Dietary Patterns, Immune Response, and Their Role in the Prevention and Management of Hepatitis B in Adults

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Abstract

Introduction: Hepatitis B virus (HBV) infection remains a major global health challenge, with approximately 254 million people living with chronic infection and 1.1 million deaths annually. Despite effective vaccination and antivirals, treatment coverage is below 5%, and host factors — including nutritional status — strongly influence vaccine response, immune control, and progression to cirrhosis and hepatocellular carcinoma. Objective: To synthesize current evidence on the role of dietary patterns and individual nutrients in modulating immune response to HBV, supporting vaccine immunogenicity, and influencing disease progression and management in adults. 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," "HBV," "diet," "nutrition," "Mediterranean diet," "vitamin D," "zinc," "polyphenols," and "immune response." In vitro studies, randomized controlled trials, cohort studies, systematic reviews, and meta-analyses published in English were eligible. Results: The Mediterranean diet and other plant-rich, anti-inflammatory dietary patterns are associated with reduced chronic liver disease risk and improved metabolic profiles relevant to HBV outcomes. Vitamin D deficiency is highly prevalent in chronic HBV and correlates with disease severity and impaired antiviral response. Zinc, selenium, vitamin E, and lactoferrin support immune competence and modulate HBV replication. Polyphenols including epigallocatechin-3-gallate, curcumin, and resveratrol exhibit direct anti-HBV activity through inhibition of viral entry, transcription, and replication. Older age, male sex, obesity, smoking, and undernutrition reduce hepatitis B vaccine seroconversion. **Conclusion:** Dietary patterns and targeted nutritional interventions represent a clinically meaningful complement to vaccination and antiviral therapy in HBV. Integration of nutrological assessment into routine hepatology care is recommended, though large, well-designed randomized trials with HBV-specific endpoints remain needed.

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Introduction

Hepatitis B virus (HBV) infection remains one of the most consequential chronic viral diseases worldwide. According to the World Health Organization 2024 Global Hepatitis Report, an estimated 254 million people are living with chronic HBV infection, and viral hepatitis caused approximately 1.3 million deaths in 2022, of which 83% were attributable to HBV [1,2]. Despite the availability of an effective vaccine and well-established nucleos(t)ide analog therapies, treatment coverage remains critically low, with fewer than 5% of eligible individuals receiving antiviral therapy globally [1,3]. The disease continues to drive a heavy burden of cirrhosis and hepatocellular carcinoma (HCC), particularly in the WHO African and Western Pacific regions [2,3].

The outcome of HBV infection — whether spontaneous clearance, immune-tolerant chronic carriage, immune-active hepatitis, cirrhosis, or HCC — is determined by a complex interaction between viral factors and host immunity [4,5]. Innate immune responses, including type I interferons and natural killer cell activity, together with adaptive CD4+ and CD8+ T-cell responses, are central to viral control [5,6]. Importantly, host factors that modulate immune function — including age, sex, body composition, comorbidities, and nutritional status — substantially influence both the natural history of infection and the response to vaccination and treatment [7].

Nutrition occupies a unique position at the intersection of host immunity, hepatic metabolism, and viral replication. The liver is the principal organ for the metabolism of macronutrients, vitamins, and trace elements, and chronic liver disease itself precipitates micronutrient deficiencies that further impair immunity [8,9]. Conversely, specific dietary patterns and individual nutrients — vitamin D, zinc, selenium, vitamin E, omega-3 fatty acids, and a wide range of polyphenols — have been shown to modulate immune responses and, in some cases, directly inhibit HBV replication [10,11]. Plant-rich, anti-inflammatory dietary patterns such as the Mediterranean diet have also been linked to a reduced risk of chronic liver disease and hepatocellular carcinoma in adult populations [12–14].

From a nutrological perspective, the management of chronic HBV is no longer limited to antiviral suppression. It increasingly encompasses prevention of metabolic comorbidities (obesity, type 2 diabetes, metabolic dysfunction-associated steatotic liver disease), optimization of vaccine response, attenuation of hepatic inflammation and fibrosis, and reduction of HCC risk [15,16]. Dietary counseling and targeted micronutrient supplementation may therefore complement immunization and pharmacotherapy as core components of integrated HBV care.

Despite a growing body of literature, the translational evidence is heterogeneous. Many studies are observational, use disparate dietary assessment methods, or rely on surrogate biomarkers rather than HBV-specific clinical endpoints. The present narrative review aims to provide a critical, mechanism-oriented synthesis of current evidence on the role of dietary patterns and nutrients in HBV prevention and management in adults, with attention to immune modulation, vaccine response, viral replication, disease progression, and nutrological integration in clinical practice.

Materials and Methods

Study design

This is a structured narrative review designed to map and critically appraise the current evidence on dietary patterns, immune response, and hepatitis B virus infection in adults. The review was conducted following the general principles of the SANRA (Scale for the Assessment of Narrative Review Articles) framework [17] and incorporated key recommendations from the PRISMA

2020 statement [18] regarding transparency of search strategy and study selection, although a formal systematic review protocol was not registered.

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," "HBV," "chronic hepatitis B," "hepatocellular carcinoma," "cirrhosis"; (ii) intervention/exposure — "diet," "dietary pattern," "Mediterranean diet," "nutrition," "vitamin D," "vitamin E," "zinc," "selenium," "polyphenol," "curcumin," "resveratrol," "epigallocatechin gallate," "lactoferrin"; and (iii) outcomes — "immune response," "vaccine response," "seroconversion," "viral load," "liver fibrosis," "HBV replication," "interferon." Boolean operators "AND" and "OR" were used to combine blocks.

Eligibility criteria

Studies were eligible if they (i) involved adult populations (≥18 years) with HBV infection, prior HBV exposure, or HBV vaccination, or evaluated nutrients with documented anti-HBV activity in pre-clinical models; (ii) reported outcomes relevant to immune response (vaccine seroconversion, cytokine profiles, T-cell function), viral parameters (HBV DNA, HBsAg, HBeAg), liver disease progression (fibrosis, cirrhosis, HCC incidence), or mortality; and (iii) were published in English. In vitro studies, animal experiments, randomized controlled trials, cohort and case-control studies, and systematic reviews and meta-analyses were considered. Studies focused exclusively on pediatric populations, on hepatitis C virus or HIV without HBV co-evaluation, or on non-nutritional interventions were excluded.

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, dietary pattern or nutrient evaluated, dose and duration of exposure, comparator, primary and secondary outcomes, follow-up duration, and adverse events. Particular emphasis was placed on mechanistic insights linking nutrients to immune modulation and HBV biology.

Synthesis of evidence

Given the heterogeneity of study designs, dietary assessment methods, and outcome measures, evidence was synthesized narratively, organized by exposure (dietary patterns, individual nutrients, polyphenols) and by clinical endpoint (vaccine response, viral control, disease progression). Risk of bias was considered when interpreting clinical evidence using domains adapted from the Cochrane RoB 2 tool [19]. No formal meta-analysis was conducted because of the descriptive scope of the review.

Results

Global epidemiology and host determinants of HBV outcomes

HBV is endemic in the WHO African and Western Pacific regions, where chronic prevalence exceeds 5% in some countries; intermediate prevalence (2–5%) is reported in Eastern Mediterranean, South-East Asian, and parts of European populations [1,2,20]. Half of the global burden of chronic HBV and HCV is concentrated in adults aged 30–54 years, and men account for approximately 58% of cases [1]. Adult outcomes of HBV depend not only on age at infection and viral genotype but also on modifiable host factors including obesity, smoking, alcohol use, and nutritional status [7,16,21].

A systematic review and meta-analysis of 37 studies including more than 21,000 adults found

that hepatitis B vaccine seroprotection was significantly reduced in adults aged ≥40 years, men, those with body mass index (BMI) ≥25 kg/m², smokers, and those with concomitant disease [7]. These findings underscore the importance of metabolic and nutritional status as determinants of immune competence and, by extension, vaccine response.

Table 1. Principal nutrients and dietary components with documented relevance to hepatitis B virus infection and immune response.

Nutrient / component	**Principal dietary sources**	**Principal mechanism**	**HBV-relevant targets**
Vitamin D (25-OH-D)	Fatty fish, fortified dairy, sunlight exposure	VDR-mediated modulation of innate and adaptive immunity; antifibrotic; antitumor	HBV DNA suppression; IFN response; cirrhosis & HCC risk
Zinc	Red meat, shellfish, legumes, seeds	Cofactor for T-cell development; IL-17 modulation; antioxidant defense	T-cell function; hepatic inflammation; vaccine response
Selenium	Brazil nuts, seafood, whole grains	Glutathione peroxidase cofactor; antioxidant; immunoregulatory	Oxidative stress; HCC chemoprevention
Vitamin E (α-tocopherol)	Vegetable oils, nuts, seeds	Lipid-soluble antioxidant; T-cell membrane stabilization	HBeAg seroconversion; hepatic oxidative stress
Lactoferrin	Bovine milk, dairy, whey-based foods	Blocks HBV–hepatocyte receptor interaction; immunomodulatory	HBV viral entry; innate immunity
Epigallocatechin-3-gallate (EGCG)	*Camellia sinensis* (green tea)	Induces degradation of HBV entry receptor (NTCP); autophagy	HBV entry; viral particle clearance
Curcumin	*Curcuma longa* (turmeric)	Down-regulates PGC-1α; NTCP binding; anti-inflammatory	HBV transcription/replication; viral entry
Resveratrol	*Vitis vinifera* (grapes), berries, red wine	SIRT1/AMPK modulation; antioxidant; anti-inflammatory	HBV replication; hepatic inflammation
Omega-3 PUFAs (EPA/DHA)	Oily fish, flaxseed, walnuts	Resolves inflammation via specialized pro-resolving mediators	Hepatic inflammation; steatosis
Mediterranean dietary pattern	Fruits, vegetables, olive oil, fish, whole grains, nuts	Composite anti-inflammatory, antioxidant, anti-fibrotic effects	Chronic liver disease risk; HCC incidence

Note: VDR, vitamin D receptor; IFN, interferon; IL-17, interleukin-17; NTCP, sodium taurocholate co-transporting polypeptide; PGC-1α, peroxisome proliferator-activated receptor gamma coactivator 1-alpha; PUFA, polyunsaturated fatty acid; EPA, eicosapentaenoic acid;

DHA, docosahexaenoic acid; HCC, hepatocellular carcinoma.

Dietary patterns and chronic liver disease risk

The Mediterranean dietary pattern

The Mediterranean diet (MedDiet) — characterized by high intake of vegetables, fruits, whole grains, legumes, nuts, olive oil, and fish, moderate dairy and poultry, and limited red and processed meat — has been consistently associated with reduced risk of chronic liver disease [12,13]. A 2025 meta-analysis of 20 observational studies (>1.2 million participants) demonstrated that adherence to the alternate Mediterranean Diet (aMED) was significantly inversely associated with chronic liver disease (pooled OR 0.65; 95% CI 0.56–0.75), with consistent protective effects across European and North American cohorts [14]. While most evidence relates to metabolic dysfunction-associated steatotic liver disease (MASLD), the broader anti-inflammatory profile of the MedDiet is plausibly relevant to HBV outcomes, particularly in mitigating the synergistic effects of metabolic comorbidities on liver fibrosis and HCC risk [13,15,22].

Vegetable-rich versus Western dietary patterns

In a hospital-based case-control study of 641 HCC cases and 1,002 controls in the United States, a vegetable-based dietary pattern was inversely associated with HCC risk (OR 0.66; 95% CI 0.46–0.94 comparing highest vs lowest tertile), while a Western dietary pattern characterized by red and processed meats and refined grains was directly associated with HCC (OR 1.79; 95% CI 1.19–2.69), with adjustment for HBV and HCV infection [15]. These findings suggest that dietary patterns exert effects on liver carcinogenesis independent of, and additive to, viral hepatitis status.

Alcohol and ultra-processed foods

Heavy alcohol consumption is an established modifiable risk factor accelerating HBV-related liver disease progression and HCC incidence [3,16,22]. Ultra-processed food intake, characterized by high content of refined sugars, sodium, and industrial additives, is associated with metabolic syndrome and hepatic steatosis, both of which may compound HBV-related hepatic injury [12,15]. Counseling to limit alcohol and ultra-processed foods is therefore a cornerstone of integrated nutrological management of chronic HBV.

Individual nutrients and immune modulation

Vitamin D

Vitamin D, beyond its classical role in calcium homeostasis, is a potent modulator of both innate and adaptive immune responses through the widely expressed vitamin D receptor (VDR) on macrophages and T and B lymphocytes [23,24]. Vitamin D deficiency (serum 25-OH-D <20 ng/mL) is highly prevalent — often exceeding 60% — in adults with chronic HBV and HCV infection worldwide, and correlates with advanced fibrosis, higher HBV DNA levels, and unfavorable response to interferon-based therapy [23,24,25]. Polymorphisms in VDR (TaqI, FokI, ApaI, BsmI) further modulate susceptibility to and progression of HBV-related liver disease [26]. Adequate vitamin D status appears to support both antiviral immunity and the resolution of inflammation, although the optimal supplementation strategy in HBV patients remains to be defined by larger randomized trials [11,27].

Zinc and selenium

Zinc is essential for thymulin activity, T-cell maturation, and cytokine regulation, and zinc deficiency is common in chronic liver disease due to reduced intake, malabsorption, and increased urinary losses [9,28]. In viral hepatitis, zinc has been shown to reduce IL-17 production and may support antiviral T-cell responses [28]. Selenium, through its incorporation into glutathione peroxidase and other selenoproteins, contributes to antioxidant defense and immune regulation; observational and interventional studies suggest selenium supplementation may reduce HCC

incidence in high-risk HBV populations [10,11].

Vitamin E and other antioxidants

Vitamin E (α-tocopherol) stabilizes cell membranes against lipid peroxidation and supports T-cell function. Adjunctive vitamin E supplementation has shown modest benefit in HBeAg seroconversion in selected cohorts and is well tolerated [10,11]. Other antioxidants present in fruits, vegetables, and beverages — including vitamin C, carotenoids, and a wide range of polyphenols — contribute to a composite anti-inflammatory environment relevant to chronic HBV [12,29].

Lactoferrin

Lactoferrin, an iron-binding glycoprotein abundant in mucosal secretions and dairy products, exhibits broad antimicrobial activity and immunomodulatory effects. In HBV models, lactoferrin inhibits viral entry by blocking the interaction between viral particles and hepatocyte surface receptors [10]. Clinical evidence in humans remains limited but biologically plausible, particularly as adjunctive therapy in immune-tolerant chronic HBV.

Polyphenols and direct anti-HBV activity

Epigallocatechin-3-gallate (EGCG)

EGCG, the principal catechin in Camellia sinensis (green tea), inhibits HBV entry by inducing degradation of the sodium taurocholate co-transporting polypeptide (NTCP) — the principal hepatocyte receptor for HBV — and promotes autophagy-mediated clearance of viral particles [10,29]. Epidemiological evidence linking habitual green tea consumption to lower hepatic fibrosis and HCC risk supports translational relevance, although dedicated randomized trials in chronic HBV are limited.

Curcumin

Curcumin, the principal curcuminoid of Curcuma longa, exhibits multifaceted anti-HBV activity. It down-regulates peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), a metabolic coactivator that robustly enhances HBV transcription [30]. Curcumin also binds NTCP and reduces viral attachment and internalization in immortalized hepatocyte-like cells, lowering HBV DNA, HBeAg, HBcAg, and covalently closed circular DNA (cccDNA) levels in vitro [31]. Despite limited oral bioavailability, novel delivery systems (nanoparticles, phytosomes) are expanding its translational potential as an adjunctive host-targeted therapy [10,30,31].

Resveratrol

Resveratrol, a stilbene polyphenol abundant in Vitis vinifera (grapes), berries, and red wine, exerts anti-HBV effects through modulation of SIRT1/AMPK signaling, suppression of inflammatory cytokines, and antioxidant activity [10,11]. Pre-clinical data suggest reductions in HBV replication and improvements in hepatic histology, although clinical trials specific to chronic HBV are needed.

Other polyphenols and natural compounds

Chlorogenic acid, luteolin-7-O-glucoside, baicalein, galangin, and isorhamnetin — found in coffee, vegetables, and medicinal herbs — have demonstrated hepatoprotective and, in some cases, anti-HBV activity through modulation of oxidative stress, fibrogenesis, and viral gene expression [10,29]. Milk thistle (Silybum marianum) and its principal bioactive silymarin have a long tradition of use in liver disease and may improve hepatic biochemistry, though firm evidence of HBV-specific antiviral activity is lacking [32].

Nutritional status and hepatitis B vaccine response

Hepatitis B vaccine response is markedly reduced in adults with overweight or obesity, in older

adults, and in those with comorbidities including diabetes mellitus, chronic kidney disease, and HIV infection [7]. Beyond demographic factors, micronutrient deficiencies — particularly of vitamin D, zinc, and protein — are associated with impaired seroconversion [11,23]. Adipose tissue-driven chronic low-grade inflammation appears to blunt vaccine immunogenicity, and weight management combined with optimization of nutritional status may improve responsiveness in non-responders. Practical implications include considering additional vaccine doses, intradermal administration, or adjuvanted vaccines in adults with elevated BMI or other risk factors [7,33].

Nutrology and chronic hepatitis B: clinical integration

Chronic HBV management in adults increasingly encompasses metabolic comorbidities. The convergence of HBV with MASLD, type 2 diabetes, and obesity accelerates fibrosis and HCC risk, and nutrological assessment should therefore form part of the routine hepatology workup [12,13,16]. Recommended elements include anthropometric measurements, dietary recall, evaluation of vitamin D, zinc, selenium and B12 status, and counseling on alcohol and ultra-processed food intake [8,9,11]. In patients with established cirrhosis, attention shifts to prevention of sarcopenia, adequate protein intake, branched-chain amino acid supplementation when indicated, and management of fat-soluble vitamin deficiencies due to cholestasis [8,9].

Safety, adverse events, and interactions

Most dietary patterns and nutrients reviewed have favorable safety profiles within usual dietary or recommended supplementation ranges. However, several considerations warrant attention. High-dose vitamin D supplementation requires monitoring of serum 25-OH-D and calcium, particularly in patients with cirrhosis [11,23]. High-dose vitamin E (>400 IU/day long term) has been associated with small increases in all-cause mortality in some meta-analyses. Polyphenol supplements (e.g., concentrated EGCG extracts) have rarely been linked to idiosyncratic hepatotoxicity, paradoxically in an HBV-relevant context [29]. Potential interactions of nutrient supplements with nucleos(t)ide analogs and interferons are generally limited but should be considered, particularly in patients with advanced liver disease and polypharmacy.

Discussion

From mechanism to clinical translation

The accumulated mechanistic and clinical evidence supports the view that dietary patterns and selected nutrients exert biologically meaningful effects on HBV outcomes in adults. Three principal axes of action emerge: (i) modulation of innate and adaptive immunity, exemplified by vitamin D, zinc, and selenium; (ii) direct interference with the HBV life cycle — viral entry, transcription, replication, and cccDNA stability — exemplified by polyphenols such as EGCG, curcumin, and resveratrol; and (iii) reduction of metabolic and inflammatory comorbidities that accelerate fibrosis and HCC, exemplified by the Mediterranean dietary pattern [10–14].

From a clinical standpoint, dietary patterns are best positioned as universal background recommendations applicable across the spectrum of HBV — from individuals at risk of infection awaiting vaccination, to inactive carriers, to those on long-term antiviral therapy, to patients with cirrhosis. Targeted micronutrient supplementation, particularly vitamin D in deficient individuals and zinc in those with documented deficiency, has the strongest current rationale [11,23,28].

Nutrology, vaccination, and antiviral therapy

Hepatitis B vaccination remains the cornerstone of prevention, and adult vaccine response is increasingly recognized as nutrition-sensitive. Optimization of weight, smoking cessation, and correction of micronutrient deficiencies should be considered as adjunctive measures in adults with elevated BMI, advanced age, or comorbidities undergoing primary or booster vaccination [7,11]. For patients on nucleos(t)ide analog therapy, nutrological support primarily targets fibrosis attenuation, HCC chemoprevention, and management of treatment-related metabolic effects [10,15,16].

Methodological limitations of current evidence

Despite the breadth of the literature, several methodological limitations temper interpretation. Most epidemiological evidence on dietary patterns and chronic liver disease is observational and susceptible to residual confounding by socioeconomic status, healthcare access, and lifestyle factors [13,14]. Many nutrient–HBV studies are pre-clinical or short-term clinical trials with surrogate endpoints (HBV DNA, HBeAg seroconversion) rather than disease incidence or mortality [10,11]. Heterogeneity in dietary assessment, supplement formulations, dosing, and study populations further complicates synthesis [18]. Publication bias favoring positive findings may inflate apparent efficacy of certain nutraceuticals.

Future research priorities include (i) adequately powered, multicenter randomized controlled trials of Mediterranean-pattern interventions in chronic HBV with clinically meaningful endpoints; (ii) trials of vitamin D and zinc supplementation stratified by baseline status; (iii) human studies of polyphenols (EGCG, curcumin, resveratrol) with standardized formulations and bioavailability assessment; (iv) integration of multi-omics (metabolomics, immunophenotyping) to characterize mechanisms; and (v) cost-effectiveness analyses for global HBV elimination strategies.

Implications for nutrology and integrative practice

Integrating dietary and nutrient-based strategies into HBV care requires interprofessional collaboration among hepatologists, infectious disease specialists, nutrologists, and dietitians. A practical framework includes nutritional screening at HBV diagnosis, individualized dietary counseling emphasizing a Mediterranean-style pattern, targeted laboratory assessment of vitamin D, zinc, and selenium status, and structured counseling on alcohol and ultra-processed foods [8,9,11]. Special populations — including pregnant women with HBV, patients with cirrhosis, transplant recipients, and adults with metabolic comorbidities — particularly benefit from such integrated care given their compounded risks for adverse outcomes [16,33].

Conclusion

Dietary patterns and individual nutrients exert a broad spectrum of effects relevant to the prevention and management of hepatitis B virus infection in adults. The Mediterranean dietary pattern, adequate vitamin D and zinc status, and a range of polyphenols including EGCG, curcumin, and resveratrol provide biologically plausible and clinically meaningful complements to vaccination and antiviral therapy. Their actions span immune modulation, direct interference with the HBV life cycle, attenuation of hepatic inflammation and fibrosis, and reduction of metabolic comorbidities that drive disease progression.

Nevertheless, the field is constrained by methodological heterogeneity, reliance on surrogate endpoints, and limited large-scale randomized trials. Translating the considerable preclinical and observational promise into routine clinical and public health practice will require rigorous, standardized trials, regulatory frameworks for nutraceutical interventions, and integration of nutrological care into HBV management algorithms. In the meantime, dietary patterns and targeted nutritional optimization represent a scientifically credible, patient-acceptable, and globally relevant component of contemporary hepatitis B care, particularly within an integrative, nutrology-informed model of practice.

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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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