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Review

Hepatitis and periodontal health: an emerging oral-liver axis

Ruth Rodríguez-Montaño, Melissa Martínez-Nieto, Gustavo Eder González-Alvarez, Mario Alberto Alarcón-Sánchez, Julieta Sarai Becerra-Ruiz, Artak Heboyan, Alba Ruiz-Gaitán and Sarah Monserrat Lomelí-Martínez

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***Abstract*:** Periodontitis and viral liver infections, particularly hepatitis B virus (HBV) and hepatitis C virus (HCV), are chronic inflammatory conditions with a high prevalence worldwide. Recent evidence establishes a possible bidirectional relationship between the two, based on shared immunological, microbial, and inflammatory mechanisms. The objective of this study was to analyze and synthesize the scientific literature on the interactions between viral hepatitis and periodontal health. Through a structured search of the PubMed, Scopus, and Web of Science databases, studies published in the last 20 years that explored the link between viral hepatitis and periodontitis were integrated. The findings from the reviewed studies show consistent, positive associations between HBV and HCV viruses and a higher prevalence and severity of periodontitis. Some studies show increased levels of proinflammatory cytokines (such as IL-6 and TNF-α) and immune dysfunction in participants with both diseases. Additionally, viral markers (such as HBsAg and HCV RNA) have been identified in gingival crevicular fluid, suggesting the presence of oral viral reservoirs. Ultimately, scientific evidence suggests a bidirectional relationship between viral hepatitis and periodontitis, influenced by systemic inflammation, immunological alterations, and microbial dysbiosis. The collected data support the relevance of interdisciplinary management between medical and dental professionals in patients with viral liver conditions.

Keywords: chronic inflammation, liver disease, oral microbiota, periodontitis, viral hepatitis

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Correspondence to:
Artak Heboyan
Department of Prosthodontics, Faculty of Stomatology, Yerevan State Medical University after Mkhitar Heratsi, Str. Koryun 2, Yerevan 0025, Armenia

Department of Research Analytics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India

Department of Prosthodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran
heboyan.artak@gmail.com

Sarah Monserrat Lomelí-Martínez
Department of Medical and Life Sciences, La Ciénega University Center, University of Guadalajara (CUCIENEGA-UdeG), Ocotlán 47810, Mexico.
sarah.lomeli@academicos.udg.mx

Ruth Rodríguez-Montaño
Department of Health and Illness as an Individual and Collective Process, University Center of Tlajomulco, University of Guadalajara (CUTLAJO-UdeG), Guadalajara, Mexico

Institute of Research in Dentistry, Department of Integral Dental Clinics, University Center of Health Sciences, University of Guadalajara (CUCS-UdeG), Guadalajara, Mexico

Melissa Martínez-Nieto
Department of Integral Dental Clinics, University Center of Health Sciences, University of Guadalajara (CUCS-UdeG), Guadalajara, Mexico

Introduction

Periodontitis is a multifactorial chronic inflammatory condition linked to dysbiosis of the subgingival dental biofilm, characterized by destruction of the supporting apparatus of the dental organ.[1,2] The World Health Organization estimates that these severe periodontitis cases affect 19% of adults, representing more than 1 billion cases globally.[3] Furthermore, viral hepatitis, particularly that caused by the hepatitis B virus (HBV) and the hepatitis C virus (HCV), poses a significant public health issue; an estimated 325 million people suffer from this chronic condition, which is associated with complications such as liver cirrhosis, liver failure, and hepatocellular carcinoma.[3]

The association between periodontitis and systemic conditions has received increasing scientific attention in recent years. A recent bibliometric analysis highlights how studies have focused particularly on the shared immunoinflammatory mechanisms between periodontitis, peri-implant diseases, and systemic conditions such as diabetes mellitus, cardiovascular disease, and liver disease.[4] The results support the priority of addressing periodontal health not only in isolation, but as an integral component in understanding and managing chronic systemic conditions, including viral hepatitis.

Traditionally, both conditions have been addressed in isolation from clinical medicine and

Gustavo Eder González-Alvarez
Department of Medical and Life Sciences, La Ciénega University Center, University of Guadalajara (CUCIENEGA-UdeG), Ocotlán, Mexico

Mario Alberto Alarcón-Sánchez
Institute of Research in Dentistry, Department of Integral Dental Clinics, University Center of Health Sciences, University of Guadalajara (CUCS-UdeG), Guadalajara, Mexico

Molecular Biology in Medicine Program, University Center of Health Sciences, University of Guadalajara (CUCS-UdeG), Guadalajara, Mexico

Julieta Sarai Becerra-Ruiz
Department of Clinics, Los Altos University Center, University of Guadalajara (CUALTOS-UdeG), Tepatitlán de Morelos, Mexico

Alba Ruiz-Gaitán
Departamento de Microbiología. Hospital Universitario y Politecnico La Fe, Valencia, Spain

dentistry. However, recent research has begun to highlight a significant link between chronic viral liver infections and periodontal health problems. These associations have generated a new emerging concept: the oral-liver axis, emphasizing bidirectional communication between the liver and the oral cavity, mediated by systemic immunoinflammatory mechanisms, microbiota changes, and microbial translocation pathways, with clinical consequences that transcend both spheres.[5,6] Certain epidemiological and clinical studies have found a higher prevalence of periodontitis in participants infected with HBV or HCV, particularly in those with advanced liver disease. This link may be influenced by systemic immunosuppression induced by viral infection, a chronic proinflammatory state, and dysbiosis in the oral cavity, which contributes to a more vulnerable environment for the development of periodontal pathogens.[5,6] In this same context, periodontitis can serve as a focal point of chronic systemic inflammation and contribute to liver damage, particularly through the translocation of bacteria and microbial products into the portal bloodstream. Despite growing evidence, gaps in knowledge remain that require more robust clinical and experimental research to address. From this perspective, understanding the interrelationship between periodontal health and liver dysfunction will help clarify the underlying mechanisms and open new therapeutic perspectives based on the prevention and comprehensive treatment of both pathologies.

Both viral hepatitis and periodontitis are conditions that share standard pathophysiological mechanisms, including chronic inflammation, immunomodulation, and microbial dysbiosis. In this context, it is essential to understand the potential interactions between the two diseases. This review aims to analyze and describe the available scientific evidence on the bidirectional association between HBV and HCV infections and periodontal health, identify the shared pathophysiological mechanisms that facilitate understanding of this interrelationship, and highlight the importance of a multidisciplinary approach to the diagnosis, therapeutic management, and follow-up of these patients.

Search methodology

This narrative review was conducted following a structured methodological strategy to ensure a comprehensive and evidence-based selection of the scientific literature. A search was conducted in the PubMed, Scopus, and Web of Science databases, encompassing studies published in the last 20 years (2004–2024). The selection criteria were original articles and reviews, published in English or Spanish, with observational or experimental methodological designs that analyzed the association between viral hepatitis (HBV, HCV) and periodontal health. The selected manuscripts addressed essential aspects, including shared pathophysiological mechanisms, oral manifestations of liver disease, the impact of antiviral therapy on the oral environment, and the possibility of a bidirectional interaction between the two conditions. Boolean combinations with specific terms were considered, such as: "hepatitis B," "hepatitis C," "periodontitis," "oral microbiota," "inflammation," "oral manifestations," "antiviral therapy," "dysbiosis," "bidirectional relationship."

Periodontitis

The periodontal disease group, or in other words, periodontal conditions, encompasses a series of periodontal disorders, the most common of which are gingivitis and periodontitis. These conditions affect the tissues surrounding the teeth, such as the ligaments, bones, and gums. These disorders cause inflammation and bleeding and can be reversible, like gingivitis, or irreversible, like periodontitis.[7,8] Clinically, this condition is characterized by the presence of detectable interdental attachment loss in two or more non-adjacent teeth, or buccal attachment loss $\geqslant$3 mm with a probing depth $\geqslant$3 mm. It is essential to rule out other non-periodontal causes of tissue damage, such as gingival recession due to trauma, caries in the cervical region, or endodontic defects. In severe cases, tooth mobility or loss of dental organs may occur.[2] It is a significant global public health issue linked to the emergence and evolution of several systemic diseases. It is a common condition affecting more than 40% of adults in the United States. Worldwide, severe disease has a prevalence of 11%.[9] The systematic review by Trindade et al. indicates that between 2011 and 2020, the prevalence of periodontitis in dentate adults was estimated to be approximately 62%, with severe periodontitis at 23.6%.[10] When microbial homeostasis in the periodontium is disrupted, microorganisms in the biofilm can lead to periodontitis and induce host immune responses.[11] Subgingival microbiome dysbiosis, defined by the proliferation of harmful bacteria such as *Porphyromonas*

gingivalis, Tannerella forsythia, and *Aggregatibacter actinomycetemcomitans*, plays a crucial role in the onset and development of periodontitis.[11] For decades, periodontitis has been recognized as a local inflammatory disease of the periodontal tissues of the oral cavity. Initially, the relationships between periodontitis and several non-communicable diseases were examined individually, thereby revealing their links. The relationship between periodontitis and diseases such as cardiovascular disease, rheumatoid arthritis, diabetes, and respiratory diseases has been demonstrated.[12] Like many other systemic conditions, periodontitis shares environmental, lifestyle, and genetic risk factors, as well as immunopathology. Furthermore, chronic noncommunicable diseases may increase susceptibility to developing other similar chronic conditions; one condition's systemic effects may serve as multiple risk factors for another similar disease.[12]

The etiopathogenesis of periodontitis is based on the interrelationship between a dysbiotic subgingival dental biofilm and a modified immune response.[4,5] In health, the subgingival microbiota establishes a balance with local immunity. The participation of systemic, genetic, and environmental factors can trigger dysbiosis, leading to an overgrowth of specific microorganisms and promoting a chronic inflammatory process in the periodontal tissues. Some of the main microorganisms involved are those proposed by Socransky from the red complex, such as *P. gingivalis*, *T. forsythia*, and *T. denticola*, which are highlighted as key bacteria due to their participation in activating the innate and adaptive immune responses. Likewise, bacteria from the orange complex, such as *Fusobacterium nucleatum* and *Prevotella intermedia*, promote the colonization of the most virulent bacteria, contributing to the progression of the disease.[5] This microbial dysbiosis promotes an exacerbated immune response, characterized by the continuous release of proinflammatory cytokines, matrix metalloproteinases, and mediators such as NLRP3, which promotes the degradation of the extracellular matrix, loss of clinical attachment, and bone resorption.[2] This altered immune activation is not only associated with local periodontal tissue destruction but also with systemic effects. Still, it may also have systemic implications, contributing to a chronic inflammatory state that affects other organs, such as the liver. The progression of periodontitis is regulated not only by the microbial species profile but also by host susceptibility mediated by immunogenic factors.[5,6]

Viral hepatitis

Hepatitis is an inflammation of the liver and can be caused by various factors, including viruses (hepatitis A, B, C, D, E), alcohol, medications, autoimmune conditions, and other toxic or metabolic causes. It can be acute (short-term) or chronic (long-term).[13,14] Viral hepatitis is the most common, with some types spread through blood, bodily fluids, or contact with infected individuals. The viruses that cause high-risk hepatitis are types B and C, as they can lead to chronic disease, in addition to causing cirrhosis and liver cancer.[15] The WHO estimates that in 2022, 254 million individuals were living with chronic HBV infection, with 1.2 million new cases of infection occurring annually. In 2022, hepatitis B caused the deaths of approximately 1.1 million individuals, primarily due to cirrhosis or hepatocellular carcinoma (primary liver cancer).[14]

Regarding HCV, it is estimated that there are 50 million individuals globally with chronic hepatitis C virus infection, and approximately 1.0 million new infections occur annually. The WHO estimates that around 242,000 individuals died in 2022 due to HCV, mainly from cirrhosis and hepatocellular carcinoma.[3] HBV is a double-stranded DNA virus belonging to the Hepadnaviridae family. It was first detected in 1963 and named the Australian Antigen due to the reaction of its protein with the antibodies of a hemophiliac individual. The virus has a specific trophic tendency toward hepatocytes, to which it binds and is incorporated after the initial infection. A total of 10 HBV genotypes (A–J) have been identified, along with 35 subgenotypes; the distribution of these genotypes fluctuates significantly across the globe.[16]

The HCV is a small, enveloped, positive-sense, single-stranded RNA virus identified in 1989 as a member of the Flavivirus family and the only member of the *Hepacivirus genus*. There are 7 major genotypes and 67 subgroups. HCV genotype one accounts for approximately half of all HCV infections, making it the most common genotype worldwide. HCV genotype three is the second most common, accounting for about one-third of HCV infections; it is most prevalent in

South Asia, Australia, and several European countries.[15] Individuals with chronic HBV infection are at high risk for liver problems, such as end-stage liver disease and hepatocellular carcinoma. For a long time, extrahepatic manifestations of HBV infection have been underestimated. Several extrahepatic conditions are well-characterized, including systemic vasculitis, glomerulonephritis, and skin manifestations. More recently, other manifestations have been identified, including hematologic malignancies and neurological pathologies.[17] During chronic HCV infection, approximately 70% of patients exhibit one or more extrahepatic signs such as non-Hodgkin lymphomas, cardiovascular diseases, nephropathy, insulin resistance, and type 2 diabetes mellitus, along with neurological and psychiatric disorders and rheumatic diseases not associated with mixed cryoglobulinemia.[18] There is evidence of a connection between periodontitis and hepatitis. In this context, a positive correlation has been documented between moderate periodontitis and hepatitis virus infection, with this correlation being even stronger for severe periodontitis.[6]

Emerging oral-gut–liver axis

Initially, the relationship between chronic hepatitis and periodontitis was debated because viruses such as HCV and HBV can be found in saliva. Oral fluids are efficiently used for mass screening for HBV and are recognized transmission routes for this virus.[19] Furthermore, the dysbiosis caused by periodontitis can impact the rest of the digestive system and, consequently, the liver. It is crucial to note that the microbiota includes bacteria, yeasts, and viruses, albeit to a lesser extent. In this context, if HCV and HBV can spread through saliva and reach the liver, there is a possibility that some bacteria causing periodontitis may also utilize this route.[20] It is essential to consider that the liver is one of the organs most impacted by these biological networks and pathogenic changes, as it maintains anatomical proximity and strong physiological interdependence with the intestine through metabolic exchange and the translocation of bacteria.[21] Another possible mechanism is systemic inflammation, which can trigger the release of inflammatory mediators such as IL-1, IL-6, and TNF-α by oral bacteria.

Additionally, intestinal dysbiosis is characterized by an increase in the intestinal lumen of ethanol and its metabolite, acetaldehyde.[22] These mediators can weaken the gut's tight connections, leading to an increased translocation of molecular patterns associated with microorganisms and gut metabolites, such as trimethylamine. These metabolites trigger inflammatory reactions in the gut and liver, resulting in progressive liver damage.

On the other hand, *Streptococcus* and *Veillonella*, bacteria characteristic of the oral cavity, have been observed in the feces of patients with liver cirrhosis compared to healthy individuals.[20,23] *Fusobacterium necrophorum* and *Prevotella species* have also been reported in liver abscesses.[24–26] Anti-HCV antibodies and viral RNA have been identified in gingival crevicular fluid (GCF) samples obtained from patients with HCV infection.[27] Viral molecules can infiltrate saliva, transforming the GCF into a source of contamination in the saliva of infected HCV patients. Inflammation in the oral cavity, liver, and intestine can lead to systemic inflammation, which in turn can result in endotoxemia. This is due to an increase in the relative abundance of potentially harmful microorganisms in the intestine and oral cavity, a deficient mucosal and systemic immune response, and a reduction in the liver's ability to manage these insults. Changes in bile acid composition, reduced stomach acidity, and potential neurohormonal modifications characteristic of cirrhosis also create this systemic pro-inflammatory environment[23] (Figure 1).

In addition to these mechanisms, it has been shown that periodontitis can promote a state of systemic oxidative stress, even in the absence of preexisting chronic conditions. Some studies have documented that patients with periodontitis exhibit increased levels of reactive oxygen species and decreased antioxidant activity, which contributes to local tissue destruction and a generalized inflammatory environment.[28–30] This redox alteration could amplify hepatocellular damage and positively impact the progression of liver disease.[30] Consequently, this mechanism represents a point of convergence linking both pathologies.

Certain studies have suggested that periodontitis, even in people without diagnosed systemic conditions, can induce a state of chronic inflammation, promoting immune dysfunction and increasing the predisposition to infections such as viral hepatitis. In this context, Matsuda et al. showed that

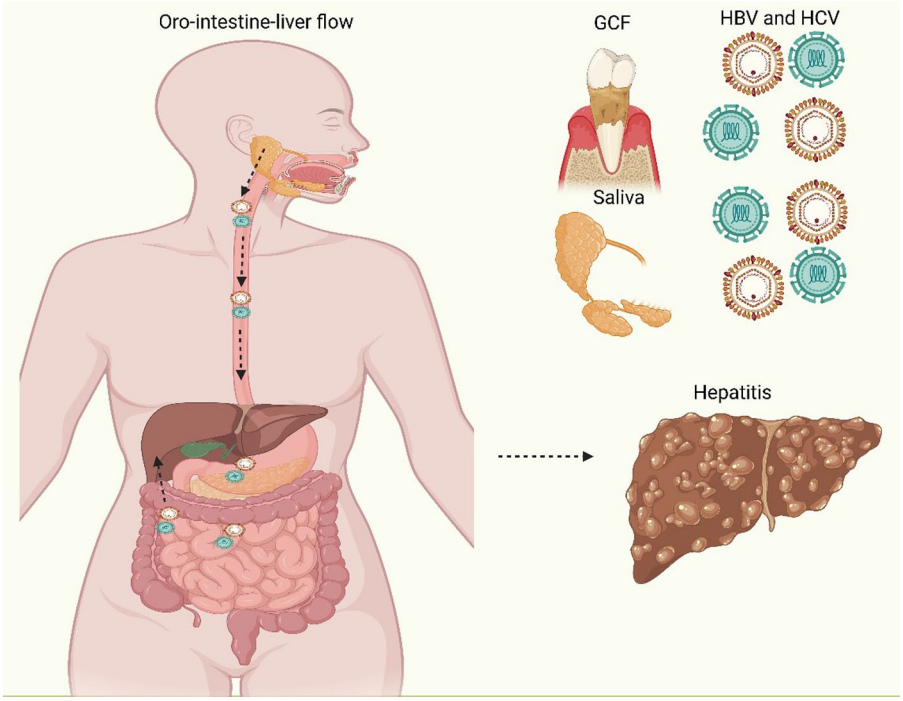

Figure 1. Oro-intestine-liver axis. People with periodontitis present microbial dysbiosis in different compartments of the oral cavity, especially in the periodontal pockets. This dysbiosis is also accompanied by dysbiosis in the intestinal microbiota. This intestinal dysbiosis can generate mucosal permeability, allowing microbiota to travel from the intestine to the liver. Similarly, this microbiota transport may travel from the small intestine to the gallbladder and liver.

patients without comorbidities diagnosed with periodontitis have elevated concentrations of systemic inflammatory markers, supporting the hypothesis that oral disease can have an effect beyond the local environment.[31] Additionally, periodontal management has been shown to not only improve oral health but also significantly reduce systemic inflammation, potentially impacting both the prevention and progression of infectious conditions such as hepatitis. These results underscore the need to consider periodontitis as a modifiable risk factor in comprehensive preventive strategies.

Cytokines in periodontitis and hepatitis

The common denominator of both diseases is chronic inflammation. Regional periodontal immunity, which includes neutrophils, helper T cells,[21] and immune-related cytokines, is vital for preserving periodontal homeostasis and responding to microbial imbalances. IL-17, IL-1β, IL-18, and IL-6 are key cytokines in the immunomodulation of this disease.[32–34] These cytokines have been observed systemically in serum and plasma samples, as well as in saliva and GCF. It is crucial to note that GCF is a specific oral fluid; although it originates in serum, it is released externally in the body, such as in the gingival sulcus. Thus, its composition and behavior during inflammation make GCF a relevant subject for study regarding the bidirectional relationships between periodontitis and HCV infection. The fluid includes elements of bacterial plaque, inflammatory cells of the immune system, connective tissue fragments, and other blood components.[35]

Regarding the cytokines detected in periodontitis, it is essential to note that they have also been observed in patients with hepatitis. IL-1α and IL-1β levels in GCF were higher in periodontitis cases of chronic HCV compared to those in healthy patients.[36] Similarly, an increase in C-reactive protein and pentraxins has been observed in patients with periodontitis and chronic hepatitis caused by the HCV.[37] The HBV has been detected in salivary samples of patients with HBV, in addition to finding blood traces in salivary samples linked to periodontal pathology.[38] Increases in IL-2, IL-10, and IFN-γ were

observed in the saliva of patients with HBV and HCV, with higher levels noted in those with HBV.[39] Likewise, chronic HBV has been reported to be positively associated with more severe periodontitis. These results suggest that people with HBV infection should adopt appropriate periodontal care measures to prevent the onset and development of periodontitis. This study was conducted using data from the National Health and Nutrition Examination Survey (2009–2014).[40] Despite the immunoinflammatory processes associated with both pathologies, patients with periodontitis and HCV have been reported to exhibit a more deteriorated periodontal status and higher levels of NLRP3, caspase 1 (CASP-1), and interleukin-18 (IL-18). Periodontitis and chronic HCV could significantly influence the hyperexpression of the NLRP3 inflammasome and its components, potentially leading to an increase in the local inflammatory reaction and clinical repercussions for periodontal health.[41] The inflammasome is a multi-protein oligomeric complex.

The NLRP3 complex, one of these inflammasomes, plays a crucial role in innate immunity and inflammation. It is a Nod-like receptor that controls the activation of protease enzymes (CASP-1) and regulates the release of essential pro-inflammatory cytokines, such as IL-18.[42] A change in the systemic immune profile during periodontitis may exacerbate persistent liver inflammation and/or viral persistence in liver cells. Circulating CD56low $CD16^+$ Natural Killer (NK) cells are anergic in the peripheral blood of individuals with periodontitis, which could enhance the survival of HBV and HCV.[43] Increased levels of IL-6 and IL-1β released by peripheral $CD14^+$ macrophages lead to a decrease in the ability of $CD4^+$ and NK T cells to produce IFN-γ. This phenotypic shift further compromises antiviral defense.[44] The systemic increase in $CD4^+$ $CCR7^+$ and $CD8^+$ $CCR7^+$ T lymphocytes may also contribute to the exacerbation of the inflammatory response in chronic liver diseases.[45]

Clinical evidence

Recently, the association between periodontitis and viral hepatitis has been supported by several epidemiological and clinical studies. However, the diversity of patient subgroups allows for a more nuanced view of the interaction between these conditions. Differences in liver disease stages, periodontitis severity, the presence of co-infections, and various sociodemographic factors provide opportunities to establish precise patterns of prevalence and correlation. Accordingly, an analysis of the most notable studies is presented, highlighting the importance of subgroup characteristics in the link between periodontal health and liver function (Table 1).

The study by Nagao et al. represents one of the first direct links between periodontitis and the progression of liver fibrosis in participants infected with hepatitis B and/or C. Through a retrospective approach involving 351 participants, it was found that those with active periodontitis (according to salivary occult blood tests) exhibited higher levels of significant liver markers (AST, ALT, LDH, ALP), as well as greater fibrosis. Another interesting finding was the identification of an increased prevalence of the fimA type II genotype of *P. gingivalis* in participants with cirrhosis or a history of hepatocellular carcinoma. In particular, this link suggests that periodontopathic bacteria not only affect the oral cavity, but that shared systemic immunoinflammatory mechanisms may also be involved in liver progression.[5] Chen et al. analyzed data from the National Health and Nutrition Examination Survey (NHANES, USA) to explore this interrelationship in a representative sample of 5755 individuals. Participants with viral hepatitis had a higher probability of suffering from periodontitis, particularly in moderate (OR: 2.13) and severe (OR: 3.58) forms. These findings corroborate the hypothesis that a chronic inflammatory process caused by liver infection generates a systemic microenvironment that triggers and enhances periodontal destruction.[6] Within this same framework, a second analysis of the NHANES database (2009–2014) was conducted but focused solely on chronic HBV, which included 5957 participants and determined a 38% increase in the probability of developing periodontitis in patients with this type of hepatitis, even when adjusting for confounding factors such as age, gender, educational level, health habits, and chronic diseases.[40] The rigorous control of variables and confirmation of the relationship through multivariate analysis presented in this study provide a higher level of epidemiological evidence for the link. These findings are consistent with the study by Fang et al., the most recent

Table 1. Original studies of periodontitis and viral hepatitis.

Author (year)	Type of hepatitis	Country	Study design	Sample size	Measured variables	Periodontal/ hepatic diagnosis	Key findings	OR/*p*-valor	Result
Nagao et al. (2014)[5]	HCV/HBV	Japan	Retrospective	351	Liver fibrosis, oral habits, presence of *P. gingivalis*	Salivaster® and fimA genotype by PCR/HCV-HBV clinical data	Higher prevalence of fibrosis in participants with periodontitis. FimA type II is more prevalent	Adjusted OR: 5.80 ($p < 80{,}000$); $p < 0.05$	Controlling periodontitis is essential for managing liver fibrosis
Chen et al. (2024)[6]	HCV/HBV	EE.UU.	Transversal (NHANES 2003–2018)	5755	Periodontitis, hepatitis, comorbidities alcohol	CDC/AAP periodontitis parameters/ NHANES serology	Significant association between hepatitis and severe periodontitis	OR: 2.13 (moderate); 3.58 (severe); $p < 0.001$	Increased risk of periodontitis in patients with viral hepatitis
Chen et al. (2024)[40]	HBV	EE.UU.	Transversal (NHANES 2009–2014)	5957	HBV, periodontitis, lifestyle	NHANES periodontal/ HBV serology	HBV is associated with an increased risk of moderate/severe periodontitis	Adjusted OR: 1.38 (CI: 1.08–1.75); $p < 0.01$	HBV significantly increases the risk of active periodontitis
Fang et al. (2024)[46]	HCV/HBV	EE.UU.	Transversal (NHANES 2009–2014)	10,714	Periodontitis comorbidities	CDC/AAP periodontitis parameters/ HBV-HCV serology	HCV had higher odds of periodontitis, especially severe periodontitis	HCV: OR 1.41, 95% CI [1.07–1.85], $p < 0.05$	Significant association between periodontitis and HCV
Anand et al. (2001)[47]	HBV/HCV/ Alcohol	India	Comparative prospective	231 Group A (83): Patients with CLD Group B (75): Healthy controls without liver disease Group C (46): Alcoholics without liver disease Group D (27): Patients with portal hypertension but no liver disease	Caries, number of teeth, plaque index, clinical attachment loss	Dental clinical examination/ Hepatological clinical history	Alcoholism (with or without cirrhosis) with worse periodontal parameters	$p < 0.01$ (plaque); $p < 0.001$ (dental care)	Alcoholism is more influential than cirrhosis in periodontal disease
Shoukat et al. (2024)[48]	HCV	Pakistán	Transversal	200 Cases (100) Controls (100)	Periodontal Disease, Oral Hygiene, Brushing Technique	Periodontal clinical evaluation/ Medical diagnosis of HCV	Higher prevalence of periodontal disease in patients with HCV	$p = 0.001$	HCV influences periodontal health; oral prevention is recommended for these patients

CDC/AAP: Centers for Disease Control and Prevention/American Academy of Periodontology; CI: confidence interval; CLD: chronic liver disease; HBV: hepatitis B virus; HCV: hepatitis C virus; NHANES: National Health and Nutrition Examination Survey; OR: odds ratio; PCR: polymerase chain reaction.

analysis of the NHANES database, which showed a significant association between viral infections and periodontal condition.[46] Participants with systemic viral infections, including hepatitis, were found to have a higher prevalence of periodontitis, even after adjusting for confounding factors such as age, gender, socioeconomic status, comorbidities, and smoking. This supports the hypothesis that chronic viral infections can trigger a systemic inflammatory environment, leading to periodontal tissue destruction and further promoting the bidirectional connection between systemic diseases and oral health.[46]

An interesting aspect is the role that alcohol plays as a cofactor in the association between liver and periodontal health. A prospective study conducted in India by Anand et al. compared oral parameters among four groups: patients with chronic liver disease, healthy controls, alcoholics without liver disease, and patients with non-cirrhotic portal hypertension. The findings demonstrated that alcoholics (with or without cirrhosis) had deficient plaque indices, greater periodontal attachment loss, and a higher number of decayed or missing teeth. Furthermore, patients with non-alcoholic liver disease did not show significant differences compared to controls; this suggests that alcoholism and associated habits (poor diet, poor hygiene, and limited access to dental services) have a direct impact on oral health, perhaps more relevant than liver disease alone.[47] From a public health perspective in developing country settings, the study by Shoukat et al. in Pakistan consolidates the findings highlighted from a community-based approach. A descriptive cross-sectional study involving 200 participants (100 with HCV and 100 controls) reveals a statistically significant difference in the prevalence of PD, poor oral hygiene, and incorrect brushing techniques among participants with HCV.[48] This manuscript presents interesting data, indicating that the PD burden in patients with HCV is influenced by both immunological factors and behavioral and social determinants that compromise access to preventive oral care. However, deficiencies in the selection criteria must be considered; specifically, the exclusion of patients with diabetes mellitus is noted, but it is not described whether there is control for other confounding factors such as smoking, alcohol consumption, nutritional status, or medication use. This study highlights the importance of a multidisciplinary approach (hepatology and dentistry) in patients with HCV. It paves the way for future research into shared immunological, salivary, and vascular mechanisms between the two conditions.[48]

Additionally, a possible link has been proposed between chronic viral infections such as HCV, periodontitis, and neurodegenerative conditions such as Alzheimer's disease. This association could be regulated by common mechanisms such as chronic systemic inflammation, oral dysbiosis, and the dissemination of periodontal microorganisms to other organs, including the central nervous system.[49,50] These results support the importance of a multidisciplinary approach that considers not only liver and oral health but also the monitoring of potential neurological disorders in this patient group.

Hepatitis management in periodontal health

Patients with liver conditions require multidisciplinary management, with oral health as a fundamental pillar. Epidemiological findings show a significant association between hepatitis virus conditions and periodontitis, suggesting that liver dysfunction can exacerbate inflammation in periodontal tissues and vice versa.[5,6] Adequate oral health fosters a close collaboration between hepatologists and dentists. Proper dental follow-up includes periodic evaluations, early diagnosis, control of dental biofilm, and oral hygiene education.[51,52] Periodic periodontal assessments are performed essentially every 3–6 months, depending on the individual patient's risk (Gheorghe et al.[53]). An early diagnosis of oral signs of hepatitis, such as persistent ulcers, petechiae, and excessive gingival bleeding, may suggest underlying liver dysfunction. The design and implementation of personalized periodontal prophylaxis programs for plaque control and topical antimicrobial strategies to decrease bacterial load are unpredictable; periodontal management should be tailored to the severity of liver dysfunction and the patient's medications.[51] In advanced liver disease, patients may present with coagulation disorders; therefore, it is crucial to request blood tests before performing periodontal treatments.[52,53]

Additionally, pharmacotherapy in patients with hepatitis must be approached with caution since altered hepatic metabolism can lead to changes in response to local anesthetics and antibiotics frequently administered in periodontal management. Given that the immune response of these

patients is often compromised, maintaining good oral hygiene is crucial in preventing secondary infections. Therefore, personalized instruction in brushing and flossing techniques is recommended. For regular use, alcohol-free antimicrobial mouthwashes (such as 0.12% chlorhexidine) may reduce the bacterial load without causing xerostomia. In specific cases, such as severe dry mouth, artificial saliva or salivary stimulants may be indicated to increase lubrication and reduce the risk of caries and oral candidiasis.[52]

In addition, recent studies have demonstrated that non-surgical periodontal management can have a broader impact beyond the oral environment. Isola et al. showed that subgingival mechanical decontamination in patients with periodontitis, with or without the addition of chlorhexidine, significantly reduces systemic levels of inflammatory markers, positively contributing to the control of systemic conditions[54] and strengthening the hypothesis that periodontal treatment modulates the immunoinflammatory response and could improve the clinical picture in patients with viral liver conditions.

Treatment with antivirals, such as interferon and ribavirin, can trigger side effects in the oral cavity.[51] Therefore, ongoing monitoring for potential complications such as xerostomia, ulcerations, lichenoid lesions, and decreased healing capacity in gingival tissue is suggested, which consequently compromises the response to periodontal treatments.[51,52] Dentists should be alert to these adverse effects and adjust therapeutic strategies according to patient tolerance; in some cases, it may be necessary to consult a hepatologist to consider adjustments to medication.[53,55] Ongoing coordination between hepatologists and dentists is essential to optimize the quality of life for patients with liver conditions. Due to the bidirectional link between periodontal health and liver dysfunction, comprehensive care management should include both monitoring of the systemic condition and the prevention and treatment of periodontal complications.

Future perspectives

A growing recognition of the bidirectional relationship between periodontitis and viral hepatitis, especially HBV and HCV, raises the need for more in-depth and detailed research to clarify the underlying mechanisms and their clinical impact. Therefore, several lines of research are suggested that could be addressed in the years to come. The link between periodontitis and hepatitis remains unclear, likely due to shared immunological and microbiological factors. The chronic inflammatory process characterized by periodontitis may contribute to and favor the progression of liver damage; on the other hand, the immune modifications generated by hepatitis suggest a predisposition to a more severe periodontal condition. Some studies have shown that patients with HCV infection present more severe periodontitis compared to uninfected individuals. However, it is necessary to determine whether this association is causal or attributed to confounding factors, such as associated comorbidities or lifestyle; therefore, future longitudinal studies and/or clinical trials will provide more conclusive findings. Exploring the development of specific biomarkers will enable the optimal characterization of patients with both conditions, allowing for personalized prevention and treatment management. Some studies have demonstrated increased levels of the NLRP3 inflammasome and inflammatory cytokines (such as IL-18 and caspase-1) in patients with chronic hepatitis and periodontitis, suggesting their potential use as biomarkers of disease progression. Likewise, the presence of HCV viral RNA in the saliva and GCF of patients with hepatitis has been analyzed, supporting the need to determine its role in periodontal pathogenesis and its potential use in early diagnosis.

Future therapeutic strategies should consider analyzing the impact of periodontal management on the development and progression of liver disease. Certain studies propose periodontal therapy to modify the composition of the intestinal microbiota in patients with cirrhosis, which would have significant therapeutic implications. Likewise, given the availability of direct-acting antivirals for HCV and the progress in therapeutic regimens for HBV, it would be interesting to evaluate whether the resolution of liver infection improves periodontal health in patients. Consideration should be given to exploring combined interventions that integrate gut–liver axis modulation through probiotics or specific anti-inflammatory agents. Recent studies suggest an interrelationship between periodontitis and hepatitis; however, there are still gaps in the scientific evidence. Longitudinal research analyzing the bidirectional relationship, the impact of chronic inflammation, the role played by the oral microbiota and its

translocation to the hepatic system, and studies on the effectiveness of new therapeutic strategies applied in the prevention and management of both conditions are essential.

Conclusion

The scientific evidence analyzed in this review supports a bidirectional association between viral hepatitis, particularly HBV and HCV, and periodontitis. This link is based on shared pathophysiological mechanisms, including chronic systemic inflammation, microbial dysbiosis, and immunological changes. Furthermore, the participation of viral markers in the oral ecosystem has been identified, supporting the possibility that the oral cavity functions as a viral reservoir and modulates the progression or transmission of the infection.

In light of this perspective, it is necessary to promote an interdisciplinary approach between dentistry and hepatology, emphasizing prevention, early diagnosis, and comprehensive management. Furthermore, future research should further elucidate the shared molecular mechanisms, identify diagnostic biomarkers, and analyze the impact of periodontal treatments on the progression of liver conditions. Understanding and managing the oral-hepatic axis presents a strategic opportunity to improve the quality of life for patients affected by these conditions and promote control of two of the world's leading chronic diseases.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Author contributions

Ruth Rodríguez-Montaño: Conceptualization; Formal analysis; Investigation; Supervision; Validation; Visualization.

Melissa Martínez-Nieto: Investigation; Writing – original draft; Writing – review & editing.

Gustavo Eder González-Alvarez: Formal analysis; Software; Writing – review & editing.

Mario Alberto Alarcón-Sánchez: Conceptualization; Formal analysis; Investigation; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

Julieta Sarai Becerra-Ruiz: Software; Validation; Writing – original draft; Writing – review & editing.

Artak Heboyan: Formal analysis; Validation; Visualization; Writing – original draft; Writing – review & editing.

Alba Ruiz-Gaitán: Formal analysis; Software; Writing – original draft; Writing – review & editing.

Sarah Monserrat Lomelí-Martínez: Conceptualization; Formal analysis; Investigation; Project administration; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The data supporting this study's findings are available from the corresponding author upon reasonable request.

ORCID iDs

Mario Alberto Alarcón-Sánchez https://orcid.org/0000-0001-6727-7969

Artak Heboyan https://orcid.org/0000-0001-8329-3205

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