Review

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A critical review of diagnostic and prognostic markers of chronic hepatitis B infection

https://doi.org/10.1515/mr-2024-0022
Received March 3, 2024; accepted April 19, 2024;
published online May 8, 2024

Abstract: A major worldwide health concern, chronic hepatitis B necessitates precise prognostic and diagnostic indicators for clinical guidance. This article highlights the clinical importance and current issues of the major markers used in both the detection and prognosis of chronic hepatitis B. An important indicator of an ongoing and persistent infection is the hepatitis B surface antigen. Hepatitis B virus DNA quantification monitoring aids in assessing viral load and hepatic cancer risk. While limited evidence of liver damage is provided by alanine aminotransferase levels, the hepatitis B core antibody verifies acute infection. Seroconversion to the hepatitis B e antibody is linked to a lower risk of disease development, and the hepatitis B e antigen status is a critical prognostic factor. Treatment choices are guided by a biopsy of the liver or minimally invasive liver fibrosis detection. Genotypes of the hepatitis B virus and host variables influence the prognosis by adding to the disease's variability. Noninvasive techniques to evaluate the severity of the disease are provided by serum markers of fibrosis, such as the fibrosis score based on four criteria and the aspartate aminotransferase-to-platelet ratio index. The requirement for indicators that distinguish between distinct viral phases and increase specificity in evaluating liver damage is one of the challenges facing chronic hepatitis B research. Even though it is quite difficult to find reliable biomarkers for resistance especially when it comes to hepatocellular cancer risk estimation, there are advanced methods, which include imaging and omics that can help in improving the accuracy of the diagnostics and prognosis. Interventions early point that improve patient outcomes are made possible using diagnostics and prognostics as they are quite effective in managing the complicated landscape of chronic hepatitis B. Key in addressing these challenges today and improving the diagnostic and prognostic markers in the future, particularly those that would support the development of successful treatment plans for people living with chronic hepatitis B virus (HBV), are scientific research, technological advances and collaborations.

Keywords: chronic hepatitis; prognostic scores; seromarkers; surrogate markers

Introduction

The chronic hepatitis B infection epidemiology reveals that it is a major global public health concern. About 400 million people are currently infected with the hepatitis B virus (HBV), and about 2 billion individuals have antibody evidence of exposure to the virus [1]. According to prevalence surveys, the prevalence of HBV infections is 2.5 % worldwide on average, with a recent decline in the frequency of acute infections with HBV and HBV-induced cirrhosis [2]. According to retrospective cohort analysis, different nations have different rates of chronic HBV infection; Africa south of the Sahara and Southeast Asia as a whole has greater rates [3, 4]. Comparable overall estimates of global prevalence have been produced by many sources; however, estimates for some populations, like children under five and nations in sub-Saharan Africa, differ [5]. A major worldwide health concern is chronic hepatitis B (CHB) infection which is the persistence of HBV in the body for six months or longer, and has significant effects on morbidity and death [6]. It is essential to comprehend the prognostic and diagnostic markers to implement and treat patients effectively. Hepatitis B surface antigens (HBsAg), are antibodies that are generated by the immune system in response to the hepatitis B surface antigen, regardless of whether it was acquired through a previous infection or vaccination. The detection of anti-HBs following vaccination serves as

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confirmation of successful immunization against hepatitis B [7]. However, its inability to distinguish between cured and chronic infections makes additional markers necessary. HBV DNA quantification sheds light on the virus's replication levels [8]. Elevated viral loads are linked to a heightened risk of transmission and acceleration of the disease. Determining the ideal intervention threshold and the importance of low-level viral infection in the dearth of liver disease presents difficulties, though. Conversely, the confirmation of acute infection is aided by the existence of hepatitis B core antibody (Anti-HBc) an antigen that is located on the inner core of the hepatitis B virus. It is not present in the bloodstream, but its presence can be detected in liver tissue during a biopsy, and its detection of HBcAg indicates active viral replication and ongoing liver damage, specifically its IgM version [9]. This is important when there is persistent active infection even though HBsAg may be negative. Its function in forecasting the course of an illness is less clear, though.

The degree of HBV replication is reflected in the predictive value of the hepatitis B e antigen (HBeAg) status which is a protein associated with the active replication of the hepatitis B virus. Its presence indicates high levels of viral replication and increased infectivity. The detection of HBeAg is typically associated with a high viral load and a higher risk of transmission [10, 11]. A decreased risk of liver disease development is linked to seroconversion to anti-HBe and seroclearance of HBeAg [12]. It is not without difficulties to anticipate the course and results of HBeAg seroconversion, though. Similarly, fibrosis score based on four components (FIB-4) and aspartate aminotransferase-to-platelet ratio index (APRI), two non-invasive blood markers, offer a practical way to measure liver fibrosis [13]. However, more improvement is necessary before they can be widely used in clinical settings because their accuracy varies depending on the environment. To enhance clinical management strategies and deepen our understanding, it is essential to integrate different markers, leverage advanced technologies, and address the limitations of our current prognostic and diagnostic methods. To address the changing problems presented by CHB, the scientific community must foster research and collaboration. Here, we conduct a critical assessment of the prognostic and diagnostic indicators available for CHB, looking at their advantages, disadvantages, and the field's changing body of research.

Diagnostic markers

These diagnostic markers and other laboratory tests, such as liver function tests and HBV DNA quantification are utilized to diagnose HBV infection, stage disease activity, monitor the response to therapy and guide patient management, as outlined in Table 1. Early detection and monitoring using these markers is important to facilitate effective patient management and prevent complications associated with HBV infection.

Surface antigen of hepatitis B

One important diagnostic indicator for hepatitis B infection is HBsAg. Its presence confirms the diagnosis of persistent infection and points to ongoing viral replication. When diagnosing CHB infection, HBsAg is a useful diagnostic tool. It is advised for CHB patient diagnosis and follow-up [14]. During an HBV infection, HBsAg is generated in excess and released into the blood, acting as a signal for infectivity and active infection [15]. To determine the treatment prognosis and HBV chronicity, quantitative HBsAg (qHBsAg) quantification is crucial [16]. For HBV e antigen-positive patients only, there is no significant association found between qHBsAg and HBV DNA levels [17]. One plausible therapeutic objective in the management of CHB is HBsAg seroclearance, which is linked to lower qHBsAg levels [18]. Nevertheless, because HBsAg seroclearance occurs at a low yearly rate, attempts are being made to increase it and use biomarkers like qHBsAg to forecast it early. In summary, qHBsAg can offer extra information for evaluating the course of the disease and the effectiveness of treatment, while HBsAg is a valuable diagnostic marker for CHB infection. There are restrictions on the use of HBsAg as a diagnostic marker for persistent hepatitis B infection. One disadvantage is that HBsAg can be detected in both acute and chronic infections, making it impossible to differentiate between the two [15]. Another drawback is that heterophilic antibody interference might cause HBsAg seropositivity to be a false-positive result, which could result in a misdiagnosis [16]. Furthermore, the illness stage may affect the efficacy of HBsAg as a diagnostic sign. A study indicated that the late cohort had a poorer sensitivity of HBsAg in predicting severe hepatitis activity than the early cohort [18]. As a result, although HBsAg is a useful marker for detecting the hepatitis B virus, its limitations should be taken into account. Furthermore, further testing might be required to accurately diagnose and treat CHB infection.

HBV DNA quantification

Assessing the level of viral replication in the blood requires quantifying the HBV DNA. A greater risk of progression of disease and transmission is linked to higher viral loads.

Table 1: Overview of markers and parameters used to diagnose and monitor HBV infection and when to select which marker.

Items	HBsAg	HBsAb	HBcAg	HBeAg	HBeAb	HBV DNA	Liver function tests
Indicates	Active infection	Immunity	Active infection	Active infection	Decrease viral load	Confirmation of the viral presence	Evaluate liver health and function
Diagnostic use	Screening for infection, monitoring treatment response	Confirming immunity, post-vaccination	Identifying active viral replication, liver biopsy	Assessing infectivity, treatment guidance	Assessing decreased viral replication, disease progression	Quantifying viral load helps in treatment decision-making	Assesses liver damage and inflammation
Clinical significance	Indicates active HBV infection, transmission risk	Confirms immunity, vaccine response	Indicates active viral replication, liver damage	Indicates high infectivity, potential for transmission	Suggests reduced infectivity, lower risk of transmission	Monitoring disease progression	Evaluate liver health and function
When to choose	Initial screening for hepatitis B infection	Screening for immunity against hepatitis B	Evaluation of liver pathology in suspected cases of hepatitis B	Monitoring disease progression and infectivity	Monitoring disease progression	Assessing response to treatment, and predicting the risk of liver disease progression	Monitoring liver health and disease progression
Interpretation	Positive indicates active HBV infection	Positive indicates immunity to HBV	Not routinely measured in blood	Positive indicates active viral replication and infectivity	Positive indicates immunity to HBV	Abnormal results may indicate liver damage or disease	High levels indicate active viral replication and low levels may indicate viral suppression

As diagnostic indicators for chronic HBV infection, HBV DNA levels have significant clinical ramifications. It can be used to ascertain the infection's phase, evaluate the effectiveness and duration of therapy, and provide guidance for the safe cessation of antiviral medication with a decreased risk of recurrence [19]. Elevated HBV DNA levels are a major risk factor for the emergence of serious long-term consequences and the advancement of chronic HBV infection, which is why HBV DNA levels are also linked to the progression of the disease [20]. Furthermore, in untreated HBV-infected patients, HBV DNA levels may indicate natural illness phases, emphasising the need for clinical management techniques and liver inflammation [21]. HBV DNA quantification can assist in clinically classifying CHB patients and directing treatment choices in addition to other clinical markers such as HBsAg levels [22]. In general, the levels of HBV DNA offer significant insights into the diagnosis, treatment, and outlook of persistent HBV infection. One of the possible drawbacks of utilising HBV DNA levels as markers of diagnosis is that they may not be able to identify viral genome mutations that lead to diagnostic escape [23]. Moreover, low antigen titres in research samples may cause the viral burden to be underestimated [24]. Developing highly homologous oligonucleotide sets for quantitative PCR assays is difficult due to the significant genetic variability of the virus, which can lead to lower primer/probe affinity for binding and misdetection of some HBV variants [25]. Another major obstacle to expanding HBV diagnostic services is the restricted availability of nucleic acid testing (NAT) to measure HBV DNA levels in nations with limited resources [26]. Liver histology, the most commonly used method for HBV diagnosis, is non-standardized and invasive, which can make it unfeasible [27]. The sporadic reproduction of HBV in individuals with hidden HBV infection and the sensitivity limitations of serological testing add to the inaccuracy of these tests for diagnosing HBV infection.

Antibody to hepatitis B core

Anti-HBc, or the hepatitis B core antibody, is frequently used to diagnose or confirm hepatitis B infection. It could be IgM, which denotes an acute infection, or IgG, which denotes a persistent or healed illness. When diagnosing CHB infection, anti-HBc is essential. Mostly present throughout life, it is a highly immunogenic particle antigen that first occurs in the early stages of infection [28]. It has been demonstrated that liver pathology, the prognosis of the disease, and HBV-related hepatitis activity are correlated with quantitative anti-HBc (qAnti-HBc) levels [29, 30]. In addition to

predicting therapy response and providing a prognosis for the disease, qAnti-HBc can distinguish between distinct phases of CHB [31]. It is also linked to the inflammatory condition of the host liver and the immunological activation associated with HBV infection [32, 33]. The diagnostic and prognostic potential of qAnti-HBc can be increased by combining it with other diagnostic indicators including HBV DNA, HBeAg, qHBsAg, and anti-HBs antibodies. Better treatment outcomes, such as HBeAg loss, prolonged response, and HBsAg reduction or clearance, are linked to higher levels of anti-HBc. Anti-HBc is a useful marker for identifying and tracking CHB infection as a result. The potential of Anti-HBc as a non-invasive biomarker for forecasting clinical outcomes and treatment success is one of the prospects for the use of HBcAb in the detection of CHB infection [28, 34]. Promising correlations have been found between HBcAb quantification (qAnti-HBc) and infection phases, hepatic fibrosis and inflammatory levels, flare-ups throughout chronic infection, and the existence of occult infection [29, 35]. Additionally, it is predictive of recurrence following medication cessation, viral reactivation upon immunosuppression, re-infection following liver transplantation, and spontaneous or treatment-induced seroclearance of HBeAg and HBsAg [36]. Nevertheless, qAnti-HBc should not be used as a stand-alone diagnostic test; in fact, when paired with other biomarkers including HBV DNA, HBeAg, qHBsAg, and anti-HBs antibodies, its diagnostic and prognostic potential can be increased [37]. Standardisation of cut-off values is required for improved result comparison, and getting hold of commercially available qAnti-HBc test kits needs to be improved [14, 38]. The following are the restrictions on the use of anti-HBc in the diagnosis of CHB infection. (1) Since anti-HBc can also be seen in people with cured or occult hepatitis B infection, it is not a reliable indicator of CHB infection [29]. (2) Anti-HBs antibodies, HBV DNA, HBeAg, qHBsAg, and other indicators can enhance the diagnostic efficacy of anti-HBc [9]. (3) There is a need to increase the accessibility of commercial diagnostic kits for measuring anti-HBc [32]. (4) The use of semi-quantitative methodologies impedes the ability to compare data from various investigations and create standard cut-off values for anti-HBc. Finally, those with “anti-HBc only” status may be at risk for reactivation. Anti-HBc alone does not suggest immunological control of HBV.

Aminotransferase alanine

As indicated in Table 2, elevated alanine transaminase (ALT) levels are indicative of liver inflammation and are used to gauge the severity of liver disease. Normal ALT values do not, however, rule out serious liver disorders in CHB patients. In individuals with CHB infection, ALT levels are crucial biomarkers for the development of the disease [39]. High ALT and HBV DNA levels are important risk factors for the development of CHB infection and are linked to dangerous long-term consequences [40]. Hepatic cancer, cirrhotic events, and death can still be risks for patients with normal or slightly elevated ALT levels [41]. Antiviral therapy is advised by the most recent Chinese guidelines for CHB patients who have identifiable HBV DNA and consistently have ALT levels over the threshold of normal [42]. On the other hand, new research has demonstrated that liver biopsies from HBeAg-negative individuals who consistently have normal ALT levels may exhibit severe inflammation and fibrosis. As a result, there is disagreement regarding whether these individuals should begin antiviral therapy. Antiviral therapy has been proposed as a potential treatment for CHB patients who have normal or slightly elevated ALT levels, particularly those who underwent interferon-based treatment. It is crucial to remember that ALT levels might change over time and that the degree of liver damage or the course of the disease may not be completely captured by a single measurement. Furthermore, for a thorough evaluation of CHB infection, ALT levels need to be analysed together with other clinical indicators and diagnostic testing. Acute liver inflammation and damage are indicated by a substantial rise in ALT values. It is frequently seen in patients with severe hepatic disease, like cirrhosis or hepatocellular carcinoma, who have a CHB infection.

Table 2: Illustrate various interpretations of alanine transaminase related to hepatitis B infection.

ALT levels, IU/L	Interpretation
Normal (≤30 for men, ≤19 for women)	ALT levels within the normal range suggest the absence of significant liver inflammation or injury.
Mildly elevated (31–100)	Mild elevation in ALT levels may indicate minor liver inflammation and can be seen in chronic hepatitis B infection with minimal or moderate liver damage.
Moderately elevated (101–200)	Moderate elevation in ALT levels suggests more significant liver inflammation and injury. It is commonly seen in chronic hepatitis B infection with moderate liver damage.
Markedly elevated (>200)	Marked elevation in ALT levels indicates severe liver inflammation and injury. It is often observed in chronic hepatitis B infection with advanced liver disease, such as cirrhosis or hepatocellular carcinoma.

Prognostic markers

The significance of these prognostic markers in risk stratification, disease monitoring, and treatment decision-making for patients with chronic hepatitis B infection is illustrated in Figure 1. It is essential to regularly monitor and assess their levels to ensure optimal patient care and improve clinical outcomes. Examples of these markers include.

Non-invasive testing and liver biopsy

Predicting the course of liver disease can be aided by measuring liver inflammation and fibrosis using a tissue sample from the liver or non-invasive testing methods like FibroScan. The prognosis of a CHB infection can be predicted more accurately by non-invasive diagnostics than by liver biopsy. The prognostic efficacy of liver biopsy and non-invasive testing in determining the prognosis of chronic liver disease has been assessed. Because liver biopsy is invasive and has limits, non-invasive fibrosis markers have become popular as an alternative to the procedure [43]. To predict the severity of chronic liver disorders, such as hepatitis C virus (HCV) and non-alcoholic fatty liver disease (NAFLD)/non-alcoholic steatohepatitis (NASH), several tissues and circulating markers of angiogenesis have been studied [44]. Several non-invasive fibrosis markers have been assessed for biopsy findings in patients with CHB [45]. These markers include the Goteburg University cirrhosis index (GUCI), Hui score, AST platelet ratio index (APRI), AST ALT ratio (AAR), and fibrosis four scores (FIB-4). Despite the increased use of non-invasive techniques, liver biopsies remain the most common method for grading and grading several chronic liver disorders [46].

Guidelines on the use of non-invasive tests have been published by the European Association for the Study of the Liver [47], emphasising their value in diagnosing and classifying chronic liver disease. Numerous studies have demonstrated the accuracy with which non-invasive models, such as the FIB-4 and APRI indices [45], the ALT, Age, PLT, and LS model [48], the AAR, API, APRI, KING, Zeugma scores, and Hudu's score [49, 50], can evaluate liver histology and forecast substantial liver injury. It has been discovered that these non-invasive models exhibit remarkable accuracy, with values of the area under the curve ranging from 0.595 to 0.870 [51, 52]. They can assist in determining whether antiviral therapy is necessary without requiring an invasive biopsy of the liver, which carries some risk. Though these non-invasive diagnostics have shown potential, it needs to be noted that they ought to be employed together with clinical judgement as they could still not be able to replace liver biopsy. The conventional approach to determining the prognosis of CHB infection involves liver biopsy; however, there are several drawbacks to this method, including cost, potential problems, and invasiveness [45, 48, 49]. An alternate method that has benefits including becoming kinder to the body, safer, and more economical is to use non-invasive diagnostics [51, 52]. To forecast liver histological alterations and fibrosis in CHB patients, several non-invasive models were created utilising various indicators [53–55]. With no requirement for a liver biopsy, these models have demonstrated encouraging outcomes in precisely evaluating liver histology and forecasting the requirement for antiviral medication. Though these non-invasive procedures have demonstrated high diagnostic performance, it is crucial to remember that they might not always be able to fully replace liver biopsy. To ascertain the best application and constraints of non-invasive testing in assessing the likelihood of CHB infection, more investigation and validation are required.

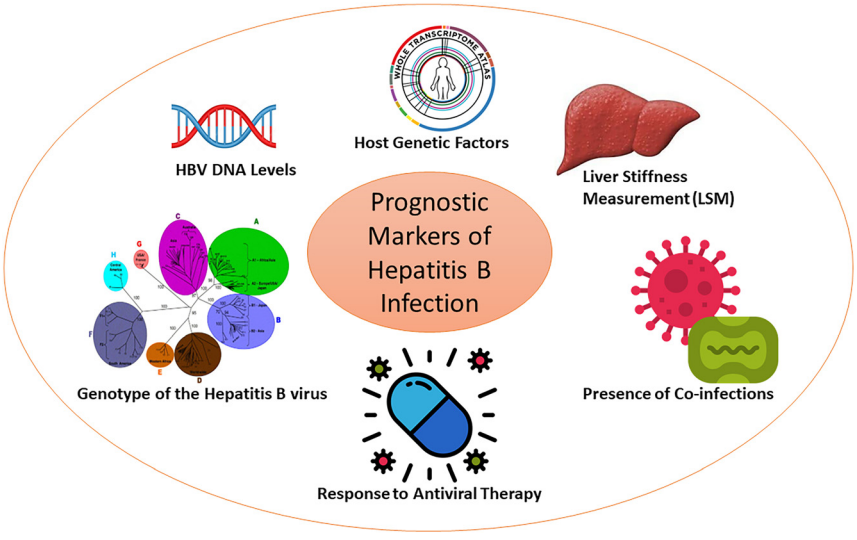

Figure 1: Illustrate prognostic markers commonly used in hepatitis B infection.

Antigen for hepatitis B e

The presence of HBeAg is a significant predictive factor [10]. Patients who test positive for HBeAg are more likely to have increased infectivity and active viral replication (Table 1). An inverse relationship exists between the advancement of liver disease and HBeAg seroconversion to anti-HBe. A predictive marker for CHB infection is thought to be HBeAg [10]. High replication of viruses and enhanced contagiousness are linked to it [15]. Research has demonstrated a correlation between HBeAg seropositivity and more advanced phases of liver fibrosis, such as cirrhosis, severe fibrosis, and substantial fibrosis [56]. Furthermore, there is a correlation between HBV DNA viral load and HBeAg status, whereby individuals who test positive for HBV DNA have higher quantities of HBV circulating DNA [10, 57]. HBeAg seroconversion, however, was not discovered to be connected to liver function tests, transmission routes, chronicity duration, marriage history, gender, or age [58]. In general, HBeAg can be utilised as a marker to forecast the severity and course of a CHB infection, especially when it comes to fibrosis of the liver and viral load [12]. Regarding the prospects of CHB infection, HBeAg is a major factor. Its presence is connected to increased levels of HBV serum DNA and is linked to enhanced replication of viruses and infectivity [58]. Loss of HBeAg, or HBeAg seroconversion, is a sign of either the reactive or inactive stages of CHB [59]. Further research is needed to fully understand the relationship between HBeAg seroconversion and various factors, such as liver function tests, mode of transmission, duration of chronicity, marital status, gender, and age [60]. Lower levels of HBsAg are linked to a higher likelihood of a sustained response in HBeAg-negative individuals. The level of HBsAg after completion of treatment can be used to predict prolonged off-treatment response [61]. Furthermore, in HBeAg-positive patients, the degree of hepatitis B core-related antigen (HBcrAg) helps forecast the clinical phase and response to treatment [62]. In patients with CHB infection, HBeAg level is an indicator of disease progression. HBeAg-negative individuals may be in an inactive or aggressive phase of the disease, whereas HBeAg-positive patients have increased replication of viruses and infectivity [63]. A better prognosis is linked to HBeAg seroconversion, which is a significant treatment outcome where HBeAg turns negative [58]. HBeAg seroconversion is predicted by HBcrAg levels at the beginning and two years following antiviral medication, where lower levels are linked to a higher chance of seroconversion [64]. In HBeAg-negative individuals, HBsAg levels at the end of therapy can also predict a persistent off-treatment response; lower levels are linked to a decreased likelihood of virological resurgence [59]. HBV DNA levels and quantitative HBsAg have different capacities for defining the natural history stages of long-term HBV infection [18].

Genotype of the hepatitis B virus

Variations in HBV genotype can affect how an antiviral treatment works and how quickly the disease progresses. For instance, in certain groups, genotype C is linked to an increased risk of hepatocellular cancer (HCC). Table 3 illustrates that the HBV genotype does not seem to have a substantial impact on the clinical manifestations of hepatitis B patients [65]. Numerous investigations have demonstrated that there is no meaningful correlation between HBV genomes and clinical characteristics such as liver histology, ALT levels, liver fibrosis, and HBeAg status [66, 67]. Nonetheless, some research has indicated that a greater viral load may be linked to specific HBV genotypes [68]. Furthermore, a study discovered that HBV genotypes can affect the longitudinal HBsAg serodecline and the extent of HBsAg seroclearance, indicating a potential interaction between HBV genotype and HLA variations [69]. In general, further investigation is required to precisely ascertain the influence of the HBV genome on the clinical progression of hepatitis B. The given abstracts don't seem to specifically address the HBV genotype. The relevance of HBV mutations and HLA genes in the risk of hepatocellular carcinoma (HCC) is covered in the abstracts, nevertheless. According to one study, there is a correlation between a higher risk of HCC and HBV mutations at the core promoter region, namely A1762T/G1764A, C1653T, and T1753V [70]. An elevated risk of HBV-related HCC was found to be significantly correlated with an HLA gene haplotype that is common in Asian populations [71]. Furthermore, an uncommon signal within the CDK14 gene was found to be associated with the prognosis and susceptibility of HBV-related HCC by a genome-wide association investigation [72]. Although the HBV genotype alone might not be a reliable indicator of the likelihood of developing HCC, these results imply that HBV mutations and HLA genes might influence an individual's susceptibility to HCC in those with HBV infection. The HBV genotype is not a reliable indicator of HBV infection. The levels of HBV DNA do not exhibit significant variations based on the HBV genotype. Nevertheless, the levels of qHBsAg, which serve as prognostic indicators, are subject to influence. To ensure proper interpretation, genotype-specific cut-off levels must be established, as different genotypes exhibit variances in qHBsAg levels [73]. HBV DNA and qHBsAg levels can also be impacted by mutations in the preCore, basal core promoter, and preS sections of the HBV genome [74]. These alterations

Table 3: Summarized the association between HBV genotypes and their prognostic implications in chronic hepatitis B infection.

Hepatitis B genotype	Prognostic implications
Genotype A	It is generally associated with mild liver disease progression and responds well to antiviral therapy.
Genotype B	It is typically associated with mild to moderate liver disease progression and is generally responsive to antiviral treatment.
Genotype C	It is associated with more severe liver disease progression, including higher rates of liver cirrhosis and hepatocellular carcinoma. It also tends to have lower response rates to antiviral therapy, especially with certain medications.
Genotype D	Similar to genotype C, associated with more severe liver disease progression, higher rates of liver cirrhosis, and hepatocellular carcinoma and response to antiviral therapy may vary depending on the specific drug regimen.
Genotype E	Limited data is available on the prognostic implications and believed to have a relatively mild disease course similar to genotypes A and B.
Genotype F	Predominantly found in South America. Prognostic implications are still being studied, but they may be associated with more severe disease progression.
Genotype G	Prognostic implications are not well-established. Limited data suggests it may have a similar disease course to genotypes A and B.
Genotype H	Found primarily in Central America. Prognostic implications are still being investigated, but it may be associated with more severe liver disease.

can impact the virus's ability to replicate and release HBsAg, and they are genotype-dependent [75]. As such, using the HBV genotype alone for prognostication may not yield reliable findings; instead, a thorough evaluation of HBV infection necessitates taking into account the effects of certain mutations and qHBsAg levels [76].

Challenges and future directions

Chronic hepatitis B (CHB) infection is a major global health concern that impacts millions of people globally. Even with improvements in diagnosis and treatment, correctly identifying and forecasting CHB is still difficult. This essay examines the difficulties that exist now with CHB diagnostic and prognostic markers and offers possible solutions for the future. Results from CHB diagnostic tests can be inconsistent due to wide variations in test accuracy. The diagnostic procedure can become more difficult when disparate assays yield contradicting results. The sensitivity and specificity of current diagnostic markers may be insufficient for the timely identification and precise diagnosis of CHB. This restriction may raise the chance of illness progression and postpone necessary action. It might be difficult to obtain diagnostic tests, especially in environments with low resources. The prompt identification and treatment of CHB are hampered by the absence of readily available, reasonably priced point-of-care testing.

It is still difficult to identify people who are at risk of developing severe liver disease or hepatocellular carcinoma (HCC) from chronic hepatitis B. Patients may not be appropriately stratified according to their risk profile by current prognostic markers, which could result in less-than-ideal therapeutic approaches. The dynamic nature of CHB infection is typified by changes in liver enzyme levels, viral load, and histological characteristics throughout time. For prognostic markers to reliably predict illness outcomes, they need to take these dynamic changes into account. The predicted accuracy of prognostic models can be increased by incorporating several biomarkers. On the other hand, determining which biomarkers are most pertinent and developing standard operating procedures for their evaluation present formidable obstacles. To find new biomarkers with better specificity, sensitivity, and predictive accuracy for CHB evaluation and prognosis, more study is required. The fields of proteomics, metabolomics, and genomics are examples of omics technology advancements that have the potential to identify novel biomarkers. Large datasets can be analysed by artificial intelligence techniques, such as machine learning as well as deep learning algorithms, to find associations and trends that might not be obvious to human researchers. The accuracy and dependability of diagnostic and prognostic algorithms may be improved by including AI. Technological advancements in point-of-care testing have the potential to enhance accessibility to diagnostic services, especially in underprivileged areas. For the early diagnosis and treatment of CHB, portable, reasonably priced testing instruments with good sensitivity and specificity for viral indicators are crucial. The accuracy of CHB diagnosis and prognosis can be increased by implementing personalised medicine techniques based on unique patient factors, such as familial susceptibility and viral genotype. Customising treatment plans to meet the specific needs of every patient can improve therapeutic results and reduce side effects. Innovative technology, multidisciplinary teamwork, and persistent research are needed to address the problems with CHB infection diagnostic and prognostic markers. Enhanced patient outcomes and disease control methods are anticipated in the long run for CHB prognosis and diagnosis through the development of new biomarkers,

the use of artificial intelligence, the advancement of point-of-care testing, and the adoption of personalised medicine approaches.

Conclusions

In conclusion, this critical review underscores the intricacies of both diagnostic and prognostic markers in chronic hepatitis B infection. While significant progress has been achieved regarding the identification of biomarkers to assist in making the diagnosis as well as to predict outcomes, several hurdles remain, which include the various assay techniques, the non-standardized assays, and the dynamic evolution in the natural history of the disease. Moving forward, progress must be combined with interdisciplinary teamwork, further research, and advancements in technology to augment the precision and validity of these markers. A personalized approach considering individual patient characteristics and the evolution of the disease is likely to be most fruitful for the optimal management of this condition and, particularly, its results in the years ahead.

Acknowledgements: The authors of this article would like to express their profound appreciation to Zarqa University for providing crucial assistance in publishing this study.
Research ethics: Not applicable.
Informed consent: Not applicable.
Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Competing interests: Authors state no conflict of interest.
Research funding: None declared.
Data availability: Not applicable.

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