Human & Veterinary Medicine
International Journal of the Bioflux Society HVM

OPEN ACCESS
Research Article

Assessments of periodontal parameters in patients with liver fibrosis according to Metavir score

[1]Alexandru Mester, [1]Ondine Lucaciu, [2]Lidia Ciobanu, [3]Dragos Apostu, [1]Dan Buhatel, [1]Radu S. Campian

[1] Department of Oral Rehabilitation, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [2] Department of Gastroenterology and Hepatology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [3] Department of Orthopedics and Traumatology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Abstract. Objective: The present study was carried out to evaluate the relationship between periodontal disease and Metavir Score. Material and Methods: This was a prospective, observational study consisted of 100 patients diagnosed with hepatitis B virus, hepatitis C virus, autoimmune or alcoholic hepatitis, who underwent a basic periodontal examination. The following parameters were recorded O'Leary Index, Gingival Bleeding Index (GBI), Probing Depth (PD) and Clinical Attachment Loss (CAL) to asses the presence of periodontitis. Results: Firstly, patients were divided in 2 groups according to their Metavir Score, as follows: F0-F2 group (n=33) and F3-F4 group (n=63). O'Leary Index (p=0.125), GBI (p=0.021) was lower in F0-F2 group compared to F3-F4. PD (p=0.66) for the patients with F0-F2 was higher compared to F3-F4. CAL was lower in F0-F2 compared to F3-F4 (p=0.04). Periodontal disease was found in 16 patients with F0-F2 and 44 patients with F3-F4 (p=0.109). Secondly, same patients were divided in 2 groups according to their hepatitis ethology as follows: group 1 (hepatitis B virus, alcoholic hepatitis, autoimmune hepatitis) (n=38) and group 2 (hepatitis C virus) (n=62). Both, O'Leary Index and GBI were found lower in group 1 compared to group 2 ($p<0.001$ and $p<0.001$). PD was higher in group 1 compared to group 2 (p=0.578). Further CAL revealed that patients from group 1 had lower values compared to group 2 (p=0.000). Periodontal disease was found in 45 patients in group 1 and in 38 patients group 2 ($p<0.001$). Conclusion: Although the study did not establish the existence of a pathogenesis link between the two pathologies, it has showed an association between hepatic fibrosis and periodontal disease. Patients with advanced liver fibrosis had higher values in clinical periodontal parameters.

Key Words: periodontal disease, liver fibrosis, Fibroscan, Metavir score, oral health.

Corresponding Author: O. Lucaciu; Email: ondineluc@yahoo.com

Introduction

Periodontal disease is a local infection that occurs in supporting tissues of the tooth and is represented either by a reversible (gingivitis) or an irreversible (periodontitis) process. Gingivitis is an inflammation of the soft tissues surrounding the tooth; which can progress into periodontitis (Rebelo et al 2011). Periodontitis is defined as the damage of the periodontal ligament of the teeth and leads to a progressive loss of gingival tissues and bone destruction. The stages of periodontal disease can be clinically diagnosed by the pocket depth (PD) and the clinical attachment loss (CAL) in combination with radiographic examination (Cekici et al 2014; Nomura et al 2006; Grønkjær 2015).

The degree of liver fibrosis is one of the most important diagnostic and prognostic assessments in chronic liver disease. Clinical manifestations of liver dysfunction accompany architectural changes of the liver parenchyma that are a result of advanced stage of fibrosis. The main causes of hepatic fibrosis are hepatitis B virus (HBV), hepatitis C virus (HCV), autoimmune disease and alcohol abuse. Also, the rising obesity rates have increased the risk of liver injury because of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. Other potential causes are drug-induced toxicity, genetic alteration, autoimmune disorders and cholestatic liver diseases (Shiha et al 2017).

There is no agreement in the correlation between liver disease and periodontal disease in current literature. Patients with non-alcoholic cirrhosis presented a tendency of a larger CAL compared with healthy volunteers, but no significant difference was found within any of the age groups (Novacek et al 1995). Two studies found that patients who had suffered with cirrhosis exhibited greater CAL, dental plaque and calculus when compared to patients without cirrhosis (Movin 1981; Raghava et al 2013). The negative effects on periodontal health, which are caused by liver fibrosis may be due to decreased blood supply of the mucogingival junction (Funatsu el al 1989) and to an increased levels of serum alkaline phosphatase (Jaiswal et al 2011). Thus, the effects of liver fibrosis on periodontitis has not been fully investigated and more studies are required to establish a link between these two diseases (Han et al 2016).

The aim of this study was to evaluate the relationship between periodontal disease and Metavir Score.

Materials and methods

The study protocol has been approved by the ethics committee of the University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, Romania (protocol no. 6/12.01.2018) and an

Table 1. Comparison of periodontal parameters between liver fibrosis groups

Variables	F0 - F2 (n=33)	F3 - F4 (n=67)	P
O'Leary Index % (median, IQR)	50 (54.9)	65.21 (64.7)	0.1
GBI % (median, IQR)	40 (51.3)	67.64 (64.19)	0.02
PD mm (median, IQR)	2.5 (1)	2 (1)	0.6
CAL mm (median, IQR)	1 (4)	3 (6)	0.04
Periodontal disease Yes (%)	16	44	0.1
No (%)	17	23	

mm: millimeters; IQR: interquartile range; GBI: gingival bleeding index; PD: probing depth; CAL: clinical attachment loss

Table 2. Comparison of periodontal parameters between hepatitis groups

Variables

Hepatitis	Group 1 (n=38)	Group 2 (n=62)	P-value
Metavir Score (median, IQR)	4 (3)	3 (2)	0.7
F0-F2 (%)	12	21	
F3-F4 (%)	26	41	
O'Leary Index % (median, IQR)	79.24 (28.77)	26.97 (26.97)	**<0.001**
GBI % (median, IQR)	78.57 (24.43)	27.52, (21.75)	**<0.001**
PD mm (median, IQR)	0 (1.5)	2 (0)	0.5
CAL mm (median, IQR)	5 (3)	0 (0)	**<0.001**
Periodontal disease Yes (%)	38	45	**<0.001**
No (%) 0		17	

Group 1: HBV, autoimmune or alcoholic hepatitis patients; Group 2: HCV patients; mm: millimeters; IQR: interquartile range; GBI: gingival bleeding index; PD: probing depth; CAL: clinical attachment loss

informed consent was obtained from each patient before any study-specific procedure.

This prospective, observational study examined the oral health of 100 patients who were enrolled between September - December 2017 The Regional Institute of Gastroenterology and Hepatology in Cluj-Napoca, Romania, with the diagnosis of HBV, HCV, alcoholic hepatitis or autoimmune hepatitis. Complete laboratory biomarkers were measured: hematology (platelet count, prothrombin), biochemical (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamiltransferase, total bilirubin, direct bilirubin, albumin), virology (AgHBs, Ac anti-HCV); transient elastography (FibroScan) (Ratziu et al 2006). Fibrosis was assessed according to the Metavir scoring system on a five-points scale (F0 = no fibrosis, F1 = portal fibrosis without septa, F2 = few septa, F3 = numerous septa without cirrhosis and F4 = cirrhosis) (Poynard et al 1997). Criteria for exclusion were underage patients (<18 years), patients without written consent, patients with hepatocellular carcinoma or other causes of liver disease (e.g. steatohepatitis) and pregnant women.

A clinical periodontal examination was performed and the following parameters were recorded: O'Leary Index (O'Leary et al 1972), Gingival Bleeding Index (GBI) (Ainamo et al 1975), Probing Depth (PD) and Clinical Attachment Loss (CAL) was performed on probing at six sites per tooth using a millimeters-scaled periodontal probe. The diagnosis of periodontal disease was based on clinical oral measurements and Armitage classification (Armitage 1999).

All data were statistically analyzed using SPSS Statistics software, version 22.0 (SPSS Inc., USA). The quantitative data were calculated as median and interquartile range (IQR). A comparison between patients with early stages of liver fibrosis (F0-F2) and late stages (F3-F4) regarding O'Leary Index, GBI, PD and CAL was performed using Student's test for parametric data. Another comparison was made between patients with HCV and other hepatitis etiology using Student's test for parametric data. The level of statistical significance was defined as $p<0.05$.

Results

Firstly, patients were divided in 2 groups according to their Metavir Score, as follows: F0-F2 group (n=33) and F3-F4 group (n=63). O'Leary Index was lower in F0-F2 group [50 (54.9)] compared to F3-F4 [65.21 (64.7)], but no statistical significance was found (p=0.1). Likewise, GBI was found lower in F0-F2 group [40 (51.3)] compared to F3-F4 [67.64 (64.19)], showing statistical significance (p=0.02). PD in patients with F0-F2 [2.5 (1)] was higher compared to patients F3-F4 [2 (1)] (p=0.6). CAL was lower in F0-F2 [1 (4)] compared to F3-F4 [3 (6)], achieving a statistical significance (p=0.04). Periodontal disease was found in 16 patients with F0-F2 and 44 patients with F3-F4. These difference was not statistical significant (p=0.1).

Secondly, same patients were divided in 2 groups according to their hepatitis etiology as follows: group 1 (HBV, alcoholic hepatitis, autoimmune hepatitis) (n=38) and group 2 (HCV) (n=62). Regarding the distribution of Metavir Score, group 1

[3 (2)] was lower compared to group 2 [4 (3)], but no statistical significance was found (p=0.7). Both, O'Leary Index and GBI were found lower in group 1 [26.97 (26.97) and 27.52 (21.75)] compared to group 2 [79.24 (28.77) and 78.57 (24.43)]. These differences were statistically significant ($p<0.001$ and $p<0.001$). PD was higher in group 1 [2 (0)] compared to group 2 [0 (1.5)], but the difference was not significant (p=0.5). Further comparison of CAL revealed that patients from group 1 [0 (0)] had lower values compared to group 2 [5 (3)], achieving statistical significance ($p<0.001$). Periodontal disease was found in 45 patients in group 1 and in 38 patients group 2, reaching statistical significant ($p<0.001$).

Discussion

Clinical data reported in this study showed a high prevalence of periodontal disease in liver fibrosis. This link can be explained due to poor oral hygiene, infrequent dental care, dental plaque, calculus, bad condition of teeth and periodontium. Several factors such as age, smoking habits and alcohol intake also contributed to the presence of these pathologies.

Novacek et al concluded that poor condition of teeth and periodontium in alcoholic patients with/without cirrhosis could be explained due to poor oral hygiene, dental care, low socioeconomic status and smoking consumption (Novacek et al 1995). O'Leary Index and GBI scores were both higher in patients with advanced liver fibrosis compared to those in incipient stages. Previous studies reported that liver cirrhosis patients demonstrated a higher gingival inflammation and calculus despite the same plaque and gingival score (Movin 1981; Oettinger-Barak et al 2002). Lins et al have stated that patients with liver cirrhosis exhibited higher prevalence of poor oral status and an early treatment is needed for the reduction of mortality (Lins et al 2011).

Patients with incipient stages exhibited the low levels of PD and CAL compared to those in advanced liver stages. A series of studies have related that cirrhosis patients exhibited higher levels of PD and CAL and an increased of periodontal destruction (Raghava et al 2013; Jaiswal et al 2011; Alazawi et al 2017). In the current literature, the association between oral and systemic diseases, such as diabetes, obesity and cardiovascular risk has been established. On the other side, the potential link between periodontitis and liver fibrosis has not received so much attention. Alazawi et al mentioned that perceived barriers to such studies may include lack of infrastructure in most centers that can bring dental and hepatology assessments together in a research environment (Alazawi et al 2017).

There are several limitations that may have affected our results. One limitation was that patients were not equally distributed regarding hepatitis etiology according to Metavir score and for this reason our results showed statistical significance in few periodontal parameters. Grønkjær has stated in his systematic review that the majority of studies had less than 100 patients and future studies should be made with larger sample size (Grønkjær 2015). Another potential bias is whether the association is a result of liver fibrosis or of other variables such as background, age, gender, smoking, alcohol, comorbidities and medication.

Several papers have stated that liver cirrhosis, as a single disease, does not initiate the development of periodontal disease (Grønkjær 2015; Novacek et al 1995). A retrospective study found that periodontal disease can influence the clinical course of liver disease (Aberg et al 2014). A positive correlation was found in periodontal breakdown and serum alkaline phosphatase level in liver cirrhosis (Jaiswal et al 2011).

Although, periodontitis is a common disease which, in most cases, can be prevented and treated, seems to be relatively harmless compared to liver cirrhosis or hepatocellular carcinoma. It is common for patients with advanced liver fibrosis to neglect their oral hygiene even when they present gingivitis or periodontitis (Han et al 2016). It is hypothesized that patients with liver diseases should have established a specific dental care which will be beneficial both to dental practitioners and patients (Novacek et al 1995; Han et al 2016).

Conclusion

The results from this study showed that different stages of liver fibrosis are associated to periodontal disease. Although the study did not establish the existence of a pathogenesis link between the two pathologies, it has showed an association between hepatic fibrosis and periodontal disease. Patients with advanced liver fibrosis had higher values in clinical periodontal parameters; this finding opens a new line of research in determining one or more exogenous or endogenous factors involved.

References

Aberg F, Helenius-Hietala J, Meurman J, et al. Association between dental infections and the clinical course of chronic liver disease. Hepatol Res 2014;44:349-53.

Ainamo J, Bay J. Problems and proposals for recording gingivitis and plaque. Int Dent J 1975;25(4):229-35.

Alazawi W, Bernabe E, Tai D, et al. Periodontitis is associated with significant hepatic fibrosis in patients with non-alcoholic fatty liver disease. PLoS ONE 2017;12(12):e0185902.

Armitage GC. Development of classification for periodontal diseases and conditions. Ann Periodontal 1999;4(1):1-6.

Cekici A, Kantarci A, Hasturk H, et al. Inflammatory and immune pathways in the pathogenesis of periodontal disease. Periodontol 2000 2014;64(1):57-80.

Funatsu K, Yamada M, Kawishima Y, et al. Microcirculatory disturbances of oral mucosa and periodontal disease in patients with liver cirrhosis. J Gastroenterol Hepatol 1989;4 Suppl 1:99-102.

Grønkjær LL. Periodontal disease and liver cirrhosis: A systematic review. SAGE Open Medicine 2015;3:2050312115601122.

Han P, Sun D, Yang J. Interaction between periodontitis and liver diseases. Biomedical Reports 2016;5(3):267-76.

Jaiswal G, Deo V, Bhongade M, et al. Serum alkaline phosphatase: A potential marker in the progression of periodontal disease in cirrhosis patients. Quintessence Int 2011;42(4):345-8.

Lins L, Bittencourt PL, Evangelista MA, et al. Oral health profile of cirrhotic patients awaiting liver transplantation in the Brazilian Northeast. Transplant Proc 2011;43:1319-21.

Movin S. Relationship between periodontal disease and cirrhosis of the liver in humans. J Clin Periodontol 1981;8(6):450-8.

Nomura Y, Tamaki Y, Tanaka T, et al. Screening of periodontitis with salivary enzyme tests. J Oral Sci 2006;48(4):177-83.

Novacek G, Plachetzky U, Pötzi R, et al. Dental and periodontal disease in patients with cirrhosis - role of etiology of liver disease. J Hepatol 1995;22(5):576-82.

O'Leary TJ, Drake RB, Nayor JE. The plaque control record. J Periodontol 1972;43(1):38.

Oettinger-Barak O, Machtei EE, Barak S, et al (2002). Periodontal changes in liver cirrhosis and post-transplantation patients, II: radiographic findings. J Periodontol 2002;73:313-6.

Poynard T, Bedossa P, Opolon P. Natural history of liver fibrosis progression in patients with chronic hepatitis C. The OBSVIRC, METAVIR, CLINIVIR and DOSVIRC groups. Lancet 1997;349(9055):825–32.

Raghava KV, Shivananda H, Mundinamane D, et al. Evaluation of periodontal status in alcoholic liver cirrhosis patients: a comparative study. J Contemp Dent Pract 2013;14(2):179-82.

Ratziu V, Massard J, Charlotte F, et al. Diagnostic Value of Biochemical Markers (FibroTest- FibroSURE) for the Prediction of Liver Fibrosis in Patients With Nonalcoholic Fatty Liver Disease. BMC Gastroenterol 2006;6:6.

Rebelo MAB, Queiroz AC. Gingival Indices: State of Art, Gingival Diseases - Their Aetiology, Prevention and Treatment, Dr. Fotinos Panagakos (Ed.), InTech 2011;42-54.

Shiha, G, Ibrahim A, Helmy A, et al. Noncirrhotic portal fibrosis/idiopathic portal hypertension:APASL recommendations for diagnosis and treatment. Hepatol Int 2017;1(3):398-413.

Authors

•Alexandru Mester, Department of Oral Rehabilitation, University of Medicine and Pharmacy "Iuliu Hatieganu", 15 Victor Babes Street, 400012, Cluj-Napoca, Romania, email: alexandrumester@yahoo.com

•Ondine Lucaciu, Department of Oral Rehabilitation, University of Medicine and Pharmacy "Iuliu Hatieganu", 15 Victor Babes Street, 400012, Cluj-Napoca, Romania, email: ondineluc@yahoo.com

•Lidia Ciobanu, Department of Gastroenterology and Hepatology, University of Medicine and Pharmacy, 19-21 Croitorilor Street, 400162, Cluj-Napoca, Romania, email: ciobanulidia@yahoo.com

•Dragos Apostu, Department of Orthopedics and Traumatology, University of Medicine and Pharmacy, 47-49 Traian Mosoiu Street, 400132, Cluj-Napoca, Romania, email: apostu.dragos@umfcluj.ro

•Dan Buhatel, Department of Oral Rehabilitation, University of Medicine and Pharmacy "Iuliu Hatieganu", 15 Victor Babes Street, 400012, Cluj-Napoca, Romania, email: dbuhatel@yahoo.com

•Radu Septimiu Campian, Department of Oral Rehabilitation, University of Medicine and Pharmacy "Iuliu Hatieganu", 15 Victor Babes Street, 400012, Cluj-Napoca, Romania, email: rcampian@email.com

Citation	Mester A, Lucaciu O, Ciobanu L, Apostu D, Buhatel D, Campian RS. Assessments of periodontal parameters in patients with liver fibrosis according to Metavir score. HVM Bioflux 2018;10(2):42-45.
Editor	Ştefan C. Vesa
Received	23 March 2018
Accepted	10 April 2018
Published Online	5 May 2018
Funding	None reported
Conflicts/ Competing Interests	None reported