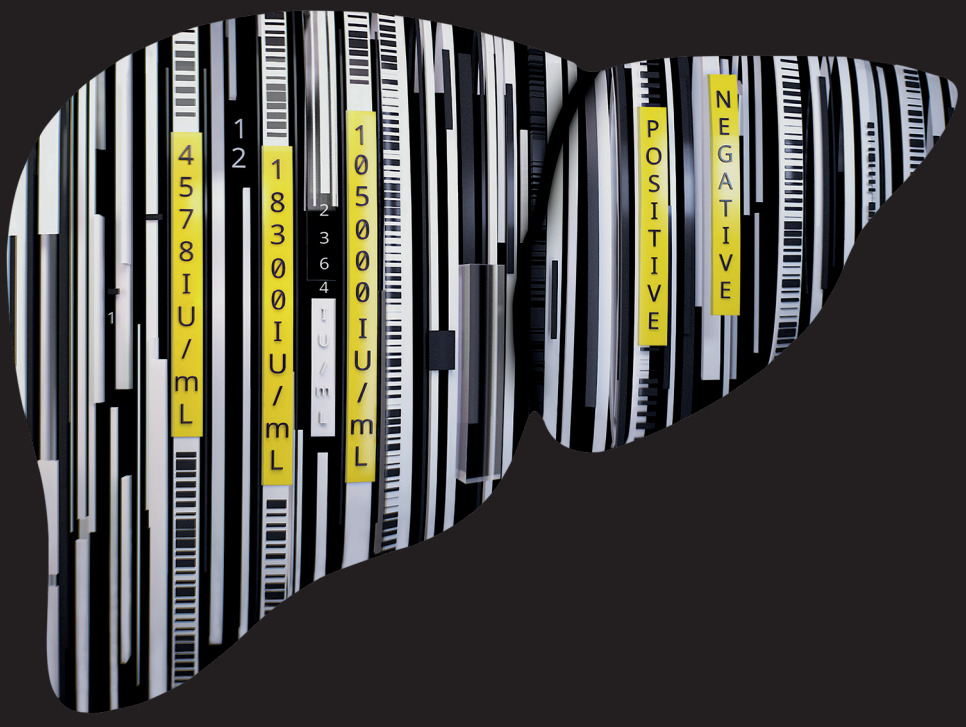

Chronic Hepatitis B (CHB)

KNOW IT BY THE NUMBERS

Your guide to comprehensive biomarker testing, including quantitative and qualitative HBsAg, for more informed clinical decisions.[1-4]

Visit KnowHepBTesting.com to know the complete picture

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Comprehensive biomarker testing may offer more clinical insights[5,6]

Real-world monitoring practices may diverge from the guideline recommendations for chronic hepatitis B (CHB)

MONITORING OF PATIENTS NOT ON TREATMENT	MONITORING OF PATIENTS ON TREATMENT	ADHERENCE TO MONITORING AND FOLLOW-UP CARE
~50% did not receive ALT and either HBV DNA or HBeAg testing within 12 months of CHB diagnosis[7]	>60% did not receive ALT + HBV DNA testing after antiviral treatment initiation[8]	40%–53% of Asian-American patients with CHB adhered to monitoring and follow-up care, which is notably low because, despite making up 6% of the US population, Asian Americans account for 58% of Americans living with CHB[9]

Insufficient biomarker testing and subsequent delay in treatment initiation can increase the risk of disease progression and serious liver-related outcomes.[10-14]

CHB may lead to cirrhosis, liver failure, or HCC in **15%–40%** of patients.[10,15]

Persistent viremia due to inadequate monitoring and lack of treatment adjustment contributes to **ongoing liver injury and fibrosis progression.**[12-14]

In 2022, HBV-related cirrhosis or HCC caused an estimated **1.1 million deaths globally.**[11]

ALT=alanine aminotransferase; DNA=deoxyribonucleic acid; HBeAg=hepatitis B e-antigen; HBV=hepatitis B virus; HCC=hepatocellular carcinoma.

Emerging biomarkers may reveal clinical insights that complement AASLD guidelines[13]

AASLD recommendations are based on HBeAg, HBV DNA, and ALT levels[13]

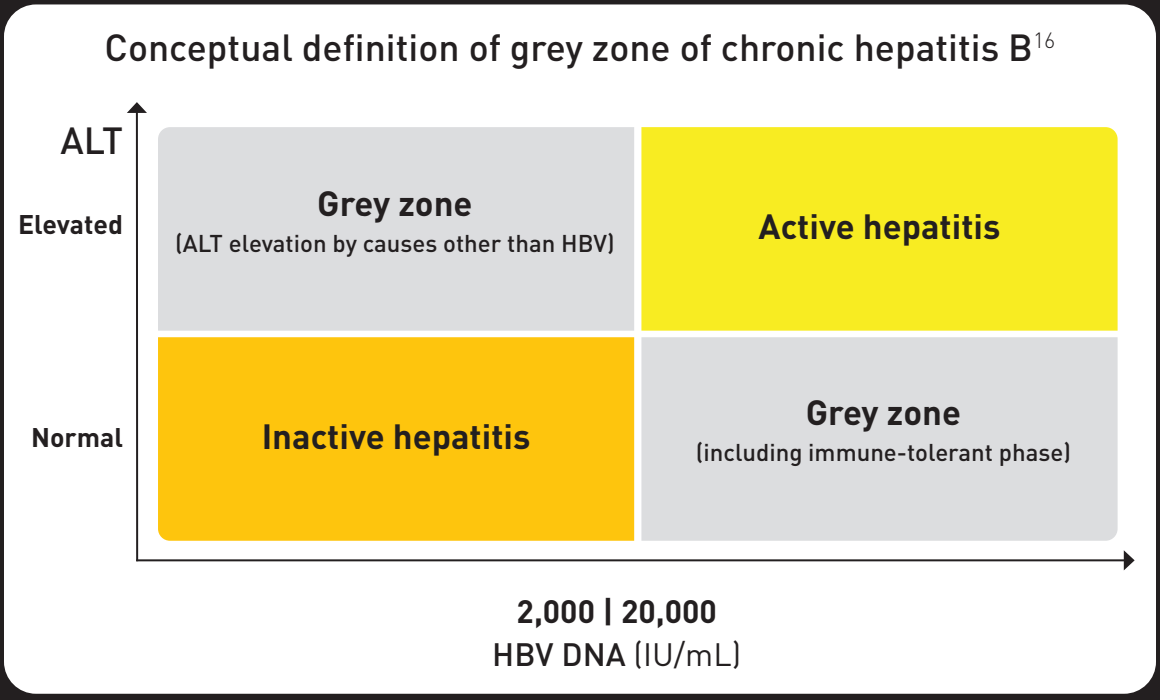

Figure used with permission. © 2024 Lim YS. Grey zone of hepatitis B virus infection. *Saudi J Gastroenterol.* 2024;30(2):76-82. https://journals.lww.com/sjga/fulltext/2024/30020/gray_zone_of_hepatitis_b_virus_infection.2.aspx

28%–55% of patients with CHB are viremic, but fall into a "grey zone" without clear guidance on optimal management and treatment. The "grey zone" refers to patients who are HBeAg-positive or -negative with HBV DNA levels and/or ALT levels outside those with immune-tolerant, immune-active, or inactive CHB.[17,18]

- Quantitative HBsAg testing is an emerging biomarker gaining traction in international guidelines (EASL, CASL) due to its predictive and prognostic value, but it remains underutilized in US practice[19-21]

Quantitative HBsAg testing can help guide management of "grey zone" patients.[13]

AASLD=American Association for the Study of Liver Diseases; CASL=Canadian Association for the Study of the Liver; EASL=European Association for the Study of the Liver; HBsAg=hepatitis B surface antigen.

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Comprehensive testing with key biomarkers allows for more clarity in chronic hepatitis B (CHB)[13,17,19,20]

This clarity supports characterization of disease phase and severity, assessment of patient prognosis, and evaluation of treatment response

KEY BIOMARKERS				
HBV DNA	Quantitative HBsAg	Qualitative HBsAg	HBeAg	Anti-HBe antibodies

Full hepatic function panel:

ALT, AST, total bilirubin +/– direct bilirubin, alkaline phosphatase, and albumin[1]

Noninvasive tests of fibrosis:

Serum APRI or FIB-4,* and elastography (vibration-controlled transient elastography, ultrasound, or MRI)[1]

For both cirrhotic and noncirrhotic patients, include HCC surveillance with ultrasound and alpha-fetoprotein.[13,19]

*APRI and FIB-4 are formulaic tools to help determine stage of fibrosis and assess risk for liver-related morbidity and mortality.[22]

Anti-HBe=anti–hepatitis B e-antigen; APRI=aspartate aminotransferase to platelet ratio index; AST=aspartate aminotransferase; FIB-4=fibrosis-4; MRI=magnetic resonance imaging.

KEY BIOMARKER: Quantitative and qualitative HBsAg testing

HBsAg testing in the management of CHB

- HBsAg is a viral surface protein and an important marker of active chronic HBV infection[2]
- It is a measure of the total transcriptional activity of both covalently closed circular DNA (cccDNA) and integrated HBV DNA in liver cells[23]
- HBsAg is believed to promote immune evasion and disease chronicity[23]

HBsAg tests for CHB:

Qualitative HBsAg	Quantitative HBsAg
Detects only presence or absence of HBsAg in serum via standard immunoassays (eg, ELISA, CLIA)[23,24]	Measures serum concentration of HBsAg in IU/mL via automated immunoassay[3,19]
Clinical utility[1,13,24]: • Initial diagnosis of HBV and screening for at-risk individuals • Cannot inform disease activity, treatment response, or prognosis, except in rare cases of HBsAg loss	Clinical utility[24]: • Quantitative HBsAg testing may help deliver more comprehensive evaluation—informing prognosis, treatment decisions, and tracking progress toward functional cure*

*Functional cure is defined as sustained loss of HBsAg (<0.05 IU/mL) and undetectable HBV DNA (<10 IU/mL), maintained for 6 months post–treatment cessation.[19,24]

CLIA=chemiluminescence immunoassay; ELISA=enzyme-linked immunosorbent assay.

Clinical utility of quantitative HBsAg

Quantitative HBsAg (qHBsAg) may help inform clinical decisions

Inform treatment eligibility[13]

- Support shared decision-making and guide treatment decisions in HBeAg-negative grey-zone patients
- Identify true inactive HBV carriers and those at risk of disease progression

Monitor treatment response and cessation[17,19,24]

- Help assess progress toward functional cure
- Support decisions on NA cessation

Provide prognostic value[13]

- Evaluate probability of spontaneous HBsAg loss
- Predict risk of liver fibrosis and HCC

Quantitative HBsAg and its interpretation

qHBsAg	Interpretation	Cirrhosis risk[24]	HCC risk[24]
Below reference (<100 IU/mL)	**Suggests inactive chronic hepatitis B (CHB)**[13,25] • Risk of viral relapse reduced, varying by ethnicity • Increases the specificity of identifying patients with inactive CHB, but reduces sensitivity to 35%	HR 1 (reference)	HR 1 (reference)
Low (100–<1,000 IU/mL)	**Suggests inactive CHB**[13] • May predict spontaneous HBsAg clearance in HBeAg-negative patients with a low viral load • May require less frequent monitoring	HR 1.96	HR 3.2
Elevated (≥1,000 IU/mL)	**Elevated risk of cirrhosis and HCC**[24]	HR 3.5	HR 5.4

HR=hazard ratio; NA=nucleos(t)ide analog.

HBsAg loss may be associated with improved clinical outcomes[19,26,27]

Two studies examined the relationship between HBsAg loss and its association with long-term outcomes[26,27]

In a retrospective cohort study that examined 15,760 patients living with CHB, HBsAg loss was associated with[26]:

89% REDUCED RISK of HCC

aHR=0.11 (95% CI: 0.01–0.76)

62% REDUCED RISK of all-cause mortality

aHR=0.38 (95% CI: 0.20–0.74)

In a separate retrospective cohort study of 20,263 patients, HBsAg loss was associated with[27]:

76% REDUCTION in HCC risk,

after 8 years of follow-up, compared with complete viral suppression alone.

aHR=0.24 (95% CI: 0.06–0.97); *P*=0.045

HBsAg loss can also be used to determine when a patient can discontinue NA therapy.[17,19]

HBsAg loss and treatment discontinuation are key components of functional cure.[17,19]

As treatment goals evolve, functional cure is increasingly becoming recognized as a treatment goal for CHB.[17,19]

Functional cure is defined as sustained loss of HBsAg (<0.05 IU/mL) and undetectable HBV DNA (<10 IU/mL), maintained for 6 months post–treatment cessation.[19,24]

aHR=adjusted hazard ratio; CI=confidence interval.

KEY BIOMARKER: HBeAg

HBeAg indicates immune activity, helps define disease phase, and differentiates between active* and inactive chronic hepatitis B (CHB)[3,6,13]

HBeAg and its association with long-term outcomes[19,23,28]

HBeAg/ANTI-HBe SEROCONVERSION HAS BEEN ASSOCIATED WITH:		
Favorable prognosis	**Lower incidence of cirrhosis**	**Lower incidence of HCC**

Earlier HBeAg seroconversion may also be associated with improved long-term outcomes.[29]

In a long-term follow-up study (N=770), patients who experienced HBeAg seroconversion **after age 40 had a higher risk of cirrhosis and HCC** compared with those who seroconverted **before age 30** (HR=17.6 [95% CI: 7.15–43.5; *P*<0.0001] and HR=5.22 [95% CI: 1.17–23.3; *P*=0.030], respectively).[29]

*Per AASLD guidelines, immune-active CHB is defined by ALT ≥2X ULN or significant histologic disease with HBV DNA >2,000 IU/mL (HBeAg-negative) or >20,000 IU/mL (HBeAg-positive).[13]

ULN=upper limit of normal.

KEY BIOMARKER: HBV DNA

HBV DNA is a measure of viral replication and guides treatment decisions, but levels can fluctuate[13]

- Serial monitoring is more reliable than cutoff values
- Levels should be interpreted alongside other clinical variables

HBV DNA and its association with long-term outcomes[19]

ACHIEVING SUSTAINED HBV DNA SUPPRESSION IS ASSOCIATED WITH A DECREASED RISK OF SERIOUS LIVER-RELATED OUTCOMES, INCLUDING:				
Cirrhosis	Hepatic decompensation	HCC	Liver transplantation	Death

In a retrospective cohort study that examined 20,263 patients, **lack of complete viral suppression** (HBV DNA undetectable) significantly **increased the risk of HCC by 69%** (aHR=1.69 [95% CI: 1.36–2.09]; *P*<0.001).[27]

Additionally, the risk of liver-related death was **~6x higher** versus patients who did achieve complete viral suppression (aHR=6.85 [95% CI: 4.59–10.23]; *P*<0.001).[27]

KNOW THE NUMBERS.

KNOW THE COMPLETE PICTURE.

Start comprehensive biomarker testing, including quantitative and qualitative HBsAg, for more informed clinical decisions.[1-4]

- Comprehensive biomarker testing may offer clinical insights[5,6]
- HBV DNA and HBeAg are complementary biomarkers that guide chronic hepatitis B (CHB) management—HBV DNA is a measure of viral replication that requires serial monitoring, while HBeAg helps define disease phase and differentiates between active and inactive CHB[3,11,13,30]
- HBsAg is an important marker of active chronic HBV infection[2]
  - **Qualitative HBsAg[23,24]:** Detects presence or absence of HBsAg to assist with diagnosis
  - **Quantitative HBsAg[24]:** Informs prognosis and clinical decisions, and tracks therapeutic progress

Quantitative and qualitative HBsAg, HBeAg, and HBV DNA tests are commercially available.[24]

For the management of CHB, explore comprehensive biomarker testing at:

KnowHepBTesting.com

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