REVIEW ARTICLE

A Narrative Review on the Specific Pattern of HBV Genotype in Bangladesh: Clinical Implications for Management

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Abstract

Background and aims: Bangladesh's unique epidemiological landscape presents an intriguing puzzle. This South Asian nation, with its complex sociodemographic and environmental factors, is home to a diverse array of hepatitis-B virus (HBV) genotypes, identified as Genotype C, with Genotypes D and A also making a significant contribution to the viral landscape. Reviewing such insights is necessary not only to underscore the country's regional diversity in HBV strains but also to bring into focus the clinical implications these genetic variations may have on disease progression and management.

Methods: A thorough database search covered various sources using relevant keywords like "Hepatitis B virus genotypes", "HBV genotypes in Bangladesh", and "HBV clinical implications". The review synthesized findings and analyzed HBV genotype prevalence and clinical implications in Bangladesh.

Results: Genotypes C and D collectively represent 82% of chronic hepatitis-B infection (CHB) cases in Bangladesh, underscoring their regional prevalence. The geographic context is pivotal in understanding HBV infection dynamics and disease progression in this area. Notably, genotype C and the presence of A1762T/G1764A mutations appear to have a distinct impact on disease development, potentially affecting the immune response in CHB patients. This highlights the need for tailored management approaches in this specific region. Further research is vital to confirm and elaborate on these findings, particularly in relation to how these mutations influence the host's immune response.

Conclusion and clinical significance: In summary, studies on HBV genotypes in Bangladesh stress the need for genotype-specific clinical considerations and more research to improve diagnostics and therapies.

Keywords: Chronic hepatitis B, Liver cancer, Liver cirrhosis.

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Introduction

Infection with the hepatitis-B virus (HBV) is still a major global public health concern. According to the World Health Organization (WHO), in 2019, there were approximately 296 million individuals living with chronic hepatitis-B infection (CHB), and about 1.5 million new infections occurred each year. In the same year, hepatitis B was responsible for an estimated 820,000 deaths, predominantly resulting from liver cirrhosis (LC) and primary liver cancer (hepatocellular carcinoma).[1] The cumulative estimated prevalence of HBV infection in the general population from 1995 to 2017 was 4.0% in Bangladesh, indicating a notably elevated risk of infection. The clinical presentation and management of HBV, however, can exhibit significant variation, influenced by the specific genotypes of the virus.[2]

Bangladesh's unique epidemiological landscape presents an intriguing puzzle. This South Asian nation, with its complex sociodemographic and environmental factors, is home to a diverse array of HBV genotypes. As of now, the predominant genotypes in Bangladesh have been identified as Genotype C, with Genotypes D and A also making a significant contribution to the viral landscape. Such insight not only underscores the country's regional diversity in HBV strains but also brings into focus the clinical implications these genetic variations may bear on disease progression and management.[3]

Understanding this unique HBV genotype pattern is of paramount importance. It lays the foundation for more targeted and effective strategies for HBV diagnosis, management, and prevention, particularly within the Bangladeshi context. By unraveling the genotype puzzle and delving into the associated clinical implications, we seek to provide valuable data-driven insights that will ultimately empower healthcare professionals, policymakers, and public health practitioners to enhance the management and mitigation of HBV in Bangladesh.

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Methods

Several scholarly databases, such as PubMed, Google Scholar, and Web of Science, were thoroughly searched. The search covered papers, reviews, and reports that have been published since the databases were first created. Relevant terms and phrases that were used in the search were "Hepatitis B virus genotypes", "HBV genotypes in Bangladesh", "HBV clinical implications", and synonyms for these terms. Key themes were discovered by synthesizing the findings from the chosen papers. Subsequently, the review examined the prevalence and distribution of HBV genotypes in Bangladesh, as well as their clinical implications.

Global Prevalence of HBV

There have been notable global differences observed in the prevalence of CHB infection in various regions. This variation is suggestive of the heterogenicity of the global HBV epidemiology. In fact, considerable variations in HBV prevalence were reported among different parts of the same country as well. The diverse nature of HBV epidemiology may be contributed by historical perspective, economic status, healthcare delivery system, and political conditions of the country. In addition to these, social and religious practices may also have profound impact on HBV epidemiology. The African (6.1%) and Western Pacific (6.2%) regions are the most endemic for chronic HBV infection, followed by Southeast Asia (2.0%), East Mediterranean (3.3%), and European (1.6%) regions. The American regions have the lowest incidence of HBV infection (0.7%). However, this geographical distribution is not homogeneous. Some parts of China show very high prevalence of HBV, whereas the prevalence is not so high in other areas.[4] Mongolia exhibits one of the highest HBV prevalence in the world.[5] The prevalence of HBV is highly heterogeneous in India, which is in accordance with its size and heterogeneous nature of population.[6] Data recorded for HBV prevalence largely depend on the nature of the study. For instance, evaluation of HBV prevalence among blood donors will mainly include male population in active working age. The prevalence of HBV may be extremely high among some specific population groups, such as people with coinfection of other viruses or drug users. In some countries, HBV prevalence has been accomplished as a pilot study with a very small sample size. Based on these diversities and the heterogeneous nature of studies, there is an urgent need for proper evaluation of HBV prevalence in different population groups, which will further help in designing appropriate HBV containment programs.

HBV Virology: Insights into the Complex Viral Genome

Hepatitis-B virus is hepatotropic and a member of the Hepadnaviridae family of viruses. It is characterized by its small size and the presence of partially double-stranded DNA. Hepatitis-B virus infects individuals of all ages and possesses a genome consisting of four overlapping open-reading frames. These four open-reading frames give rise to four critical genes within the HBV genome, labeled as *C, X, P,* and *S*. The *S* gene is of particular interest, as it contains three "start" codons (ATG). This division results in three distinct regions: pre-S1, pre-S2, and S. The pre-S–S (pre-surface–surface) region is responsible for encoding three viral surface antigens. The most well-known among these antigens is the 24 kDa S protein, commonly referred to as hepatitis-B surface antigen (HBsAg), with a sequence of 226 amino acids. In addition to HBsAg, two more surface proteins of HBV have been identified: M (or pre-S2) protein, featuring a 55-amino acid extension at the N-terminal, and L (or pre-S1) protein, which includes either 108 or 119 amino acids, based on the genotype of HBV. While the functions of M proteins remain poorly understood, the L protein has been identified as essential for the virus's binding to host-cell receptors.[7] The pre-C–C (pre-core–core) region of the HBV genome encodes two crucial antigens: hepatitis-B core antigen (HBcAg) and e antigen (HBeAg). The viral X protein (HBx), which regulates signal transduction inside host cells and X open-reading frame, encodes it. The polymerase, an enzyme with multifunctional roles in DNA synthesis and RNA encapsidation, is encoded by the P coding region.[8]

In individuals infected with HBV, various expression proteins and antigens are detected, often in varying proportions. These variations depend on the different stages of pathological processes. However, the precise roles of these proteins and antigens in inducing liver damage remain poorly understood. It is plausible that the association of these antigens and their titers may have implications for the pathological status and HBV infection prognosis.

HBV Genotype Variations and Their Global Distribution

The genome of the HBV, infects human consisting of roughly 3200 base pairs. Inside hepatocytes, HBV undergoes replication through reverse transcription, making it prone to substitutions of nucleotides at a rate predicted to be between 1.4 and 3.2 × 10−5/sites/year. This replication method can result in the emergence of diverse forms of HBV, including genotypes, subtypes, mutants, recombinants, and quasi-species, attributed to immunogenic or host-induced pressures. These variations are likely pivotal for the virus's survival.[9,10] Genotypic classification of HBV has been achieved with insights into these molecular events. Based on more than 8% genetic difference, HBV genotypes are currently divided into 10 (A-J) genotypes, and several subtypes with 4–8% genetic divergence have been found.[11] There are notable regional preferences in the HBV genotype distribution. While genotypes B and C are primarily found in the Asia-Pacific region, which includes Japan, Taiwan, and China, genotype A is more widespread in Africa, Europe, some regions of India, and America. Northern India, the Mediterranean region, Europe, and Africa are among the regions where genotype D is most common. West Africa harbors genotype E, Central and South America harbor genotype F, France, Germany, and the Americas harbor genotype G, Central America and Mexico harbor genotype H, and Vietnam and Laos harbor genotype I.[9]

The initiation of this diversity in HBV genotypes remains enigmatic. Typically, most countries are dominated by two major HBV genotypes, except in immigrant countries, where multiple genotypes may coexist. Japan, for example, has HBV genotypes C and B as the primary ones, while Africa and Europe feature HBV genotypes A and D. India, with its diverse population, accommodates genotypes A, C, and D, suggesting migration from different parts of the world. Because of perinatal or mother-to-infant transmission, genotypes B and C are more common in highly endemic areas, whereas in areas where horizontal transmission is the primary mode of HBV infection, other genotypes are more frequently detected. However, the scenario is different in India and Bangladesh, where perinatal transmission is common, yet genotype B is rarely found.[11] Global research has established a connection between the HBV genotype and the degree of liver damage, as well as the development of liver LC and HCC. Progressive liver disorders are more common in areas like the Asia-Pacific region where both HBV genotypes B and C are common, particularly with genotype

C infections displaying a greater propensity for severe outcomes when compared with genotype B.[12,13] This association is often accompanied by high viral loads, with genotype-C-infected patients having higher HBV loads than genotype-B-infected patients[13] and HBV genotype C has greater pathogenicity than genotype B.[14] Moreover, HBV genotype-B infections often result in HCC developing earlier in life than genotype C infections, which usually cause HCC to develop later in life.[15] In areas where genotype D is prevalent, such as North America and Western Europe, the incidence of HCC is greater than genotype A.[16,17] A prospective study involving HBV carriers who were native to Alaska found that HBV genotype F carried a considerably greater chance of developing HCC than genotypes A–D. It has also been documented that the pathological state of HBV patients is related to HBV genotypes F, G, and H. The reduced incidence of cirrhosis and HCC in Mexico may be explained by the pathogenicity of genotype H, which is distinct from other HBV genotypes in high endemic regions.[18–20] Even though a number of studies have shown differences in the association between HBV genotypes and the severity of liver diseases, a comprehensive understanding of the underlying mechanisms responsible for these variations is still lacking.

Genomic Mutations and Their Role in Hepatitis B Pathogenesis

Given that the hepatitis-B virus is noncytopathic, naturally occurring mutants within the HBV genome carry significant implications for the development of liver damage induced by HBV. These alterations are essential for changing how the host immune system recognizes the virus, increasing the virus's pathogenicity by increasing its replication and affecting cell attachment and penetration.[21] One well-known mutation is the HBV pre-core nucleotide 1896 stop codon mutation, which is strongly associated with the presence or lack of the HBeAg. This mutation has been recognized for decades. Contrary to the belief that HBeAg-negative CHB is a benign condition, it is now understood that viral replication and liver damage can be prominent features in HBeAg-negative patients. Chronic hepatic inflammation may be prolonged by mutations that sustain HBV DNA replication even after HBeAg seroconversion, such as the basal core promoter (BCP) A1762T/G1764A variations.[22] Moreover, the cytoplasmic location of intracellular HBcAg has been connected to these BCP mutations, and this is directly related to the active necroinflammation of hepatocytes.[23] In studies comparing genotypes D and A, genotype D displayed more progressive liver disease and a larger frequency of BCP A1762T/G1764A variants compared with genotype A.[24] Several important discoveries have been made after a more thorough examination of these mutations and variations. Compared with genotype B, genotype C exhibits a greater incidence of pre-S deletion mutations and BCP A1762T/G1764A variations. Furthermore, genotype C had a greater serum HBV viral load than genotype B, exhibits increased intracellular HBV DNA expression, higher intracellular core protein expression, and secretes more HBeAg compared with genotype B. These findings may provide some understanding into why genotype C is associated with more severe liver disease than other genotypes.[25] In addition, relative to genotype B, genotype C is linked to a greater prevalence of BCP A1762T/G1764A variations. Individuals who carry these variations are far more likely to develop HCC.[12] Notably, an independent predictor of the pathogenesis of HCC has been found for the BCP mutation at A1762T/G1764A. A summary risk ratio of 3.79 for HCC in relation to BCP A1762T/G1764A variations has been found through meta-analysis.[23] It was shown by a recent qualitative and quantitative study conducted in Taiwan that BCP A1762T/G1764A polymorphisms constitute a separate threat for the development of cirrhosis. Patients with these variations had an increased risk of cirrhosis, according to a quantitative study employing pyrosequencing.[12] Because the HBV genome overlaps, BCP A1762T/G1764A mutations also affect the carboxy-terminal codons 130 and 131 of the X protein. In light of these data, BCP A1762T/G1764A polymorphisms, independent of HBV genotypes, may increase fibrogenic activity and encourage hepatocarcinogenesis.[26] In a different investigation, Takahashi et al. identified the complete HBV genome's nucleotide sequence in sera from forty Japanese patients who had HBsAg-expressing HBV-related HCC. Overwhelmingly, patients with HBV genotype C provided 95% of the serum samples, and nucleotide positions 1762 (A-to-T) and 1764 (G-to-A) showed alterations in almost 90% of these isolates.[27] Collectively, these findings suggest that increased pathogenicity and a greater propensity to cause LC and HCC are related to HBV genotype C. However, it is important to note that this study's comparison was primarily between HBV genotypes C and B due to the geographical distribution of HBV genotypes.

Hepatitis B in Bangladesh: Prevalence and Genotype Distribution

Bangladesh, the eighth most populous country globally, is geographically surrounded by India on almost all sides, sharing borders with Myanmar while being in close proximity to Nepal and Bhutan. Like many other developing nations with limited resources, Bangladesh lacked a thorough investigation on HBV and its effects. In 1991, a study at a Dhaka-based medical college involving 500 individuals who had undergone major surgeries revealed a HBsAg positivity rate of 8.6% in Bangladesh.[28] In 2006, Mahtab et al. reported a HBsAg prevalence of 5.5% among 1018 individuals, encompassing diverse age groups, sexes, and backgrounds.[29] However, this study, conducted over a decade ago, may not be entirely representative of the current prevalence rate. Subsequent studies shed light on the ongoing situation in Bangladesh. In 2010, Ashraf et al. conducted research in Dhaka involving 1997 subjects from a municipal corporation and reported a 5.8% prevalence of HBV infection.[30] A further study conducted in 2013 on patients receiving standard medical checkups at a hospital in Dhaka found a prevalence rate of 4.90%.[31] Collectively, these studies place Bangladesh in the intermediate prevalence category (2–7%) for chronic HBV,[30] with an estimated 3–12 million chronically HBV-infected individuals. Notably, the past two decades have seen improvements in HBV infection rates among infants and children born during the post-vaccination era. This progress reflects the success of the nationwide universal vaccination program initiated in 2004, with a remarkable coverage rate of 94.2%.[32] The prevalence of HBsAg has dramatically decreased to less than 0.1% after the HBV vaccination was implemented in children. In 2018, Paul et al. reported HBsAg prevalence of 0.05% among post-vaccine era children and 1.7% among pre-vaccine era children.[33] All these reports underscore the immense success of the universal vaccination program in Bangladesh.

Hepatitis-B virus genotype prevalence in Bangladesh has been explored in only few studies, most involving fewer than 100 subjects. In 2006, Mahtab et al. reported a higher prevalence of genotype D (50%) and genotype C (39%) among the 45 subjects studied, marking the first report on HBV genotype prevalence in

Bangladesh.[29] In a subsequent study of 19 HBV-infected patients, HBV genotype D (74%) exhibited the highest prevalence, followed by genotype A (15.8%) and genotype C (10.0%).[34] However, more recent research has shown that CHB patients in Bangladesh had a greater prevalence of HBV genotype C.[35,36] Rahman et al. in 2016 observed a predominance of genotype C (48.7%), D (28.2%), and A (23.1%) among 39 patients. In a different study, Munshi et al. found that among the 53 patients they studied, the prevalence of genotype C was greater at 45.3%, followed by genotype D at 35.8% and genotype A at 18% in 2017. A different study that involved 97 HBV-sequenced isolates and ran from 2005 to 2017 discovered that genotype C predominated (43%), followed by genotype D (39%) and A (18%). Research conducted by Raihan et al. in 2019 also observed a higher prevalence of genotype C (46%), with genotypes D and A at 35% and 18%, respectively, among 360 CHB patients which is the largest cohort till date in the country.[3]

Diverse HBV Genotypes Prevalent in Bangladesh and Their Clinical Significance

In most countries and regions, two predominant HBV genotypes are typically identified, with occasional exceptions due to the migration patterns of populations in immigrant-receiving nations. For instance, Japan, China, and Taiwan predominantly harbor HBV genotypes B and C, while Europe and certain regions of Africa exhibit HBV genotypes A and D. Bangladesh, however, is noteworthy for its substantial prevalence of three major genotypes: C, D, and A. Historical migration movements, like the Mongol invasion in the 16th century and the East India Company's occupancy of Bangladesh in the 18th century, might be blamed for the cohabitation of different genotypes in the area.[10]

One intriguing observation stemming from studies of HBV genotypes in Bangladesh is the conspicuous absence of HBV genotype B among the isolates. This finding has been consistently confirmed in various studies, including the largest cohort study conducted by Raihan et al. in 2019. None of the prior studies in Bangladesh, conducted by Mahtab et al.,[29] Shaha et al.,[34] Rahman et al.,[36] and Munshi et al.,[35] reported genotype B in Bangladesh. A similar pattern has also been observed in India, as reported by Datta et al. This absence of genotype B highlights the significant role of perinatal transmission of HBV infection in Bangladesh. In this context, it suggests that the mothers in Bangladesh are more likely to transmit HBV genotypes A, C, and D to their offspring, with genotype B being the least prevalent. Moreover, the presence of genotypes D and A in significant numbers indicates a high rate of horizontal transmissions as well.[37]

The presence of these three major HBV genotypes in Bangladesh carries potential clinical and public health implications. Studies conducted in Japan, Taiwan, Korea, and Europe have previously demonstrated that certain HBV genotypes exhibit a stronger association with the progression of liver diseases compared with others. These investigations have shown, so far, that genotype C is more pathogenic than genotype B. The pathogenic potential of genotypes C and B has been studied in nations like China, Taiwan, and Japan because of the predominance of these genotypes in these areas. Likewise, comparisons have been made to assess the pathogenic potential of HBV genotypes A and D, as these genotypes predominate in Europe.[38]

Nonetheless, there is a scarcity of research on this kind being done in underdeveloped nations. An essential study by Raihan et al. carried out in Bangladesh offers valuable insights into the connection between the prevalence of liver disorders and HBV genotypes. This study compared HBV genotypes A with C and HBV genotypes C with D, representing a unique research effort in Bangladesh. Their results showed that patients with elevated HBV DNA levels, elevated ALT levels, LC, and HCC were more likely to have HBV genotype C. On the other hand, patients with consistently low HBV DNA levels and normal ALT levels were more likely to have HBV genotypes D and A.[3] There is evidence linking genotype C to severe liver disorders associated with HBV in many parts of the world, especially in locations where genotypes B and C are more common. Higher levels of HBV replication have been observed to indicate greater pathogenicity for genotype C. Furthermore, HCC is more common in people with HBV genotype C than in people with genotype B.[10]

In Taiwan, 4,841 CHB patients without HCC participated in a study. It was discovered that patients with genotype C had higher viral loads and a 26-fold higher chance of developing HCC than patients with other genotypes.[13] In a similar vein, a prospective research involving 2,762 community-based chronic HBV patients in Taiwan found that those with genotype C were more likely to develop HCC.[39] In a subsequent hospital-based cohort research, Tseng et al. observed 2,688 HBsAg-positive patients without cirrhosis for an average of 14.7 years before discovering that genotype C was more strongly associated with the development of HCC than genotype B.[14] The impact of genotype C on the clinicopathological characteristics of long-term HBV patients has also been noted in earlier investigations. Wu et al. discovered that compared with genotype-B patients, those with genotype C had greater viral loads and inflammation of the liver.[40] It was claimed in a recent study by Chuon et al. that CHB individuals with genotype C in Cambodia had a higher risk of developing HCC. All of these results support the notion that individuals with HBV genotype C have a higher chance of developing HCC.[41]

The precise factors and mechanisms underpinning the relationship between genetics and the development of liver disease remain largely unknown and inadequately understood. Therefore, there is a pressing need for dedicated research efforts aimed at unraveling the mechanisms responsible for the higher virulence of genotype C, especially concerning the pathogenesis of LC and HCC.

The length of time that an individual has been HBeAg-positive and the degree of viral replication are two possible contributing variables to the observed variations in disease development between genotypes. Sumi et al. provided evidence in support of this theory, demonstrating that earlier HBeAg seroconversion occurred in patients with genotype B, which may have reduced viral replication in a subset of patients once HBeAg seroconversion was attained. This could provide some insight into why patients with genotype B had a lower risk of getting HCC and hepatic fibrosis advancement than those with genotype C.[42,43] A better clinical outcome seemed to be associated with early HBeAg seroconversion as opposed to late or missing HBeAg seroconversion. Numerous cross-sectional investigations have revealed a stronger correlation between genotype C and a higher possibility of cirrhosis, liver fibrosis, hepatitis flare-ups, and inflammation of the liver.[25,43] Nevertheless, there was no discernible difference between HBV genotypes B and C in terms of the lifetime risk of developing advanced fibrosis and HCC.

Furthermore, it is possible that variations in the HBV genome could increase the likelihood of LC and HCC development, either on their own or in combination with other genotypes. A1762T/G1764A mutations were shown to be substantially more frequent in individuals with genotype C and LC or HCC.[44] Genotype C or mutations at A1762T/G1764A were linked to a ninefold increased

risk of LC and/or HCC development according to a study conducted in Bangladesh.[3] Similar results have been observed in several other countries. The first of such findings was reported by Takahashi et al. in 1995.[27] Later, in 2004, Kao et al. conducted research on a cohort of patients with genotypes B and C and discovered that the frequency of mutations at A1762T/G1764A was more in genotype C and was firmly linked to progression of HCC.[25] In another long-term study involving approximately 1526 HBV carriers, it was proposed that the A1762T/G1764A mutation might function as a stand-alone predictor of the development of HCC.[39] A meta-analysis conducted in China on HBV-infected individuals further substantiated these findings regarding the association between A1762T/G1764A mutations, genotype C, and the progression of LC and HCC.[45] According to a Taiwanese study, individuals with persistent HBV infection of genotype C or B who also had cirrhosis also had the A1762T/G1764A mutation. Furthermore, additional research has suggested that the A1762T/G1764A mutation may function as an independent predictor of HCC.[23,45] Given the overlapping nature of the HBV genome, mutations in the BCP may alter the carboxy-terminal codons of the X protein and alter the amino acid sequences at 130 and 131 positions. This may further stimulate fibrogenic activity in the liver, leading to HCC development, irrespective of genotypes. In another recent study conducted in Cambodia, 26 CHB patients were examined, revealing the presence of genotype C1 in 24 patients. Furthermore, a great deal of mutations was found, most notably the double mutation at A1762T/G1764A in 18 isolates (75.0%) and the combination of mutations at C1653T and/or T1753V and A1762T/G1764A in 14 isolates (58.3%). In addition, 340 registered C1 strains from GenBank were screened for mutations, with 113 of them (33.2%) displaying combination mutations, the majority of which were reported in the group suffering from LC and HCC. These findings collectively emphasize that Cambodian CHB patients with genotype C1 and mutations are at a heightened risk of progressing to LC and HCC.[41] Together, these studies provide valuable insights into the association between HBV genotypes and HBV mutations and their role in HBV-induced liver damage.

Hepatitis-B virus, as a noncytopathic virus, lacks a clearly defined direct role in inducing liver injury, hepatic fibrosis, and hepatocarcinogenesis. Nevertheless, HBV has been associated with various disease manifestations, spanning acute infection, chronic HBV infection leading to conditions like LC and HCC, and even acute liver failure (ALF) and acute-on-chronic liver failure (ACLF). Prolonged infection of hepatocytes by the virus results in chronic inflammation characterized by the ongoing expression of inflammatory cytokines. This process recruits various immune cells to the liver. The persistent presence of inflammation, with periodic exacerbations and remissions, culminates in a state commonly known as chronic hepatitis B (CHB). This sets the stage for an inflammatory microenvironment or mucosal milieu,[46] which may contribute to hepatic fibrosis. As fibrosis progresses and distorts the hepatic parenchymal structure, it ultimately leads to cirrhosis of the liver.[47] The presence of fibrosis and cirrhosis increases the susceptibility of the liver to hepatocarcinogenesis, eventually progressing to HCC. In total, the inflammatory mucosal milieu, coupled with fibrotic activity, is likely linked to the pathogenesis of progressive liver diseases in CHB patients with mutations, though questions remain as to why all patients do not follow the same pathogenic course.

Activated inflammatory cells are known to release free radicals, including reactive oxygen species (ROS) and nitric oxide (NO)-reactive species. These compounds can inflict damage to DNA, resulting in gene mutations, thereby promoting neoplastic transformation.[48,49] Hepatic oxidative stress has indeed been strongly associated with an elevated risk of HCC in patients with chronic HBV infections. Furthermore, high levels of nitrite were reported in HCC patients in two separate studies conducted in 1997 and 2000 by Moriyama et al.[50,51] Another study involving Bangladeshi CHB patients also revealed that genotype C and mutations at A1762T/G1764A resulted in significantly higher levels of proinflammatory cytokines (IFN-γ, TNF-α, TGF-β, IL-2, and IL-12) and nitrite production in culture supernatants.[52] These findings suggest a possible role of mutant HBV in amplifying an inflammatory microenvironment, potentially increasing the risk of LC and HCC development, although other contributing factors cannot be ruled out.

Conclusion

The studies in Bangladesh have revealed the unique geographical importance of HBV genotypes in this region. This area exhibits a distinctive genetic diversity with the prevalence of three primary HBV genotypes: C, D, and A. This regional genetic landscape has significant implications for health care and disease management. Genotypes C and D collectively constitute 82% of CHB cases in Bangladesh, emphasizing the regional dominance of these genotypes. The geographic context plays a vital role in understanding HBV infection dynamics and disease progression within this specific region. Furthermore, the link between genotype C and the presence of HBV mutations at A1762T/G1764A underscores the regional genetic impact on disease development. This suggests that genotypic variations uniquely influence the clinical course of the disease, requiring tailored management approaches specific to this geographic setting. An intriguing discovery is the potential impact of A1762T/G1764A mutations on the immune response in CHB patients in Bangladesh. These mutations appear to induce a pro-inflammatory cytokine pattern, raising questions about their distinct role in host immunity within this geographic context. Further research is essential to confirm and expand upon these findings, given the region's unique genetic characteristics. Comprehensive studies involving various cytokine types will be crucial in validating these observations and understanding how these mutations affect the host's immune response.

Clinical Significance

The studies on HBV genotypes in Bangladesh highlight the geographic importance of understanding viral genetics in the context of hepatitis B. These findings stress the significance of genotype-specific clinical considerations and the potential immunological implications of regional HBV mutations. More extensive research in this region is needed to enhance our understanding of chronic HBV infections and improve diagnostic and therapeutic strategies for the local population and beyond.

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