Nutritional Status and Non-Invasive Biomarkers in the Assessment of Liver Fibrosis among Patients with Chronic HBV Infection

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Abstract

Introduction: Liver fibrosis is the principal determinant of long-term outcomes in chronic hepatitis B virus (HBV) infection, predicting progression to cirrhosis, hepatocellular carcinoma (HCC), and mortality. Liver biopsy remains the histological reference standard but is invasive, costly, and prone to sampling error; non-invasive serum biomarkers and transient elastography have therefore emerged as central tools for fibrosis staging. In parallel, nutritional status — encompassing malnutrition, sarcopenia, and micronutrient deficiencies — is increasingly recognized as an independent prognostic factor in chronic HBV. Objective: To synthesize current evidence on nutritional status and non-invasive biomarkers in the assessment of liver fibrosis among adults with chronic HBV infection, and to propose an integrated, nutrology-informed framework for clinical use. Methods: A structured narrative review was conducted using PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library for studies published between January 2000 and December 2025. Search terms combined "hepatitis B," "liver fibrosis," "non-invasive biomarker," "FIB-4," "APRI," "transient elastography," "FibroScan," "malnutrition," "sarcopenia," and "nutritional assessment." Original research, systematic reviews, and clinical guidelines published in English were eligible. Results: FIB-4 and the AST-to-platelet ratio index (APRI) are the most extensively validated serum-based scores in chronic HBV, with strong diagnostic performance for advanced fibrosis and cirrhosis and inclusion in WHO and EASL guidelines. The gamma-glutamyl transpeptidase-to-platelet ratio (GPR), albumin–bilirubin (ALBI), and AST-to-ALT ratio (AAR) provide complementary information. Transient elastography (FibroScan) consistently outperforms simple serum scores and predicts liver-related events, mortality, and fibrosis regression on antiviral therapy. Malnutrition and sarcopenia are highly prevalent in advanced HBV-related liver disease and independently predict decompensation, HCC, and survival. Vitamin D deficiency, hypoalbuminemia, and low handgrip strength carry independent prognostic value beyond conventional scoring systems. Conclusion: Integrating nutritional assessment with validated non-invasive biomarkers provides a clinically meaningful, biopsy-sparing approach to fibrosis staging and prognostication in chronic HBV. Standardized algorithms combining FIB-4, APRI, transient elastography, and structured nutritional screening should be incorporated into routine hepatology and nutrology practice.

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DOI: 10.70102/IJARES/V6IS1/6-S1-01

Keywords: Hepatitis B; Liver Fibrosis; Biomarkers; Elasticity Imaging Techniques; Nutritional Status; Sarcopenia.

1. Introduction

Chronic hepatitis B virus (HBV) infection affects an estimated 254 million people globally and was responsible for approximately 1.1 million deaths in 2022, the majority due to cirrhosis and hepatocellular carcinoma (HCC) [1,2]. The principal determinant of long-term outcomes in chronic HBV is the extent and progression of liver fibrosis, which evolves from minimal portal expansion (F1) to bridging fibrosis (F3) and frank cirrhosis (F4) over years to decades of chronic necroinflammation [3,4]. Accurate fibrosis staging is therefore central to clinical decision-making — informing antiviral treatment initiation, prognosis, and HCC surveillance — and is a cornerstone of contemporary chronic HBV management [5,6].

For more than five decades, percutaneous liver biopsy has served as the reference standard for fibrosis assessment. However, biopsy is invasive, costly, and associated with rare but serious complications, including bleeding and biliary injury; it is further limited by sampling error, intra- and interobserver variability, and reduced acceptability to patients [7–9]. These limitations have motivated the development of non-invasive alternatives, which now occupy a central role in international guidelines for chronic HBV [5,6,10].

Non-invasive fibrosis assessment in chronic HBV broadly comprises two complementary approaches. The first uses serum-based composite scores derived from routine laboratory parameters — including the aspartate aminotransferase-to-platelet ratio index (APRI), the fibrosis-4 (FIB-4) score, the gamma-glutamyl transpeptidase-to-platelet ratio (GPR), the AST-to-ALT ratio (AAR), and the albumin–bilirubin (ALBI) score — which are inexpensive, broadly available, and well validated [9,11–14]. The second uses physical measurement of liver stiffness, most commonly via transient elastography (TE; FibroScan), which provides higher diagnostic accuracy than simple scores and prognostic information for liver-related events and mortality [15–18].

Parallel to advances in non-invasive fibrosis assessment, an extensive literature now establishes nutritional status as a critical, independent determinant of clinical outcomes in chronic liver disease, including HBV-related cirrhosis [19,20]. Malnutrition affects up to 50–90% of patients with advanced liver disease, and sarcopenia — the progressive loss of skeletal muscle mass and function — is present in approximately 10% of Child–Pugh A, 34% of Child–Pugh B, and 54% of Child–Pugh C cirrhotic patients [21–23]. Sarcopenia, vitamin D deficiency, and protein-energy malnutrition independently predict ascites, hepatic encephalopathy, infections, HCC incidence, and mortality, often beyond the prognostic information provided by conventional scoring systems [24–26].

The convergence of these two lines of evidence — non-invasive fibrosis biomarkers and structured nutritional assessment — offers an opportunity to refine risk stratification, monitor disease progression, and individualize therapy in chronic HBV without relying on biopsy. From a nutrological perspective, integrating dietary and metabolic assessment into hepatology workflow allows simultaneous identification of modifiable risk factors and treatable nutritional deficits that may accelerate or attenuate fibrosis progression. The present narrative review aims to provide a critical, mechanism-oriented synthesis of current evidence on nutritional status and non-invasive biomarkers in the assessment of liver fibrosis among adults with chronic HBV, and to propose an integrated, nutrology-informed framework for clinical use.

2. Materials and Methods

2.1 Study design

This is a structured narrative review designed to map and critically appraise the current evidence on nutritional status and non-invasive biomarkers in the assessment of liver fibrosis in adults with chronic HBV infection. The review was conducted following the general principles of the SANRA

(Scale for the Assessment of Narrative Review Articles) framework [27] and incorporated key recommendations from the PRISMA 2020 statement [28] regarding transparency of search strategy and study selection, although a formal systematic review protocol was not registered.

2.2 Information sources and search strategy

Electronic searches were conducted in PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials, and Google Scholar for studies published between January 2000 and December 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms grouped into three blocks: (i) condition — "hepatitis B," "chronic hepatitis B," "HBV," "liver fibrosis," "cirrhosis"; (ii) non-invasive assessment — "biomarker," "FIB-4," "APRI," "GPR," "ALBI," "AST-to-ALT ratio," "transient elastography," "FibroScan," "liver stiffness," "magnetic resonance elastography"; and (iii) nutritional assessment — "nutritional status," "malnutrition," "sarcopenia," "body composition," "vitamin D," "handgrip strength," "subjective global assessment." Boolean operators "AND" and "OR" were used to combine blocks.

2.3 Eligibility criteria

Studies were eligible if they (i) included adult populations (≥18 years) with chronic HBV infection or HBV-related cirrhosis; (ii) evaluated at least one non-invasive fibrosis biomarker or nutritional assessment tool against histological, elastographic, or clinical outcomes; and (iii) were published in English. Diagnostic accuracy studies, prospective and retrospective cohort studies, randomized controlled trials, systematic reviews, meta-analyses, and authoritative clinical guidelines were considered. Studies exclusively in pediatric populations, in hepatitis C or HIV without HBV evaluation, or in liver transplantation outcomes without reference to fibrosis were excluded.

2.4 Study selection and data extraction

Titles and abstracts retrieved from each database were screened for relevance. Full texts of potentially eligible articles were retrieved and assessed against the eligibility criteria. Data extracted from included studies covered: study design and population, biomarker or nutritional tool evaluated, reference standard (biopsy, elastography, or clinical outcomes), diagnostic performance metrics (sensitivity, specificity, area under the curve [AUC]), prognostic associations (fibrosis progression, decompensation, HCC, mortality), follow-up duration, and adverse events.

2.5 Synthesis of evidence

Given the heterogeneity of study designs, reference standards, and biomarker formulations, evidence was synthesized narratively, organized by category of assessment (serum biomarkers, imaging-based elastography, nutritional tools) and by clinical purpose (diagnosis of fibrosis, prediction of progression, monitoring of treatment response). Risk of bias was considered when interpreting diagnostic accuracy studies using domains adapted from the QUADAS-2 tool, and randomized evidence was evaluated using the Cochrane RoB 2 tool [29]. No formal meta-analysis was conducted because of the descriptive scope of the review.

3. Results

3.1 Overview of fibrosis assessment in chronic HBV

Fibrosis staging in chronic HBV traditionally uses the METAVIR system (F0 — no fibrosis, F1 — portal fibrosis without septa, F2 — portal fibrosis with few septa, F3 — bridging fibrosis, F4 — cirrhosis) or the Ishak score [3,4]. Treatment decisions in current European Association for the Study of the Liver (EASL) and Asian Pacific Association for the Study of the Liver (APASL) guidelines hinge on the presence of significant fibrosis (≥F2) or cirrhosis (F4), particularly in patients with intermediate HBV DNA levels or normal alanine aminotransferase (ALT) [5,6]. The two principal non-invasive paradigms — serum biomarker panels and elastography — are complementary, and combined use improves overall diagnostic accuracy [10,15,17]. Table 1 summarizes the principal non-invasive biomarkers with documented relevance to fibrosis staging in chronic HBV.

Table 1. Principal non-invasive biomarkers and tools for liver fibrosis assessment in chronic HBV infection.

Biomarker / tool	Components / measurement	Typical HBV cut-offs	Principal clinical use
APRI	AST × 100 / (ULN of AST × platelet count [10^9/L])	>0.5 significant fibrosis; >1.0 cirrhosis (WHO)	Rule-in/rule-out advanced fibrosis; resource-limited settings
FIB-4	(age × AST) / (platelets × √ALT)	<1.45 rules out, >3.25 rules in advanced fibrosis	First-line fibrosis triage in primary and specialty care
GPR	(GGT / ULN of GGT) / platelet count × 100	>0.32 significant fibrosis; >0.56 cirrhosis	Improved performance in African and Asian HBV cohorts
AAR (De Ritis)	AST / ALT ratio	>1.0 suggests advanced fibrosis	Adjunctive marker; limited stand-alone accuracy
ALBI	$\log_{10}$ bilirubin × 0.66 + albumin × −0.085	Grade 1: ≤−2.60; Grade 3: >−1.39	Liver function and HCC prognosis; complements fibrosis scores
Transient elastography (FibroScan)	Liver stiffness measurement (kPa) by shear-wave propagation	≥F3: 7.5–12.0 kPa; F4: 11.0–13.4 kPa	Reference non-invasive tool; predicts events and mortality
2D shear-wave elastography	Ultrasound-based real-time elastography	Comparable to TE; tool-specific cut-offs	Alternative when TE unavailable; assesses heterogeneity
Magnetic resonance elastography (MRE)	MR-based liver stiffness mapping (kPa)	F2: ≥3.0 kPa; F4: ≥4.7 kPa	Highest accuracy; reserved for selected cases
Enhanced Liver Fibrosis (ELF) test	Hyaluronic acid + PIIINP + TIMP-1	>9.8 advanced fibrosis (general cut-off)	Direct serum marker of matrix turnover
FibroTest / FibroSURE	α2-macroglobulin, haptoglobin, apolipoprotein A1, GGT, total bilirubin	>0.48 significant fibrosis; >0.74 cirrhosis	Commercial composite serum panel

Note: AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transpeptidase; ULN, upper limit of normal; APRI, AST-to-platelet ratio index; FIB-4, fibrosis-4

index; GPR, GGT-to-platelet ratio; AAR, AST-to-ALT ratio; ALBI, albumin–bilirubin score; ELF, enhanced liver fibrosis; PIIINP, N-terminal propeptide of type III procollagen; TIMP-1, tissue inhibitor of metalloproteinase 1; TE, transient elastography; MRE, magnetic resonance elastography; HCC, hepatocellular carcinoma.

3.2 Serum-based non-invasive biomarkers

3.2.1 APRI

The aspartate aminotransferase-to-platelet ratio index, originally validated in chronic hepatitis C, has been extensively evaluated in chronic HBV. APRI is calculated as AST (×100) divided by the product of the upper limit of normal of AST and the platelet count, and is included in WHO 2024 guidelines as a first-line tool for cirrhosis screening in resource-limited settings [9,11]. In HBV cohorts, APRI demonstrates moderate performance for advanced fibrosis (AUC 0.70–0.80) and higher accuracy for cirrhosis (AUC up to 0.85), with optimal cut-offs typically of >0.5 for significant fibrosis and >1.0 for cirrhosis [9,12,30]. Its principal limitations include reduced performance during ALT flares and in patients with normal transaminases or low viral loads [13,31].

3.2.2 FIB-4

FIB-4, calculated from age, AST, ALT, and platelets, is among the most extensively used non-invasive fibrosis scores in chronic liver disease. In multiple HBV cohorts, FIB-4 has demonstrated the highest AUC among simple serum scores for advanced fibrosis and cirrhosis, often outperforming APRI in head-to-head comparisons (AUC for cirrhosis 0.80–0.87) [9,11,30]. The widely used dual cut-offs (<1.45 to rule out and >3.25 to rule in advanced fibrosis) have high negative and positive predictive values and are operationally useful in primary care triage [11,32]. In HBeAg-negative chronic HBV with low viral loads and normal ALT, FIB-4 retains predictive value, supporting its use in indeterminate clinical scenarios [13,31].

3.2.3 GPR, AAR, and ALBI

The gamma-glutamyl transpeptidase-to-platelet ratio (GPR) has shown superior performance to APRI and competitive performance to FIB-4 for advanced fibrosis and cirrhosis in African and Asian HBV cohorts, with reported AUCs of 0.72 for ≥F3 and 0.84 for cirrhosis [9,33]. The AST-to-ALT ratio (AAR or De Ritis ratio) is a simple but less specific indicator, with values >1.0 suggesting advanced disease but limited stand-alone accuracy. The albumin–bilirubin (ALBI) score, originally developed for HCC prognostication, captures global hepatic synthetic and excretory function and provides incremental prognostic information beyond fibrosis-focused scores, particularly in advanced disease [9,34].

3.2.4 Direct serum markers of matrix turnover

Direct biomarkers reflect extracellular matrix synthesis and degradation, including hyaluronic acid, N-terminal propeptide of type III procollagen (PIIINP), and tissue inhibitor of metalloproteinase 1 (TIMP-1) — the components of the Enhanced Liver Fibrosis (ELF) test. ELF demonstrates good diagnostic accuracy for advanced fibrosis in HBV (AUC ~0.80) and prognostic value for liver-related events [9,35]. Commercial composite panels such as FibroTest combine indirect biomarkers (α2-macroglobulin, haptoglobin, apolipoprotein A1, GGT, total bilirubin) and perform comparably to APRI and FIB-4, with the trade-off of cost and limited availability [9,35].

3.3 Imaging-based non-invasive assessment

3.3.1 Transient elastography (FibroScan)

Transient elastography (TE) measures the velocity of a low-frequency shear wave propagated through the liver and reports liver stiffness in kilopascals (kPa). In chronic HBV, TE consistently outperforms simple serum scores for the identification of advanced fibrosis and cirrhosis, with AUCs of 0.87 for bridging fibrosis (≥F3) and 0.93 for cirrhosis [15,16,36]. Typical HBV cut-offs are 7.5–12.0 kPa for ≥F3 and 11.0–13.4 kPa for F4, with lower values applicable in patients with

normal ALT and higher values during ALT flares due to confounding by necroinflammation [15,16].

Beyond diagnosis, TE provides longitudinal prognostic information. In a study of 128 chronic HBV patients with biopsy-confirmed advanced fibrosis, baseline liver stiffness was an independent predictor of liver-related events including decompensation and HCC [17]. During long-term nucleos(t)ide analog therapy, liver stiffness shows a rapid initial decline followed by slower steady reduction, and a percentage decrease ≥38% at week 78 predicts histological fibrosis regression with high accuracy [18,37].

3.3.2 Two-dimensional shear-wave elastography and MRE

Two-dimensional shear-wave elastography (2D-SWE), integrated into conventional ultrasound platforms, provides liver stiffness measurements comparable to TE and the additional advantage of real-time anatomical guidance, although tool-specific cut-offs apply. Magnetic resonance elastography (MRE) achieves the highest diagnostic accuracy of all non-invasive methods (AUC >0.95 for cirrhosis), with cut-offs of approximately ≥3.0 kPa for significant fibrosis and ≥4.7 kPa for cirrhosis [15,38]. MRE is generally reserved for selected indications because of cost and limited availability.

3.3.3 Sequential and combined algorithms

Sequential strategies that use FIB-4 as the first-line triage followed by TE in patients with intermediate or indeterminate scores reduce overall biopsy referrals while preserving diagnostic accuracy [9,11]. The European Association for the Study of the Liver guidelines recommend such combined algorithms for chronic HBV, particularly in patients with normal ALT, low viral loads, or discordant clinical and laboratory findings [5].

3.4 Nutritional status as an independent prognostic dimension

3.4.1 Prevalence and definition of malnutrition in HBV-related liver disease

Malnutrition affects 20–50% of patients with compensated HBV-related cirrhosis and up to 90% of those with decompensated disease [19,21]. The Global Leadership Initiative on Malnutrition (GLIM) criteria, endorsed by the European Society for Clinical Nutrition and Metabolism (ESPEN), require the combination of at least one phenotypic criterion (weight loss, low body mass index [BMI], or reduced muscle mass) and one etiologic criterion (reduced intake or assimilation, or disease-related inflammation) [22]. Standard biochemical markers — albumin, prealbumin, transferrin — are unreliable in advanced liver disease because they reflect hepatic synthetic function rather than nutritional intake, and edema and ascites confound anthropometric measurements [19,21,22].

3.4.2 Sarcopenia

Sarcopenia, defined as the progressive loss of skeletal muscle mass, strength, and physical performance, is a major and increasingly recognized complication of chronic liver disease. The prevalence of sarcopenia rises with Child–Pugh class: approximately 10% in class A, 34% in class B, and 54% in class C cirrhosis [21,23]. Multiple contributors interact: protein-energy malnutrition, hyperammonemia-induced anabolic resistance, systemic inflammation, gut dysbiosis, reduced branched-chain amino acid availability, and physical inactivity [23,39]. Sarcopenia independently predicts ascites, hepatic encephalopathy, infections, HCC incidence, post-transplant outcomes, and overall mortality, and contributes to the burden of decompensation in chronic HBV [23,24,39].

3.4.3 Tools for nutritional assessment in chronic HBV

Several tools are validated for use in chronic liver disease. The Royal Free Hospital–Nutritional Prioritizing Tool (RFH-NPT) and the Liver Disease Undernutrition Screening Tool (LDUST) are liver-specific screening instruments [21,22]. The Subjective Global Assessment (SGA) and patient-generated SGA remain reference clinical tools. Sarcopenia can be assessed by skeletal muscle index (SMI) at the L3 vertebral level using computed tomography or magnetic resonance imaging,

bioelectrical impedance analysis, dual-energy X-ray absorptiometry, or simple bedside measures such as handgrip strength (using the Jamar dynamometer) and gait speed [21,40]. Physical performance batteries such as the Liver Frailty Index integrate grip strength, chair stands, and balance, and have shown independent prognostic value in cirrhotic populations [22].

3.4.4 Vitamin D and other micronutrients

Vitamin D deficiency (25-OH-D <20 ng/mL) is present in >50% of patients with chronic HBV and is independently associated with advanced fibrosis, higher HBV DNA levels, and reduced response to interferon-based therapy [25,41]. The coexistence of Child–Pugh B/C cirrhosis and severe vitamin D deficiency (or sarcopenia) carries substantially worse prognosis than either condition alone, with reported hazard ratios for mortality of 3.2–8.1 [25]. Zinc, selenium, and B-vitamin deficiencies also contribute to immune dysfunction and hepatic regeneration impairment in advanced disease, and fat-soluble vitamins (A, D, E, K) are commonly deficient in cholestatic states [42].

3.5 Integrating biomarkers and nutritional assessment

Table 2 summarizes the proposed integrated, nutrology-informed framework for fibrosis assessment in adults with chronic HBV. The combination of biomarker-based fibrosis staging with structured nutritional and sarcopenia assessment allows clinicians to identify two largely independent prognostic axes — structural liver injury and host nutritional reserve — and to design correspondingly tailored interventions [10,21,23].

Table 2. Proposed integrated framework combining non-invasive fibrosis biomarkers and nutritional assessment in chronic HBV.

Clinical stage	Fibrosis assessment	Nutritional assessment	Clinical priorities
Inactive HBsAg carrier; normal ALT	FIB-4 every 1–2 years; TE if indeterminate	BMI, dietary pattern; vitamin D once	Lifestyle counseling; HCC risk stratification
Immune-tolerant chronic HBV	FIB-4 + APRI annually; TE every 1–2 years	BMI, dietary recall; vitamin D status	Surveillance; weight & metabolic optimization
Immune-active chronic HBV	TE + FIB-4 at baseline and every 6–12 months	Full nutritional screen; handgrip strength	Treatment initiation; reduce metabolic comorbidities
HBV cirrhosis (compensated)	TE every 6 months; ALBI; consider MRE	RFH-NPT / SGA; L3-SMI imaging when available	HCC surveillance; antifibrotic optimization
HBV cirrhosis (decompensated)	ALBI + MELD; TE less reliable	Sarcopenia, frailty (LFI); micronutrient panel	Nutritional therapy; transplant evaluation

Note: ALT, alanine aminotransferase; FIB-4, fibrosis-4 index; APRI, AST-to-platelet ratio index; TE, transient elastography; MRE, magnetic resonance elastography; ALBI, albumin–bilirubin score; MELD, model for end-stage liver disease; RFH-NPT, Royal Free Hospital–Nutritional Prioritizing Tool; SGA, Subjective Global Assessment; L3-SMI, L3-vertebra skeletal muscle index; LFI, Liver Frailty Index; HCC, hepatocellular carcinoma.

3.6 Monitoring response to antiviral therapy

Effective nucleos(t)ide analog therapy in chronic HBV induces measurable regression of liver fibrosis in a substantial proportion of patients over 1–5 years of treatment [18,37]. Serial monitoring with FIB-4 and transient elastography provides a feasible, biopsy-sparing approach to documenting fibrosis regression and identifying patients at residual risk of HCC despite virological suppression [18,37,43]. Nutritional improvement — gain in muscle mass, normalization of vitamin D, and resolution of low-grade inflammation — frequently accompanies sustained virological response, and concurrent nutritional monitoring may therefore complement biomarker-based assessment of therapeutic success [21,23].

3.7 Limitations of current non-invasive and nutritional assessment

Several caveats apply across non-invasive biomarkers. Inflammation (elevated ALT, ALT flares), cholestasis, hepatic congestion, and obesity can falsely elevate liver stiffness; food intake within 2–3 hours similarly increases TE values [15,16]. APRI and FIB-4 lose accuracy when transaminases are markedly abnormal or when platelets fall for non-fibrotic reasons. Nutritional assessment in cirrhosis is similarly confounded by fluid retention and altered hepatic protein synthesis, requiring liver-specific tools (RFH-NPT, LDUST) rather than generic screens [21,22]. No single test is sufficient in isolation, and clinical judgment remains essential.

4. Discussion

4.1 From individual biomarkers to integrated assessment

Two decades of research have established a robust portfolio of non-invasive tools for fibrosis assessment in chronic HBV, with FIB-4, APRI, and transient elastography now embedded in international guidelines [5,6,10,11]. The next frontier is the systematic integration of these structural biomarkers with assessment of the host nutritional and functional substrate. Sarcopenia, vitamin D status, and frailty contribute independent prognostic information that is not captured by Child–Pugh, MELD, or fibrosis-focused scores, and their identification opens specific therapeutic avenues — nutritional rehabilitation, vitamin D repletion, branched-chain amino acid supplementation, and structured exercise [21,23,25,39].

The clinical utility of an integrated framework is greatest in three scenarios. First, in patients with intermediate FIB-4 or TE results, addition of nutritional and functional metrics refines individual risk stratification beyond binary fibrosis categorization. Second, in patients with established cirrhosis under HCC surveillance, sarcopenia and frailty identify those at highest short-term mortality and prioritization for transplant evaluation. Third, in patients on long-term antiviral therapy, parallel monitoring of fibrosis regression (via TE) and nutritional recovery provides a more complete picture of treatment success than virological endpoints alone [18,23,37].

4.2 Nutrological perspective on HBV-related fibrosis

From a nutrological standpoint, chronic HBV management increasingly intersects with metabolic dysfunction-associated steatotic liver disease (MASLD), obesity, type 2 diabetes, and alcohol use. Each of these factors accelerates fibrosis progression and HCC risk independently of viral activity [44,45]. Integrating dietary patterns (Mediterranean-style or other plant-rich, anti-inflammatory regimens), correction of micronutrient deficiencies, alcohol counseling, and structured exercise into hepatology workflow extends the therapeutic toolkit beyond antivirals [44,46]. This integrated model is particularly valuable in low- and middle-income settings, where access to MRE and commercial biomarker panels is limited but nutritional intervention is universally feasible.

4.3 Methodological limitations of current evidence

Despite the breadth of the literature, several methodological limitations temper interpretation. Diagnostic accuracy studies of non-invasive biomarkers commonly suffer from spectrum bias when conducted exclusively in tertiary biopsy cohorts, and biopsy itself is an imperfect reference [7,8]. Many studies report fibrosis cut-offs without external validation, leading to heterogeneity in clinical thresholds. Nutritional research in cirrhosis is dominated by single-center observational designs

with variable assessment tools and limited reporting of confounders including alcohol intake, physical activity, and concomitant MASLD [21,22,39]. Sex- and ethnicity-specific cut-offs remain incompletely characterized for many serum biomarkers.

Future research priorities include (i) prospective multicenter validation of integrated fibrosis–nutrition algorithms in geographically diverse HBV cohorts; (ii) standardized incorporation of sarcopenia and frailty metrics into clinical trials of antiviral therapy; (iii) trials of targeted nutritional interventions (Mediterranean-style diet, vitamin D, branched-chain amino acids, structured exercise) with fibrosis and clinical endpoints; and (iv) economic evaluations to support scalable implementation in low-resource settings.

4.4 Implications for clinical and nutrological practice

Translating the evidence into practice requires interprofessional collaboration among hepatologists, infectious disease specialists, nutrologists, dietitians, and primary care physicians. A pragmatic workflow includes baseline FIB-4 and APRI at every HBV visit, transient elastography at least annually in patients with significant viremia or biochemical activity, structured nutritional screening (RFH-NPT or SGA) at diagnosis and at six-monthly intervals in advanced disease, handgrip strength as a simple bedside marker of sarcopenia, and laboratory assessment of vitamin D, zinc, and selenium in patients with cirrhosis or treatment failure [5,21,22,25]. Such an integrated framework operationalizes nutrology within hepatology and aligns chronic HBV care with the 2030 WHO viral hepatitis elimination targets.

5. Conclusion

Non-invasive biomarkers and nutritional assessment together provide a powerful, biopsy-sparing approach to evaluating liver fibrosis and prognosis in adults with chronic HBV infection. FIB-4, APRI, and transient elastography form the core of validated non-invasive fibrosis assessment, complemented by GPR, ALBI, and direct matrix-turnover markers. Malnutrition, sarcopenia, frailty, and vitamin D deficiency are highly prevalent and confer independent prognostic information that meaningfully refines risk stratification beyond fibrosis stage alone.

Translating this dual-axis assessment into routine practice requires standardized algorithms, interdisciplinary collaboration, and prospective validation. In the meantime, integrated fibrosis-and-nutrition assessment offers a clinically actionable, globally relevant framework for the contemporary management of chronic HBV, consistent with an integrative, nutrology-informed model of care and with global efforts toward viral hepatitis elimination.

Acknowledgments

The authors thank the editorial team of the International Journal of Nutrology for their consideration of this manuscript, and acknowledge the broader community of researchers in hepatology, virology, and clinical nutrition whose primary work forms the basis of this review.

Funding

This review did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical Approval

Not applicable. This review article is based exclusively on previously published literature and did not involve any new studies with human participants or animals performed by any of the authors.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author Contributions (CRediT)

Conceptualization, methodology, investigation, writing – original draft preparation, writing – review and editing: All authors. All authors have read and agreed to the submitted version of the

manuscript.

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