Hepatitis B: Viral genome, HBV and HIV co-infection, Antiviral Therapy and Diagnosis

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***Abstract*—Infection with hepatitis B is a major worldwide health concern. Frequently spread through bodily fluids such as blood, semen, and vaginal secretions and lead to wide range of liver disease including acute to chronic hepatitis, fulminant hepatitis, cirrhosis and hepatocellular carcinoma. Hepatitis B infection infects more than 262 million people worldwide that leading to around 820,000 deaths annually. In order to accomplish the objective of eradicating viral hepatitis (particularly chronic B and C), and sexually transmitted disease by 2030, the health sector is guided by global health sector strategies on viral hepatitis but currently no countries are on track to achieve this goal. All patient with hepatitis B surface antigen (HbsAg) should receive treatment until HBsAg is undetectable for 12 months. We are going to review on epidemiology, HBV and HIV coinfection, mode of transmission, antiviral therapy, as well as their Diagnostic evaluation and its future approaches**

***Index Terms*—HBV, epidemiology, viral genome, HBV / HIV coinfection, Antiviral therapy, diagnostic evaluation**

I. INTRODUCTION

HBV, a little DNA virus with peculiar characteristics resembling retroviruses, belongs to the Hepadnaviridae family. HBV can incorporate into the host's genome and replicates via an RNA intermediate (1,4). The hepatitis B virus is a partially double-stranded DNA virus that has multiple serological markers, including anti-HBc IgM and IgG, HBsAg and anti-HBs, and HBeAg and anti-HBe. Contact with contaminated blood or semen is how it is spread (5). A to H are the eight genotypes of HBV based on sequence comparison. Every genotype has a unique geographic range. Electron microscopy is used to visualize three different kinds of virus particles in infected serum. One of the viral particles is a 20 nm diameter, smaller spherical shape, while the other is a 22 nm wide filament of variable length. Since the spheres and filaments are made of host-derived lipids and the hepatitis B surface antigen (HBsAg) rather than viral nucleic acids, they are not contagious (2,4). The identification of HBsAg made it possible to screen blood donors for a potentially harmful infection for the first time. Modern virus diagnostics were developed in large part to address the need to identify clinically silent HBV infections (3,6)

II.EPIDEMIOLOGY

The global HBV epidemic has infected around two billion people, with over 350 million people suffering from chronic HBV across all countries and the death rate from viral hepatitis has risen by 63% since 1990(7). Infection with the hepatitis B virus (HBV) is a worldwide public health concern (8,9). About 257.5 million persons worldwide were infected with HBV in 2022 (hepatitis B surface antigen (HBsAg) positive), and consequences from the virus were responsible for about 550,000 fatalities (10). In the central Ethiopian region, community-based cross-sectional research of adult intrafamilial home contacts was carried out between October 1, 2023, and March 1, 2024. The distance between Addis Ababa, Ethiopia's capital, and the center Ethiopian area is 232 kilometers. The region was predicted to have 6,430,235 residents, of which 3,186,824 (49.56%) were men and 3,243,411 (50.44%) were women. In Ethiopia, the central region is the most rural with 5,425,189 people living in rural areas (84.4%) and 1,005,046 people living in urban areas (15.6%). The projected total number of households in the chosen research region was

1,312,411 (20.41%), of which 1,498,245 (23.3%) were women of reproductive age, and 222,486 (3.46%) were pregnant women. With 1,656 public and private healthcare facilities, including two comprehensive specialized hospitals (Wachemo University Nigist Eleni Mohammed Memorial Comprehensive Specialized Hospital (WCUCSH) and Worabe University Comprehensive Specialized Hospital (WUCSH)), five general hospitals, twenty-one primary hospitals, two hundred and twenty-eight health centers, 1,067 health posts, and 333 private clinics (11)), this region is divided into seven zones and three special districts. In the first phase, five purposefully selected public hospitals in central Ethiopia two teaching hospitals (WCUCSH and WUCSH) and three general hospitals (Butajira, Durame, and Halaba Kulito) were used to retrospectively select 195 pregnant women index cases who tested positive for HBV (HBsAg+). 29,400 pregnant women who visited Antenatal Care (ANC) clinics prior to a six-month period of actual data collection between April 1 and September 30, 2023, were selected as cases. Using a lottery approach, 385 individuals who were intrafamilial household contacts were chosen at random from the HBV index cases for the second phase. Until the 385-sample size was reached, all selected contacts were tracked down and examined for HBV (HBsAg). In households with multiple eligible adults, on average, two people were randomly picked (12.)

III.VIRAL GENOME

The HBV contains a 3.2 kb genome and an enveloped shape. The virally encoded capsid encloses the circular double-stranded DNA (dsDNA) genome. Open reading frames (ORFs) in the genome are highly overlapping and contain a lot of information. The HBV genome's negative strand has four open reading frames (ORFs): the P gene, the S gene (which is further subdivided into pre-S2, pre-S1, and S regions), the X gene, and the C gene (which is further subdivided into pre-C and C regions). PreCore, HBV e antigen (HBeAg), HBV polymerase, structure protein, HBsAg and HBV core antigen (HBcrAg), and HBV X protein (HBx) are among the seven proteins that are encoded by the ORFs (13). When the HBV genome enters host hepatocytes, it is repaired into covalently closed circular DNA (cccDNA), which becomes a stable episome inside the hepatocyte nucleus. Initially, the genome is found in a partially double stranded, relaxed circular DNA form (rcDNA)(14) HbsAg Three distinct HBsAgs are produced: the major HBsAg, which is encoded by the S gene; the medium HBsAg, which is encoded by the pre-S2 and S genes; and the large HBsAg, which is encoded by the pre-S1, pre-S2, and S genes (Tiollais et al., 1985; Blum et al, 1989a). It is likely that the big HBsAg facilitates the virus's attachment to the cell (Neurath et al., 1986, 1990). It is uncertain what the middle HBsAg does (15) HbcAg.The pre-core/core (HBe-C/C) gene encodes the hepatitis B core antigen (HBcAg) and its antigenically different processed product, hepatitis B envelope antigen (HBeAg). This protein, which is seen in serum as HBeAg, often indicates a high amount of liver virus replication HBxAg does not seem to be required for HBV replication or gene expression in vitro(15)

IV. MODE OF TRANSMISSION

Early childhood Vertical transmission is responsible for majority of chronic hepatitis B infections. Compared to other transmission methods, vertical transmission is linked to a higher risk of developing liver disease and is a significant source of new infections. Eleven studies on vertical transmission and 113 studies on the prevalence of HBsAg in 190,983 pregnant women were considered.

Based on data from 2014–23, the WHO African region's HBsAg prevalence among women undergoing prenatal care was 6·2% (95% CI 5·3–7·2).In the WHO African area, the hepatitis B virus (HBV) was responsible for a projected 272,000 fatalities and 771,000 new infections in 2022, which accounted for 63% of all new infections world-wide, a decline from a peak of 339 000 in 2001 (149 000–634 000; 1·2% of all live births)(16) Horizontal transmission through sexual contact, bodily fluids, and blood (Khan et al., 2021).

In Africa, horizontal transmission is well known, particularly when it occurs through intimate contact inside households.

However, the importance of horizontal transmission would be decreasing as more newborns received the three-dose hepatitis B immunization series (HepB3).

First month of life is the most vulnerable time for horizontal transmission, which occurs in early

childhood through close contact with infected caregivers and is thought to be a major route of infection. For HBV and HCV, the combined prevalence of horizontal transmission was 28.6% (95% CI: 18.2%–41.8%) and 10.8% (95% CI: 6.3%–17.8%), respectively.

Among children from infected homes, prevalence was 35.9% for HBV (95% CI, 16.3% - 61.7%) and 3.3% for HCV (95% CI, 1.6% - 7.0%). The rates of HBV and HCV intra-household transmission through sexual contact were 21.5% (95% CI, 4.3% - 62.5%) and 7.7% (95% CI, 4.9% - 11.8%), respectively (17,18,19,20,21,22,23)

V. HBV AND HIV COINFECTION

Since the two viruses share transmission pathways, about 10% of individuals with HIV also have chronic HBV co-infection. Compared to chronic HBV mono-infection, HIV/HBV coinfection speeds up the development of chronic HBV to cirrhosis, end-stage liver disease, or hepatocellular carcinoma (30). A serious global public health issue is the hepatitis B virus. Due to a shared risk of transmission, HBV–HIV co-infection is not unusual, especially in regions where HBV infection is endemic. Reference 1 Patients with HIV have a 40% higher chance of contracting HBV infection than people without HIV (31). Co-infection with HBV increases morbidity and death among HIV-positive individuals (32). Furthermore, a large number of HIV-positive individuals are not aware that they have an HBV infection, putting them at a heightened risk of liver-related illnesses (33). Although it is strongly advised to screen for HBV co-infection on a regular basis, especially in settings with limited resources, this is not often done before starting ART.HBV co-infection increases the likelihood of liver-related disease development and ongoing non-AIDS-defining morbidity in HIV-positive individuals (Citation 6–Citation 8).Third Citation There has been minimal and conflicting evidence about the impact of HBV co-infection on the course of HIV illness and liver-related problems in HIV-positive individuals using HAART(31)

HBV and HIV coinfection Pathogenesis

The exact mechanism via which HIV contributes to liver disease is still unknown. The immune response mediates HBV-related hepatotoxicity, which appears to be exacerbated by HIV-induced immunodeficiency (34). One significant aspect of HIV infection is the depletion of CD4+T cells, which inhibits the cytokine release of lymphocytes and the antigen presentation of liver-resident macrophages (Kupffer cells), leading to host immunosuppression (35). Inhibiting the host immune response significantly increases HBV replication, which further damages the liver (36,37). Hepatocytes infected with HBV are non-cytopathic, meaning they do not exhibit definite cellular damage or viral cytopathic effects. However, those who are coinfected with HIV and HBV exhibit fibrosing cholestatic hepatitis (38,39). The hepatic cytokine environment is altered by HIV/HBV coinfection. HIV glycoproteins have been shown to promote hepatocyte death by stimulating the expression of the tumor necrosis factor related apoptosis inducing ligand (TRAIL) (30). HIV envelope protein causes Huh7 cells to undergo caspase-independent apoptosis (40). HIV infection contributes to liver inflammation and fibrosis by causing hepatocyte apoptosis by phagocytosis by macrophages or hepatic stellate cells (41). The increase of hepatocyte apoptosis has been observed among HBV/HIV coinfected patients compared with HBV mono-infected patients (42). It has been shown that HIV gp120 mediates hepatic inflammation by inducing hepatic production of IL-8(43). An increase in HBV load raises the HBV X protein (HBx), which can also use NF-κB and C/EBP-like cis-elements to transactivate IL-8 expression (44). IL-8 a leukocyte chemotactic molecule, is essential for preserving the inflammatory milieu and the development of HCC (45). Additionally, HBx can increase the expression of cyclooxygenase-2 (COX-2), which is overexpressed in liver cirrhosis. There is growing evidence that HBV proteins activate IL-8 and COX-2 to maintain the inflammatory environment. The inflammatory hepatocytes secrete C-X-C motif chemokine 10 (CXCL10), which is linked to the severity of liver damage involving viral hepatitis. Once CXCL10 binds to its receptor, chemokine receptor 3 (CXCR3), immunocytes like natural killer cells and activated T cells and B cells are drawn to the inflammatory sites. Patients with HBV/HIV coinfected had elevated CXCL10, but not those with HBV mono-infected individuals (46,47,48,49,50,30)

VI. DIAGNOSIS AND CLINICAL FINDING

Hepatocellular carcinoma (HCC) represents one of the most formidable challenges in digestive system malignancies, characterized by its high morbidity and mortality, with chronic infection of hepatitis B virus (HBV) being one of the main causes. This devastating disease has caused a serious burden on the economy and medical system of China (24,25). Hepatitis B (HB) is still a major global health concern despite the availability of effective vaccines and treatment methods. It can cause acute, chronic, severe liver failure, and malignancy, which can lead to high rates of morbidity and death (51)

6.1 Serological, Genomic and Molecular Testing

6.1.1 Quantitative HbsAg

Throughout the various stages of CHB, HBsAg levels and the source of HBsAg production fluctuate. HBsAg concentrations are low during the inactive phase and high during the immune-tolerant phase (52,53). Additionally, in the younger hepatitis B e antigen (HBeAg)-positive patient, the source of HBsAg production shifts from mostly covalently closed circular DNA (cccDNA) transcription to HBV integrants in the older HBeAg-negative patient (54). In Asian HBeAg-negative patients, spontaneous HBsAg Sero clearance after 6 to 8 years is predicted by an HBsAg level of less than 100 IU/ml. The HBsAg level has recently been included in HCC risk scores since greater levels may indicate a decreased chance of spontaneous clearance (55,56). In HBeAg-positive patients, an HBsAg level of >20,000 IU/ml at week 24 confers a 96% negative predictive value (NPV) for genotype A HBV and a 100% NPV for genotypes B, C, and D. This suggests that the HBsAg level can also be helpful in predicting and/or tracking a patient's response to therapy with peginterferon (PEG-IFN). The elimination of HBeAg and an HBV DNA level of less than 2,000 IU/ml six months after treatment are considered favorable responses to HBV infection treatment. In patients who are HBeAg-negative, the best-validated model for predicting the effect of treatment is to observe a decrease in both HBsAg and HBV DNA levels at week 12. Patients with an HBV DNA level of less than 2,000 IU/ml and a normal alanine aminotransferase (ALT) level 24 weeks after therapy have an NPV of 95 to 100% if they do not have a 2-log reduction in their HBV DNA level and/or any decline in HbsAg (57,58,59)

6.1.2 HBeAg.

An essential stage of immunological clearance is indicated by the seroconversion of HBeAg. Nevertheless, high HBV DNA quantities can cause active hepatitis in certain HBeAg-negative patients. This condition is frequently described as an HBeAg-negative illness. It is possible for concurrent mutations to occur in the precure stop codon and/or the basal core promoter. The status of HBeAg is one area where current worldwide consensus includes recommendations (60).

6.1.3 Anti-HBc.

Immunoassays for total anti-HBc, which can identify both anti-HBc IgG and anti-HBc IgM, can identify the core antibody to the hepatitis B virus, or anti-HBc. The hallmark of acute hepatitis B is anti-HBc IgM, which is frequently the only indicator that can be found when HBsAg has gone undetectable. When patients experience severe and acute flare-ups of chronic hepatitis B, they also test positive for anti-HBc. Anti-HBc IgG, however, can be a sign of an HBV infection, either past or present. A positive anti-HBc test and a negative HBsAg test in patients with cryptogenic hepatocellular carcinoma (HCC) may suggest an occult HBV infection or HBV infection (61,62).

6.1.4 HBV DNA

Since HBV DNA can be a marker of viral replication and is the primary target of antiviral therapy, current guidelines recommend antiviral therapy for patients with elevated ALT levels and HBV DNA levels of 2,000 to 20,000 IU/ml, as well as for those with HBV DNA at any detectable levels in the presence of cirrhosis (63,64,65). HBV DNA testing is necessary for patients receiving nucleos(t)ide analogs (NAs) in order to evaluate therapy response and direct treatment. A higher chance of therapeutic resistance is linked to the inability to suppress HBV DNA to undetectable levels by the sixth month of telbivudine and lamivudine treatment or by the twelve months of adefovir treatment (both of which have a low barrier to resistance). Consequently, it is typically advised to employ a stronger medication to which the virus is not resistant (63,64,65)

6.1.5 HBcrAg

One potential blood indicator of the active transcriptional activity of liver ccc DNA is HBcrAg. Higher HBcrAg levels may be linked to a higher risk of liver cancer in individuals receiving NA treatment or not. Thus, serum HBcrAg levels in NA-treated participants correlate with serum HBV DNA levels but not with serum HBsAg levels. The probability of hepatitis reactivation increases with the level of HBcrAg before discontinuing NA medication, suggesting that HBcrAg may play a part in residual viral replication during NA therapy (66,67,68,69).

6.2 POC Diagnostic

In places with limited resources, a quick point-of-care (POC) assay for HBsAg offers a tenable diagnostic approach. 49 quick POC assays were assessed in a recent meta-analysis that summarized the results of 27 investigations. Individual testing's reliability varied widely and was heterogeneous, ranging from 43.5% to 99.8%, despite a solid specificity that was nearly 100% (range: 90% to 100%). The three main variables that most consistently matched the estimations and the heterogeneity were the study score, study location, and reference standard. However, in the Gambia, a country in Western Africa, three POC assays for HBsAg were evaluated both in the field and in laboratories. However, in the Gambia, a country in Western Africa, three POC assays for HBsAg were evaluated both in the field and in laboratories. The range of sensitivity and specificity they discovered was 88.5% to 90.0% and 99.8% to 100% in the field, respectively, and 93.9% to 95.3% and 93.3% to 94.7% in the lab. (70,71).

6.3 New Molecular Marker and Genomic information

Additional tar gets for therapy to lower viral loads may be indicated by host genomic factors that disrupt the viral replication cycle in HBV.A promising single nucleotide polymorphism (SNP) that could suggest a virological response to peginterferon is interferon lambda 3 (IFN-λ3), formerly known as interleukin-28B (IL-28B), which produces a polymorphism in the human leukocyte antigen (HLA) locus. HBeAg seroconversion is frequently associated with another HLA gene, HLA-DPA1. Through the increase of IP-10 production, the G-201A allele in the promoter region of the interferon-inducible IP-10 gene has been reported to be associated with the progression of hepatic illness in Chinese Han hepatitis B patients(72,73,74,75) The HBV DNA level does not precisely reflect the amounts of viral ccc DNA, RNA, or antigen synthesis in the livers of treated patients since HBV DNA is suppressed to low levels in the majority of patients receiving NA therapy. The function of HBV RNA as a possible biomarker has been investigated by several teams. The majority of HBV RNA detected in serum is believed to be progenomes RNA because mRNA is unstable in serum. According to earlier research, measuring HBV RNA may assist predict HBeAg seroconversion in individuals on NA treatment (76,77)

6.4 Detection Method for Diagnosis of HBV Infection

Detection methods	Advantages	Clinical application
Polymerase chain reaction (PCR)	quick sensitive and particular	HBV-DNA directly detect in serum
Enzyme linked immunosolvent assay (ELISA)	High sensitivity and easy operation high specificity	Blood levels of HbsAg and other HBV serum marker are typically quantitatively detected
Time resolved fluor immunoassay (TRFIA)	Increased specificity low background and broader and linear range	Very little HbsAg was found in the serum
Radio immunoassay (RIA)	Excellent specificity and sensitivity	HbsAg, HbsAb, HbeAb, HbcAb can be identify
Chemi luminescent immunoassay (CLIA)	Easy to realize full automation and reduce human operation error strong specificity	Detection of HBV serum marker (including HbsAg anti-HbsAg, anti-HbeAg anti-HBe
Good immune chromatography assay (GICA)	Simple preservation that makes it possible to identify HbsAg in blood	GIVA was only suitable for the preliminary screening og HbsAg antigen positive individuals
Microparticle enzyme immunoassay (MEIA)	Extremely sensitive high specificity easy to use and ideal for reproducibility	Accept reference method for the quantitative determination of HBV serological marker

TABLE -1. Clinical application of detection method in HBV infection (26,27,28,29)

VII. ANTIVIRAL THERAPY FOR HBV

According to studies, antiviral therapy lowers the production of immune complexes and HBsAg levels by roughly 80% (78). Interferon-alpha and pegylated interferon-alpha, three nucleoside analogs (lamivudine, entecavir, and telbivudine), and two nucleotide analog prodrugs (adefovir dipivoxil and tenofovir disoproxil fumarate) are the seven medications approved by the US Food and Drug Administration (FDA) for the treatment of CHB (79,80).

7.1 Entecavir (ETV)

Chronic hepatitis B (CHB) and its associated nephropathies are commonly treated with entecavir, a strong and highly specific HBV reverse transcriptase inhibitor (81). The World Health Organization (WHO) guidelines for 2024 state that ETV is advised for individuals who need a high genetic barrier to resistance, especially those who are at risk for osteoporosis or renal insufficiency. Additionally, the guidelines advocate ETV as a first-line treatment for children and adolescents due to its safety and effectiveness (82). The low rate of resistance, which occurs in less than 1% of patients over a 5-year period, is a significant benefit of ETV [55]. This qualifies ETV as a viable long-term treatment option, particularly for individuals who need ongoing viral suppression. Regular monitoring of resistance mutations and HBV DNA levels makes it easier to identify resistance early and modify treatment in a timely manner. Another advantage of ETV is that it has less nephrotoxicity, which makes it ideal for people with chronic renal insufficiency. The majority of patients do not see a substantial decline in their renal function, and long-term follow-up rarely results in negative reaction (83,84). The great patient adherence to entecavir is a result of its once-daily dosage schedule and outstanding tolerability. According to studies, adherence rates for ETV treatment can reach 90.8%, which is much higher than the 83.9% seen with lamivudine (85,86).

7.2 Tenofovir

A powerful nucleotide reverse transcriptase inhibitor, tenofovir disoproxil fumarate (TDF) is frequently used to treat CHB, especially in individuals with HBV-associated nephropathy (87). Tenofovir is advised as a first-line treatment in the WHO's 2024 guidelines, particularly for those who are at risk of osteoporosis or renal impairment. Research has demonstrated that TDF can alleviate proteinuria and dramatically lower serum HBV DNA levels within 48 weeks of treatment (78). Tenofovir is preferable to lamivudine and other antiviral drugs because of its high genetic barrier to resistance, which results in a resistance rate of less than 1% during long-term therapy. Clinical evidence indicates no serious resistance difficulties, despite the fact that in vitro investigations have revealed mutations such as rt181T/V and rtN236T that may influence tenofovir sensitivity. However, long-term tenofovir treatment is linked to renal tubular injury risk, which can cause some individuals to have elevated serum creatinine and decreased serum phosphorus. TDF treatment resulted in an average eGFR reduction of 4.6 mL/min in a long-term follow-up study of 308 HBV patients treated within the US Veterans Affairs system, suggesting a possible adverse effect on renal function (88,89,90,91).

7.3 Lamivudine (LAM), telbivudine (LdT), and clevudine

One of the first nucleoside analogs to be used in the treatment of hepatitis B was lamivudine (LAM) .By preventing HBV reverse transcriptase activity, it lowers viral replication Lamivudine's high rate of resistance restricts its usefulness in long-term usage, despite its effectiveness in lowering viral load and improving clinical status About half of the participants in a three-year study developed resistance. Fatigue and minor gastrointestinal pain are among the rare adverse effects of LAM, which has a good safety record. For short-term usage, it is still helpful in individuals who need quick viral suppression and have low viral levels (92,93,94,95). An oral nucleoside analog with strong HBV DNA inhibition is telbivudine (LdT). Telbivudine reduced HBV DNA in HBV-GN individuals, and in certain cases, serum HBeAg was removed.But after the second year of treatment, resistance rates rise to 25%, and some patients may experience muscle toxicity, such as increased creatine kinase levels, which calls for careful observation (96,97,98,99). In addition, clevudine has strong HBV suppression and lower rates of resistance than LAM. However, the possibility of severe muscular toxicity from extended use, such as myalgia and muscle weakening, limits its use (100,101)

7.4 Adefovir dipivoxil (ADV)

Patients who are resistant to LAM are frequently treated with the nucleotide analog adefovir dipivoxil (ADV). Adefovir decreases viral replication by blocking HBV reverse transcriptase. At week 52 of a randomized experiment, ADV-treated subjects showed decreases in serum HBV DNA and increases in the percentage of subjects with an HBV DNA level of no more than 10(5) copies/mL, with HBV DNA undetectable, and with ALT normalization. Adefovir proved successful in lowering liver inflammation and fibrosis and regulating viral load in patients with LAM resistance (102,103).

7.5 Interferon therapy

The use of interferon (IFN) therapy to treat HBV-associated nephropathy is restricted. Interferons have some therapeutic potential for patients with HBV-GN because they work by boosting the host immune response to reduce HBV infectio. In order to potentially lessen immune complex accumulation in the kidneys, interferon therapy aims to inhibit viral replication and encourage the immune system to eradicate infected cells. According to certain research, interferon and nucleoside analogs were equally successful in resolving proteinuria and clearing HBeAg. Peginterferon alfa-2b, also known as Peg-IFN α-2b, has proven to be more effective than NAs in treating CHB, especially in individuals with low HBsAg levels. The Peg-IFN α-2b group's HBsAg clearance rate was a noteworthy 52.1% by week 24. Patients who are resistant to nucleos (t)ide analogs can benefit from interferons because they inhibit HBV replication by stimulating the host immune system, which gets around the resistance that direct antiviral drugs cause. However, there are serious side effects associated with interferon therapy, especially in patients who have HBV-related nephropathy. These adverse effects include hematological abnormalities (such as neutropenia, thrombocytopenia), flu-like symptoms (such as fever, weariness), and neuropsychiatric symptoms (such as anxiety, sadness (104,105,106,107,108).

Abbreviation

HbsAg: hepatitis B surface antigen
HbcAg; hepatitis B core antigen.
HbeAg: hepatitis B E antigen
HbcrAg: hepatitis B core related antigen
ALT: alanine transferase
HCC: hepatocellular carcinoma
Ccc DNA: Covalently closed circular DNA
Anti-HBC: hepatitis b core antibody
HAART: Highly active Antiretroviral Therapy

VIII. CONCLUSIONS

The hepadnaviral family includes the hepatitis B virus, which causes hepatitis and spreads through tainted blood or other bodily fluids. Approximately 240 million people worldwide have a chronic HBV infection, which leads to over 300,000 liver disease consequences such damage, cirrhosis, or liver cancer, which ultimately cause 68600 deaths. observed evidence of a decrease in HBsAg prevalence from 1990 to 2022, and this change is expected to accelerate in coming years as the population of pregnant women increasingly includes individuals born after implementation of the HBV infant vaccination. The genome of the hepatitis B virus (HBV) is a relaxed, partially double-stranded circular DNA molecule that is roughly 3.2 kilobases (kb) in size. It has an incomplete plus-strand and a full-length minus-strand. Clinical management and public health continue to face major obstacles due to HBV-associated nephropathy. The recurrence of renal problems in the face of efficient antiviral suppression, the lack of choices for resistant patients, and safety concerns in specific populations, such as pregnant women and people with renal impairment, are important biological obstacles.

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Conflict of interests

The authors declare no competing interests

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