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Periodontal disease and liver cirrhosis: A systematic review

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Abstract

Objectives: Studies suggest that periodontal disease, a source of subclinical and persistent infection, may be associated with various systemic conditions, including liver cirrhosis. The aim of this study was to examine the literature and determine the relationship between periodontal disease and liver cirrhosis and to identify opportunities and directions for future research in this area.

Methods: A systematic review of English articles in the PubMed, EMBASE, and Scopus databases was conducted using search terms including 'liver cirrhosis', 'end-stage liver disease', 'liver diseases', 'oral health', 'periodontal disease', 'mouth disease', 'gingivitis', and 'periodontitis'.

Results: Thirteen studies published between 1981 and 2014 were found to include data on oral health and periodontal disease in cirrhotic patients. Studies indicated an increased incidence of periodontal disease in patients with liver cirrhosis, measured with several different periodontal indices. The reported prevalence of periodontal disease in cirrhosis patients ranged from 25.0% to 68.75% in four studies and apical periodontitis was found in 49%–79% of the patients. One study found that mortality was lower among patients who underwent dental treatment versus non-treated patients. Another study suggested an association between periodontal disease and the progression of liver cirrhosis, but data are sparse and conflicting as to whether periodontal disease is correlated to cirrhosis aetiology and severity.

Conclusion: Despite the clinical reality of periodontal disease in liver cirrhosis patients, there are few published studies. Before clinical implications can be addressed, more data on the prevalence of and correlation between periodontal disease and liver cirrhosis aetiology, duration, and progression are needed.

Keywords

Liver cirrhosis, oral health, periodontitis, periodontal disease, systematic review

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Introduction

Studies indicate an association between periodontal disease and different systemic diseases, although a direct relationship has not yet been established. Possible explanations may include oral hygiene neglect, shared risk factors, and chronic inflammatory processes.[1,2] The existence of periodontal disease may affect a patient's immunity, which can result in systemic infections such as respiratory infections and bacteraemia.[3] While the relationship of periodontal disease to systemic conditions such as diabetes[4] and cardiovascular disease[5] is fairly well established, the role played by liver cirrhosis needs further clarification.

Several studies have reported an association between periodontal disease and liver cirrhosis. The earliest study was published in 1960 by Sandler and Stahl.[6] In this study, the authors found a significantly higher rate of periodontal disease compared to the control group. Other cirrhotic outcomes that have been linked to periodontal disease include the progression in liver disease, accelerated Model for End-Stage Liver Disease (MELD) scores,[7] and the occurrence of systemic infections.[8]

Despite the advanced medical therapies that have greatly improved the ability to prevent and treat cirrhosis complications, bacterial infections are common and increase morbidity

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and mortality.[9,10] The affirmation of oral diseases as an independent risk factor for adverse cirrhotic outcomes would be of great importance because this disease is both preventable and treatable. Yet, dental diseases and complaints have been ignored in the already published literature, which makes the approaches of effective management questionable. This study therefore aimed to systematically review the literature to evaluate the relationship between periodontal disease and liver cirrhosis and to establish directions for future research.

Definition of periodontal disease

Periodontal disease is a common chronic disorder, with an estimated prevalence between 10% and 60% in adults.[9–11] Periodontal disease results in local infections that occur in tooth-supporting tissues and refers to a reversible (gingivitis) or irreversible (periodontitis) process. Gingivitis is a condition with inflammation of the soft tissues surrounding the tooth or gingiva; over time, it may develop into periodontitis.[12] Periodontitis destroys the connective tissues of the teeth and leads to progressive loss of the alveolar bone around the teeth, eventually leading to tooth loss. It can be diagnosed by clinical examination with a periodontal probe to determine the pocket depth and clinical attachment loss in combination with radiographic examination.[13] Periodontal disease can typically be successfully treated. The primary prevention method of gingivitis and periodontitis is the careful practice of oral hygiene, which includes daily brushing to keep teeth clean of dental plaque and calculus as well as regular dentist visits.[14]

One of the difficulties in periodontal disease–related research is the great variation in the definitions and clinical measurements used. Various indices have been developed to measure the extent of periodontal disease, but no one index has universal application or acceptance.[12,15]

Methods

Search method for the identification of studies

Before performing the search, a search protocol was prepared to document review aims, inclusion and exclusion criteria, and the search strategy. The systematic search was conducted on 6 February 2015 in the EMBASE, PubMed, and Scopus online databases. References were cross-checked to identify all studies that were relevant for inclusion. The following search terms were used as free-text, MeSH, and Emtree terms: ‘liver cirrhosis’, ‘end-stage liver disease’, ‘liver diseases’ and ‘oral health’, ‘periodontal disease’, ‘mouth disease’, ‘gingivitis’, and ‘periodontitis’. Different forms of spelling and synonyms of each term were also used.

Inclusion criteria of studies considered in this review

Types of studies. There were no inclusion criteria regarding study design and methodological quality of the included articles because part of the purpose was to discuss the aspects of study designs that were suitable for research in this area. There were no restrictions on publication year, but only studies that were written in English were considered.

Types of participants. Studies were required to include a group of cases with a clinical diagnosis of liver cirrhosis. The mean age of the study sample had to be older than 18 years.

Types of interventions. Studies investigating cirrhosis aetiology and severity as risk factors for periodontal disease were included to evaluate the pattern of periodontal disease in liver cirrhosis.

Types of outcome measures. The outcome being evaluated was the presence and prevalence of periodontal disease. No limitations were set for the technical equipment used, and all types of periodontal disease measurement were accepted.

Presentation of results. Articles were included if they reported original sample data analysis.

Data extraction

Data extraction was performed using a predefined data extraction form concerning the following: (a) the characteristics of participants (including age, gender, severity of disease, and aetiology of cirrhosis) and the participant recruitment of studies, (b) the definition of periodontal disease, and (c) the frequency and type of periodontal disease in patients with liver cirrhosis.

Assessment of methodological quality

There are no standard accepted quality scales for studies involving prevalence or with a cohort or cross-sectional design.[16] In this study, the quality of the included articles was assessed with a modified assessment tool developed by The National Heart, Lung, and Blood Institute and the Research Triangle Institute International, USA.[17]

The tools included 14 items for cohort studies and 11 items for cross-sectional studies, evaluating potential flaws in study methods including sources of bias, confounding, and the strength of causality in the association between interventions and outcomes and other factors. Each item was rated 0 = no or 1 = yes, resulting in a maximum of 14 or 11 points per article (Table 1).

Data synthesis

Because of the high level of heterogeneity in patient characteristics, periodontal disease definitions, and techniques used across studies, it was not appropriate to apply statistical methods to estimate the overall pooled risk of periodontal disease in the studies. Instead, a descriptive assessment of the results based on the extracted data was performed.

Table 1. Quality scores for articles on periodontal disease and liver cirrhosis fulfilling the inclusion criteria.

	Åberg et al.[7]	Lins et al.[8]	Guggenheimer et al.[18]	Raghava et al.[19]	Castellanos-Cosano et al.[20]	Silva Santos et al.[21]	Panov and Krasteva[22]	Jaiswal et al.[23]	Niculescu et al.[24]	Oettinger-Barak et al.[25]	Oettinger-Barak et al.[26]	Novacek et al.[27]	Movin[28]
Cohort score (0–14)	10	10	10										
Cross-sectional score (0–11)				5	7	5	4	4	3	4	4	7	6

Results

Description of studies

The searches produced a total of 3356 hits. After the elimination of duplicates, 2500 articles were reviewed by title and abstract and 22 articles were identified for full-text assessment. The references were hand searched from the identified articles. After full-text reviews, 13 articles met the inclusion criteria. A summary of the process is shown in a flow diagram, according to the PRISMA statement[29] (Figure 1). Reasons for the exclusion of reviewed full-text articles are presented in Table 2.

Description of included articles

The 13 articles meeting the inclusion criteria were based on 12 study samples and were published between 1981 and 2014.[7,8,18–28] Two studies were conducted on the same study population: one study investigated the radiographic findings and the other study investigated the clinical findings.[25,26]

Study design

Three studies were cohort studies,[7,8,18] nine of the studies were cross-sectional studies, of which eight included control groups[19–22,25–28] and the last study was a retrospective review of medical records.[24] The studies were conducted in 10 countries: one each from Austria, Bulgaria, Denmark, Finland, Romania, Spain, and United States and two each from India, Israel, and Brazil. In 11 studies, the primary aim was the investigation of oral health and periodontal disease in cirrhotic patients.[8,18–22,24–28] In the remaining studies, the association between periodontal disease and serum alkaline phosphatase, MELD score and spontaneous bacterial peritonitis (SBP) episodes,[7,23] was investigated. Two studies also investigated the outcome after treating patients for periodontal disease.[8,21]

Liver cirrhosis patients

In total, 905 patients (562 men and 283 women, two studies failed to describe the gender of the participants) with liver cirrhosis participated in the studies on which this review is based. The sample sizes varied from 13 to 280 cirrhosis patients with an age range from 22 to 87 years. Diagnoses of cirrhosis varied between the studies. In five studies, the study population consisted of patients with different aetiologies of liver cirrhosis, for example, alcohol, viral hepatitis B or C, cryptogenic, autoimmune liver disease, or non-alcoholic steatohepatitis (NASH).[7,8,18,21,27] In two studies, the population consisted of patients with chronic hepatitis B or C and cirrhosis or alcoholic cirrhosis.[19,22] In the last six studies, the aetiology of cirrhosis remained unclear.[20,23–26,28]

In one of the studies, it remained vague how and from which study population the samples were recruited.[19] The other studies recruited in- and out-patients from gastroenterology and

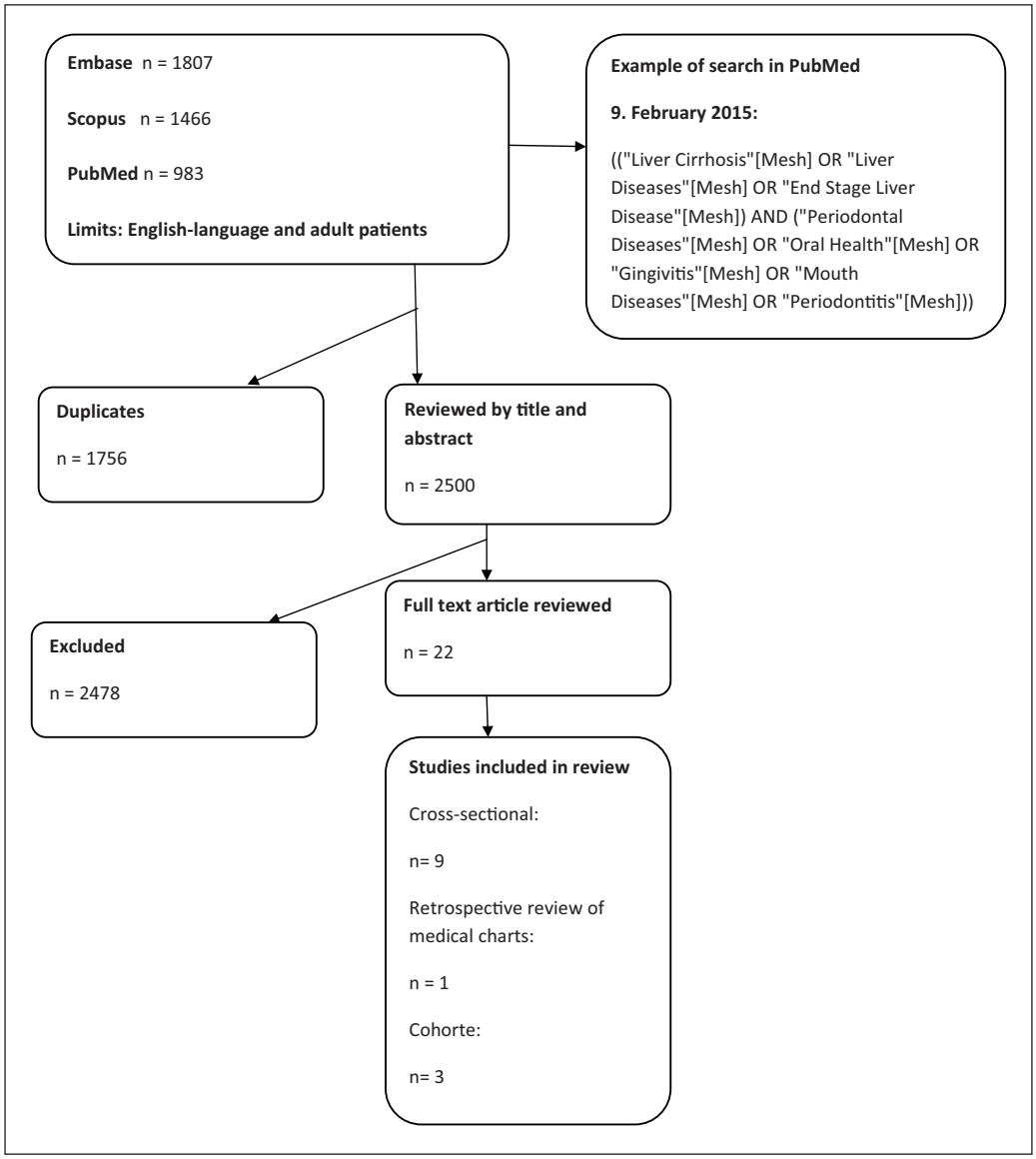

Figure 1. Flow chart of the review process.

Table 2. Reasons for excluding retrieved articles.

Study	Reasons for exclusion
Helenius-Hietala et al.[30]	Liver cirrhosis post-transplantation
Nagao et al.[31]	Not possible to extrapolate data for cirrhosis patients
Helenius-Hietala et al.[32]	Liver cirrhosis post-transplantation
Helenius-Hietala et al.[33]	Shared subject data with Åberg et al.[7]
Nagao et al.[34]	No diagnosis of liver cirrhosis
Diaz-Ortiz et al.[35]	Liver cirrhosis post-transplantation
Coates et al.[36]	No diagnosis of liver cirrhosis
Barbero et al.[37]	Non-English language
Sandler and Stahl[6]	Insufficient result presentation

Studies may have met exclusion criteria other than those listed in the table.

hepatology units; in eight of these studies, recruited patients were on a waiting list prior to liver transplantation.[7,8,18,20–22,25,26]

Methodological quality of the included studies

The quality scores of the nine cross-sectional studies and the medical review ranged from 3 to 7 points, with a mean score of 4.9. The cohort studies scored 10 out of a possible 14 points (Table 1).

In relation to the description of the participant characteristics, two studies did not fully describe the age and gender of liver cirrhosis patients or controls[19,24] and three articles had no description of the recruiting method used for liver cirrhosis patients or the control group.[19,22,23] The remaining recruited control groups were recruited from the local health district,[20] dental school,[21] or were blood donors.[27,28] Only two articles described a systematic method for the recruitment of control groups.[25,26]

Regarding the sampling methods used, one article reported the use of consecutive sampling,[18] two articles reported including all cirrhosis patients awaiting liver transplantation,[7,8] and two articles invited patients to participate.[25,26] The remaining eight failed to report on this aspect or used convenience samples. Controlling for confounding was performed adequately in relation to age,[18,20,23,25,26,28] gender,[25,26] smoking,[19,20] and socioeconomic background.[23,28]

In relation to the evaluation of periodontal disease, all studies except one had acceptable definitions describing the periodontal disease findings.[24] Nine studies used different periodontal indices, and in three studies, the researcher used their own definitions.[7,18,24]

In relation to the statistical analysis, three articles failed to fully report the confidence interval and/or p values of the periodontal findings.[8,22,24] Two articles had shortcomings in the manner in which the results were presented; the data were primarily presented as graphics.[27,28] Study characteristics and periodontal disease outcomes are presented in Table 3.

Prevalence of periodontal disease in patients with liver cirrhosis

The definition of the prevalence of periodontal disease varied in the different studies. In four studies with a total of 459 cirrhosis patients, the reported prevalence of periodontal disease ranged from 25.0% to 68.75%.[8,18,21,24] This was significantly different from that of the control group used in the study of Silva Santos et al.[21] In one study, cirrhosis patients had an average of five teeth with a pocket depth of ⩾6 mm, indicating periodontitis.[7] In two studies with 173 cirrhosis patients, the prevalence of apical periodontitis was 49%–79%.[8,20]

A study with 13 cirrhotic patients found more periodontal disease than the control group reported by gingival overgrowth, greater pocketing, attachment loss, and bone loss, despite similar plaque and gingival scores.[25,26] However, one study with 30 cirrhosis patients did not find such a difference in the loss of attachment between the cirrhosis and control groups.[28] Another study found that the loss of attachment and thereby periodontal disease in patients with cirrhosis was higher than in the healthy control group, but this tendency was only significant in the group of patients with alcoholic cirrhosis.[27] This was in accordance with a study of 50 patients with alcoholic cirrhosis who demonstrated greater alveolar bone loss and an increased incidence of periodontal disease compared to healthy controls.[19] Another study compared 60 cirrhotic patients with and without periodontitis and found that the loss of clinical attachment level and bone loss were significantly higher in the group of patients with periodontitis, despite similar plaque and gingival scores in both groups.[23] Three studies with 152 cirrhosis patients found a higher degree of gingival inflammation compared to controls.[22,27,28]

Relationship of periodontal disease with liver cirrhosis

Few studies have addressed the relationship between periodontal disease and liver cirrhosis, but those that were published show that cirrhosis as a disease itself does not contribute to the development of periodontal disease.[18,27,28] Instead, studies suggest that the aggravation of the periodontal conditions is related to increasing oral hygiene neglect. Oral hygiene neglect and infrequent professional dental care were associated with periodontal disease, extracted teeth, caries lesions, dental plaque, and calculus in seven studies.[7,18–20,22,27,28] In addition, two studies indicated that patients suffering from cirrhosis for more than 3 years showed a significantly greater loss of attachment, as well as having more plaque compared with those with disease duration of less than 3 years.[19,28] However, one study of 97 cirrhotic patients found no such association.[27]

A retrospective study found an association between periodontal disease and accelerated liver disease, as measured by the progression of the MELD score during the year preceding dental examination.[7] Furthermore, a study group found a positive correlation between periodontal breakdown and serum alkaline phosphatase level in liver cirrhosis patients.[23]

Other oral manifestations

Eight studies with a total of 671 cirrhosis patients indicated a high prevalence of poor oral health status,[8,18–22,27,28] and one study stated that the most frequent gastrointestinal disease that is associated with oral lesions is liver cirrhosis.[24] A small study with 16 cirrhosis participants found that all patients were diagnosed with at least one oral disease or condition that needed treatment. In addition to periodontal disease, petechiae were diagnosed in 18.75% of patients, ulceration and angular cheilitis were diagnosed in 6.25% of patients, and oral candidiasis was diagnosed in 12.5% of patients.[21] In another study, oral candidiasis was observed in 5.7% of patients.[18] Furthermore, in two studies, mucosal lesions were

Table 3. Study characteristics and periodontal disease outcomes.

Characteristics of studies					Definitions of periodontal disease			
Study	Study design	Sample size	Characteristics of cirrhosis patients	Age (years)	Outcome measure	Results	Confounders being controlled	Conclusions
Åberg et al.[7]	Cohort	N = 116	ALC: 37 PBC: 31 CC: 15 Others: 33 Men: 64 Women: 54 Listed for transplantation	52 ± 10	Mean number of periodontal pockets, mean number of extracted teeth, mean number of ABL, mean number of teeth	⩾4 mm periodontal pockets 8 ± 8, ⩾6 mm periodontal pockets 5 ± 3, extracted teeth 4 ± 4, ABL (mm) 3 ± 1, 22 ± 9 teeth	No	Dental infections may influence the clinical course of cirrhosis Increase in MELD score correlated with number of extracted teeth
Lins et al.[8]	Cohort	N = 131	ALC: 39 HCV: 55 CC: 18 Others: 19 Men: 100 Women: 31 Listed for transplantation	49 ± 11	CAL, PPD, number of oral manifestations, DMFT	Periodontitis 52%, mucosal lesions 17%, xerostomia 48%, PL 48%, and abscesses 49%. DMFT men 18.9 ± 9.9, DMFT women 16.9 ± 10.7	No	Patients with liver cirrhosis exhibit a high prevalence of poor oral health status as well as oral infections. Treatment of patients is associated with reduction in mortality
Guggenheimer et al.[18]	Cohort	N = 300 Cirrhosis: 280 Other patients: 20 Study compared with national surveys	ALC: 80 HBV or HCV: 95 Other cirrhosis: 105 Men: 173 Women: 127 Listed for transplantation	35–79	Number of edentulism, severe dental disease, candidiasis, gingivitis, plaque, and xerostomia	Edentulism 22.3%, severe dental disease 31.8%, OC 5.7%, plaque 63.4%, and xerostomia 43%	Yes (age)	The most significant factor for dental disease 12 months or longer since previous dental visit
Raghava et al.[19]	Cross-sectional	N = 150 Cirrhosis: 50 Controls: 100	ALC: 25 smokers, 25 non-smokers	NA	Russell's index	ALC non-smoker 3.71 ± 1.14 ALC smoker 4.74 ± 0.56 Control non-smoker 1.67 ± 0.35 Control smoker 2.10 ± 0.34	Yes (smoking)	Both ALC non-smoker and smoker demonstrate greater alveolar bone loss and increased periodontal destruction
Castellanos-Cosano et al.[20]	Cross-sectional	N = 84 Cirrhosis: 42 Controls: 42	Aetiology NA Men: 30 Women: 12 Listed for transplantation	59 ± 9	PAI index AP RFT	Cirrhosis: AP: 79% RFT: 19% Controls: AP: 50% RFT: 62%	Yes (sex, smoking, age)	Cirrhosis patients have higher prevalence of radiographic periapical lesions and lower frequency of RFT than controls

Table 3. (Continued)

Characteristics of studies					Definitions of periodontal disease			
Study	Study design	Sample size	Characteristics of cirrhosis patients	Age (years)	Outcome measure	Results	Confounders being controlled	Conclusions
Silva Santos et al.[21]	Cross-sectional	N = 32 Cirrhosis: 16 Controls: 16	ALC: 3 HCV: 5 HCV or HBV and ALC: 7 Wilson: 1 Men: 13 Women: 3 Listed for transplantation	51 (range 37–68)	Number of oral manifestations, number of caries	Patients: PD 68.75%, PTC 18.75%, OC 12.5%, GO, AC, UL, and xerostomia 6.25%, caries 81.25% Controls: PD 62.5%, OC 6.25%, caries 43.75%	No	Patients with liver cirrhosis exhibit a higher incidence of oral manifestations compared to controls
Panov and Krasteva[22]	Cross-sectional	N = 96 Cirrhosis: 25 Controls: 71	HBV and HCV Men: 13 Women: 12 Listed for transplantation	55 (range 24–87)	PBI, dental caries, number of missing teeth, OHI	Patients: PBI 2.53 ± 0.9, missing teeth 9.8 ± 9.2, OHI 2.7 ± 1.5, caries 1.26 ± 3.8 Controls: PBI 1.95 ± 0.9, missing teeth 3.0 ± 5.4, OHI 1.53 ± 1.2, caries 0.94 ± 1.3	No	Patients with liver cirrhosis have poor oral health and significant oral health needs
Jaiswal et al.[23]	Cross-sectional	N = 60	Aetiology NA 60 cirrhotic men divided into two groups: 30 with periodontitis (called test group) and 30 without periodontitis (called control group)	43 (range 32–44)	OHI GI ABL CAL	Test group: OHI 1.36 ± 0.11, GI 0.89 ± 0.06, ABL 1.62 ± 0.32, CAL 2.34 ± 0.67 Control: OHI 1.39 ± 0.16, GI 0.76 ± 0.21, ABL 0.28 ± 0.04, CAL 0.43 ± 0.14	Yes (age)	The loss of clinical attachment was significantly higher in the group of cirrhosis patients with periodontitis despite similar plaque and gingival score
Niculescu et al.[24]	Review of medical charts	N = 430 Cirrhosis: 32 Other patients: 398	Aetiology NA	46 ± 3 (range 22–76)	Number of mucosal disorders, gingival disorders, periodontal disorders	Number of mucosal disorders 16 patients, gingival disorders 16 patients, periodontal disease 8 patients	No	The most frequent GI disease associated with oral lesions was liver cirrhosis
Oettinger-Barak et al.[25]	Cross-sectional	N = 30 Cirrhosis: 13 Control: 17 Other patients: 24	Aetiology NA Men: 7 Women: 6 Listed for transplantation	46 ± 13	Radiographic alveolar bone height	Patients: 6.47 ± 0.75 Controls: 2.73 ± 0.38	Yes (age, sex)	Liver cirrhosis patients demonstrated greater bone loss compared to healthy controls

(Continued)

Table 3. (Continued)

Characteristics of studies					Definitions of periodontal disease			
Study	Study design	Sample size	Characteristics of cirrhosis patients	Age (years)	Outcome measure	Results	Confounders being controlled	Conclusions
Oettinger-Barak et al.[26]	Cross-sectional	N = 30 Cirrhosis: 13 Control: 17 Other patients: 24	Aetiology NA Men: 7 Women: 6 Listed for transplantation	46 ± 13	PI GI PPD, CAL, GO	Patients: PI 2.03 ± 0.2, GI 1.19 ± 0.1, PPD 3.32 ± 0.2, CAL 4.89 ± 0.5, GO 0.37 ± 0.1 Controls: PI 1.71 ± 0.13, GI 1.18 ± 0.09, PPD 2.45 ± 0.23, CAL 2.78 ± 0.23, GO 0.09 ± 0.02	Yes (age, sex)	Liver cirrhosis patients demonstrated greater pocketing and attachment loss compared to healthy controls despite same plaque and gingival score
Novacek et al.[27]	Cross-sectional	N = 236 Cirrhosis: 97 Controls: 71 Other patients: 68	ALC: 64 PBC: 5 CC: 1 HCV: 11 HBC: 3 Others: 13	31–60	Number of teeth, number of carious teeth, OHI, CAL	Patients: number of teeth 21, number of carious teeth non-ALC 2% in ALC 21.3%, OHI non-ALC 55% in ALC 18% Controls: number of teeth 24, number of carious teeth 1.2%, OHI 72%	Yes (multiple linear regression)	Patients with non-ALC did not differ in number of teeth, number of carious teeth, and the loss of attachment Cirrhosis does not contribute to the development of periodontal disease
Movin[28]	Cross-sectional	N = 73 Cirrhosis: 30 Controls: 43	Aetiology NA Men: 25 Women: 5	53 ± 1.5	Number of teeth, PI, GI, RC, RDF, loss of attachment	Patients: teeth 13 ± 8, CAL 4.65 ± 0.31 Controls: teeth 13 ± 8, CAL 4.12 ± 0.25	Yes (age, sex, socioeconomic background)	Liver cirrhosis patients demonstrated greater gingival inflammation and calculus compared to controls despite same plaque score and loss of attachment and tooth loss Patients with cirrhosis >3 years showed greater loss of clinical attachment, plaque, and calculus

ALC: alcoholic liver cirrhosis; PBC: primary biliary cirrhosis; CC: cryptogenic cirrhosis; HCV: hepatitis C virus; HBV: hepatitis B virus; MELD score: Model for End-Stage Liver Disease; NA: not available; ABL: alveolar bone loss in mm; PD: periodontal disease; GO: gingival overgrowth; OC: oral candidiasis; PTC: petechiae; AC: angular cheilitis; UL: ulceration; CAL: clinical attachment loss; PPD: probing pocket depth; PL: periapical lesions; PBI: papilla bleeding index; OHI: oral hygiene index; GI: gingival index; PI: plaque index; RC: retentive calculus; DMFT: dental manifestations; PAI: periapical index; AP: apical periodontitis; RFT: root-filled teeth; RDF: retentive decay and fillings.

observed in 13%–25% of the 163 liver cirrhosis patients.[8,24] Three studies investigated xerostomia and reported that salivary flow was reduced from 6.25% to 48% in patients with liver cirrhosis.[8,18,21]

Treatment of periodontal disease

In two studies with 147 cirrhosis patients, dental treatment procedures were performed after dental examination.[8,21] Although the majority of patients showed abnormal coagulation values, only one patient in the study of Lins et al.[8] had complications such as dental haemorrhage during dental surgery. After dental treatment, mortality was significantly lower among patients who underwent treatment for periodontal disease versus non-treated patients, particularly among patients with more advanced liver disease.

Discussion

The results of this review show that patients with liver cirrhosis exhibit a high prevalence of poor oral health and periodontal disease. In four studies, periodontal disease was seen in 25%–69% of the patients, and apical periodontitis was, in two studies, diagnosed in 49%–79% of the patients. In addition, the remaining studies show a significantly increased incidence of gingival inflammation, clinical attachment loss, and bone loss compared to the different control groups. However, one study from Austria by Novacek et al.[27] did not find this tendency to be significant in the group of patients with non-alcoholic cirrhosis. This is in accordance with the findings of Helenius-Hietala et al.,[33] who considered non-alcoholic cirrhosis patients to be more health conscious than those with alcoholic cirrhosis. Still, Guggenheimer et al.[18] found no difference in dental disease between alcoholic cirrhosis and non-alcoholic cirrhosis patients, making it impossible to conclude whether periodontal disease is attitude or disease dependent. Further research is required to establish the impact of cirrhosis aetiology on periodontal disease.

Many factors can induce poor oral health, such as age, education level, cognitive function, depression, lack of motivation, and use of medication and disease.[38] In this review, three studies investigated the duration of cirrhosis on periodontal disease.[19,27,28] Of these, two studies found that patients diagnosed with cirrhosis for more than 3 years had more problems with periodontal disease than those with disease duration of less than 3 years.[19,28] This indicates that the aggravation of periodontal conditions is consistent with the neglect of oral health as the cirrhosis progresses. However, further research is needed to establish the relationship between cirrhosis duration and periodontal disease.

The poor oral health status in cirrhosis patients can be attributed not only to poor oral hygiene but also to a lack of dental care access. In this review, over half of the studies indicated a high prevalence of poor oral health status among patients;[8,18–22,27,28] however, none of the studies investigated the patients' oral care habits, and only a study by Guggenheimer et al.[18] presented data on patients' dental insurance status. Therefore, it is not possible to evaluate economic conditions, insurance status, self-neglect, or dental anxiety as factors that could have affected the results. However, recent studies have shown a strong association of the effects of lifestyle and socioeconomic status on periodontal health.[39] The possible effect modification of these conditions is worth investigating.

As previously stated, periodontal disease may increase the presence of systemic infections. In this review, only one study investigated and found an association between periodontal diseases and accelerated liver disease.[7] This is in accordance with evidence suggesting an association between periodontal disease and atherosclerosis, myocardial infarction, stroke, and diabetes mellitus.[40] In addition, studies address the effect of periodontal treatment on the amelioration of these systemic diseases.[41] Periodontal disease should therefore be examined and treated. However, there are concerns about the risk of performing dental treatments in cirrhosis patients. In this review, two studies treated periodontal disease in patients with liver cirrhosis.[8,21] The results showed few complications and a low mortality rate among the treated patients. However, the authors stated that the results are not conclusive because patients with advanced liver cirrhosis were lost to follow-up. Hence, further studies are needed.[8]

There were several methodological weaknesses in the included studies that may have affected the results. First, a great variation in the definitions of periodontal disease was observed. Researchers used their own case definitions combined with probing depth and/or clinical attachment loss or used different indices to define periodontal disease. Few of the 13 included studies used the same definition. Obviously, different criteria to define periodontal disease will result in different outcomes. The lack of consensus and uniformity in the definition of periodontal disease makes findings difficult to interpret and compare. This problem has been highlighted of several researchers, who suggest establishing uniform criteria for defining periodontal disease and measuring tool in periodontal research.[42,43]

A second weakness is the confounding effects. Whether the observed association is a result of the causality of the confounding effects of other variables such as socioeconomic background, smoking, gender, comorbidity, or age[44] is questionable.

Although 8 of the 13 studies that were reviewed controlled for some confounding variables or used multivariable regression analysis, several essential confounding variables such as comorbidity with diabetes, obesity, smoking, and age were not considered, resulting in some potentially remaining residual confounding effects.

Another potential bias is the sample size. The smaller the sample size, the lesser the sample size is representative of the population studied. In this review, the majority of studies had a sample size of less than 100 cirrhosis patients.[19–28] In the future, studies with larger sample sizes need to be carried out to confirm the results observed in this review.

Because of a growing interest in the association between systemic diseases and periodontal disease, there is a need for methodologically strong observational studies with a clear definition of periodontal disease, a sufficiently large sample size of cirrhosis patients, and controls for key confounders. As more studies are conducted, the collection of more data allows for the examination of whether periodontal disease is an independent risk factor and also allows for the assessment of the effects of liver cirrhosis aetiology, severity, and duration.

Future directions of periodontal disease–related research in liver cirrhosis

In future studies of periodontal disease in liver cirrhosis, several issues must be addressed to manage therapies for periodontal disease. First, further prospective studies of the prevalence of periodontal disease in liver cirrhosis cohorts are required, particularly adjusting for periodontal risk factors and stratifying by cirrhosis aetiology, severity, and duration. Second, evaluating the component between periodontal disease and progression of liver cirrhosis and complications will guide future management principles. Furthermore, the treatment of periodontal disease to reduce mortality in cirrhosis patients must be explored. Finally, there is a need to establish preventive actions to improve oral health in patients with liver cirrhosis.

Methodological considerations of this review

The strength of this review is the systematic search of selected databases and the evaluation of the methodological quality of the included studies. At this time, this systematic review is the first to report on periodontal disease in patients with liver cirrhosis.

The weaknesses of the review are, first, the possibility that relevant articles were not included because of the language limitation and, second, that only a limited number of databases were searched. The inclusion of grey literature, such as unpublished articles, may potentially minimize the effect of publication bias, but to search and access grey literature can be challenging and were not possible with the time resources available.

In this review, there were no predetermined minimal criteria related to the quality of the included articles. If the results had varied greatly between studies, it would have been necessary to analyse the definitions and methodologies of the studies to understand such diversity.

This systematic review revealed that the methodological quality of the included studies was generally low. But since a part of the purpose was to explore study designs suitable for research in this field and make recommendations for future research, it was necessary to include these, although the low quality could possible lead to a biased result. In future research, methodologically stronger studies are needed.

This review has only one author. However, because it was prepared in connection with a PhD course in systematic reviews and meta-analysis, any disagreements or questions were settled by discussion and consensus with experiences teachers and colleagues. Therefore, the results are most likely reproducible and biases limited.

Conclusion

There is evidence of a relationship between periodontal disease and liver cirrhosis particularly due to poor oral health, but with only 13 published articles on this subject, it is not possible to come to a clear conclusion. Because periodontal disease may be a risk factor for the progression of liver cirrhosis, there is a need to understand this correlation. Based on the combined findings in this review, it is recommended that future studies have a prospective design. Factors related to periodontal disease should be explored to determine the relationships between cause and effect, the differences between cirrhosis aetiology and duration, and the role of comorbidity. Moreover, periodontal disease must be well defined and assessed with valid methods. Such studies will allow for the identification of the increased risk of periodontal disease in liver cirrhosis patients and hence allow early prevention and treatment interventions to be initiated.

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