of chronic hepatitis and liver disease.

Conclusion

HBV genotypes play an important role in the outcome of chronic HBV infection. More studies are required to define specific relationships between individual genotypes and risk for development of LC and HCC.

References

1. Ott JJ, Stevens GA, Groeger J, Wiersma ST (2012) Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. *Vaccine* 30(12): 2212-2219.
2. Kramvis A, Kew M, François G (2005) Hepatitis B virus genotypes. *Vaccine* 23: 2409-2423.
3. Kao JH, Chen DS (2006) HBV genotypes: epidemiology and implications regarding natural history. *Curr Hepat Rep* 5(1): 5-13.
4. Kramvis A, Restorp K, Norder H, Botha JF, Magnius LO, et al. (2005) Full genome analysis of hepatitis B virus genotype E strains from SouthWestern Africa and Madagascar reveals low genetic variability. *J Med Virol* 77(1): 47-52.
5. Mulders MN, Venard V, Njayou M, Edoth AP, Bola Oyefolu AO, et al. (2004) Low genetic diversity despite hyperendemicity of hepatitis B virus genotype E throughout West Africa. *J Infect Dis* 190(2): 400-408.
6. Singh J, Dickens C, Pahal V, Kumar R, Chaudhary R, et al. (2009) First report of genotype e of hepatitis B virus in an Indian population. *Intervirology* 52(5): 235-238.
7. Alvarado Mora MV, Romano CM, Gomes-Gouvêa MS, Gutierrez MF, Botelho L, et al. (2007) Molecular characterization of the hepatitis B virus genotypes in Colombia: a Bayesian inference on the genotype F. *Infect Genet Evol* 11(1): 103-108.
8. Devesa M, Loureiro CL, Rivas Y, Monsalve F, Cardona N, et al. (2008) Subgenotype diversity of hepatitis B virus American genotype F in Amerindians from Venezuela and the general population of Colombia. *J Med Virol* 80(1): 20-26.
9. Tanwar S, Dusheiko G (2012) Is there any value to hepatitis B virus genotype analysis? *Curr Gastroenterol Rep* 14(1): 37-46.
10. Olinger CM, Jutavijittum P, Hübschen JM, Yousukh A, Samountry B, et al. (2008) Possible new hepatitis B virus genotype, southeast Asia. *Emerg Infect Dis* 14(11): 1777-1780.
11. Phung TB, Alestig E, Nguyen C, Lindh M (2010) Genotype X/C recombinant (putative genotype I) of hepatitis B virus is rare in Hanoi, Vietnam-genotypes B4 and C1 predominate. *J Med Virol* 82(8): 1327-1333.
12. Tatematsu K, Tanaka Y, Kurbanov F, Sugauchi F, Mano S, et al. (2009) A genetic variant of hepatitis B virus divergent from known human and ape genotypes isolated from a Japanese patient and provisionally assigned to new genotype J. *J Virol* 83: 10538-10547.
13. Schaefer S (2007) Hepatitis B virus taxonomy and hepatitis B virus genotypes. *World J Gastroenterol* 13(1): 14-21.
14. Cao GW (2009) Clinical relevance and public health significance of hepatitis B virus genomic variations. *World J Gastroenterol* 15(46): 5761-5769.
15. Acharya SK, Madan K, Dattagupta S, Panda SK (2006) Viral hepatitis in India. *Natl Med J India* 19(4): 203-217.
16. Sanchez-Tapias JM, Costa J, Mas A, Bruguera M, Rodes J (2002) Influence of hepatitis B viral genotype on the long-term outcome of chronic hepatitis B in western patients. *Gastroenterology* 123(6): 1848-1856.
17. Chen HC, Eng HL, Lee CM, Fang YK, Kuo FY, et al. (2004) Correlations between hepatitis B virus genotype and cirrhotic or non-cirrhotic hepatoma. *Hepatogastroenterology* 51(56): 552-555.
18. Kao JH, Chen PJ, Lai MY, Chen DS (2002) Genotypes and clinical phenotypes of hepatitis B virus in patients with chronic hepatitis B virus infection. *J Clin Microbiol* 40(4): 1207-1209.
19. Kao JH, Chen PJ, Lai MY, Chen DS (2004) Hepatitis B virus genotypes and spontaneous hepatitis B e antigen seroconversion in Taiwanese hepatitis B carriers. *J Med Virol* 72(3): 363-369.
20. Chan HL, Hui AY, Wong ML, Tse AM, Hung LC, et al. (2004) Genotype C Hepatitis B virus infection is associated with an increased risk of hepatocellular carcinoma. *Gut* 53(10):1494-1498.
21. Kao JH, Chen PJ, Lai MY, Chen DS (2009) Hepatitis B genotypes correlate with clinical outcomes in patients with chronic hepatitis B. *Gastroenterology* 118(3): 554-559.
22. Lee CM, Chen CH, Lu SN, Tung HD, Chou WJ, et al. (2003) Prevalence and clinical implications of hepatitis B virus genotypes in southern Taiwan. *Scand J Gastroenterol* 38(1): 95-101.

23. Tangkijvanich P, Mahachai V, Komolmit P, Fongsarun J, Theamboonlers A, et al. (2005) Hepatitis B virus genotypes and hepatocellular carcinoma in Thailand. *World J Gastroenterol* 11(15): 2238-2243.
24. Wai CT, Fontana RJ, Polson J, Hussain M, Shakil AP, et al. (2005) Clinical outcome and virological characteristics of hepatitis B-related acute liver failure in the United States. *J Viral Hepat* 12(2): 192-198.
25. Thukar V, Guptan RC, Kazim SN, Malhotra V, Sarin SK (2002) Profile, spectrum and significance of HBV genotypes in chronic liver disease patients in the Indian subcontinent. *J GastroenterolHepatol* 17(2): 165-170.



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