Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Oral Health and Inflammatory Biomarkers in Individuals with Metabolic Dysfunction Associated with Steatotic Liver Disease

Ana Luiza Barboza Vianna
Universidade Federal do Rio de Janeiro
Taísa Coelho Guimarães
Universidade Federal do Rio de Janeiro
Davi da Silva Barbirato
Universidade Federal do Rio de Janeiro
Lohanna Palhinha do Amaral
Instituto Oswaldo Cruz
João Régis Ivar Carneiro
Medical School, Hospital Universitário Clementino Fraga Filho
Ronir Raggio Luiz
Institute of Public Health Studies- UFRJ
Patrícia Torres Bozza
Instituto Oswaldo Cruz
Maria Cynésia Medeiros de Barros
cynesiaster@gmail.com

Universidade Federal do Rio de Janeiro https://orcid.org/0000-0002-2284-3581
Cristiane Alves Villela-Nogueira
Medical School, Hospital Clementino Fraga Filho

Research Article

Keywords: periodontal diseases, periodontitis, nonalcoholic fatty liver disease, fatty liver

Posted Date: September 10th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10976174/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: The authors declare no competing interests.

Abstract

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) shares some risk factors with Periodontal Diseases (PD). The presence of chronic inflammation is a common feature. The aim of this study was to evaluate the oral conditions of users of a public health service and investigate the association between these oral conditions, the inflammatory status, and the severity of MASLD. This is a cross-sectional study evaluating oral conditions, such as dental caries and periodontal clinical profile, inflammatory status, anthropometric assessment, and bioimpedance in patients with MASLD. The individuals were divided into two groups according to liver stiffness (LSM) (Fibroscan®, Echosens,Fr), GROUP 1 ≤ 7.9 kPa e GROUP 2 > 7.9 kPa. The total study population was 58 patients (59.72 ± 8.83 yrs), 71.9% females, who underwent intra-oral examination. Of these, 44.8% of individuals showed fewer than 10 teeth or were edentulous (n = 26), and 55.2% underwent a full mouth periodontal examination, inflammatory biomarkers, and liver evaluation. Metabolic Syndrome was present in 96.88% of this population. GROUP 1 presented a DMFT (decayed-missing-filled teeth) value of 19, while GROUP 2 showed 17, indicating poor oral health status in both groups. Only 6.2% of participants exhibited periodontal health. Dental caries, periodontal diseases, inflammatory profile, and degree of hepatic impairment in patients with MASLD was similar in both groups. Considering the oral health of individuals in this sample, we observe a deficiency in oral health independently of the severity of liver disease. These findings highlight the need for including oral assessment evaluation in patients with MASLD.

INTRODUCTION

Chronic liver diseases represent a significant public health issue, responsible for substantial morbidity and mortality worldwide. The global prevalence of MASLD is 25.24%, with higher rates in the Middle East and South America. MASLD ranges from hepatic steatosis to non-alcoholic steatohepatitis (NASH), the more severe form of the disease that can progress to fibrosis and cirrhosis [1]. Transient elastography is a non-invasive, painless procedure used to measure liver elasticity based on the emission of elastic waves [2]. This method allows fibrosis estimation grade as a continuous variable in kilopascals (kPa) [3]. The presence of cardiometabolic factors are essential to the definition of MASLD, according to the new nomenclature defined in 2023. Factors associated with MASLD onset and progression include insulin resistance, diet, and genetic factors. Increasing evidence suggests that Periodontal Diseases may also impact on the pathophysiology of liver disease [4, 5, 6].

Conditions associated with MASLD include obesity (51.34%), type 2 Diabetes Mellitus (22.51%), Dyslipidemia (69.16%), Systemic Arterial Hypertension (39.34%), and MetS (42.54%). The increasing prevalence of MASLD is related to the concomitant increase in obesity and obesity-related diseases. Recently, few researches suggested that Periodontal Disease may also affect the pathophysiology of liver disease [4, 5, 6].

Periodontitis is a chronic inflammatory multifactorial disease associated with dysbiotic biofilm, characterized by progressive destruction of alveolar bone, if not treated, could lead to edentulism [7].

This condition affects more than 50% of the global adult population and increases further with age [8]. Periodontitis and MASLD are chronic conditions characterized by a low-intensity, long-duration inflammatory response with local and systemic effects [7, 8, 9, 10, 11].

Periodontal Diseases often begin with an uncontrolled inflammatory response to slow and steady bacterial colonization of the tooth surface and gingival tissues, with the host response to microbial challenge being primarily responsible for periodontal breakdown [12, 13]. Pro-inflammatory mediators, such as cytokines, play an essential role in the progression of Periodontitis [10, 14]. Furthermore, pathogens can activate acquired immunity, which in turn contributes to further progression of the inflammatory condition. Based on current evidence linking periodontal disease and MASLD, the aim of this study is to evaluate the oral conditions of individuals of a Hepatology Public Service, and investigate an association between these oral conditions, such as dental caries and Periodontal Diseases, with the inflammatory state, anthropometric characteristics and severity of MASLD.

METHODS

This cross-sectional study included patients with established MASLD diagnosis from the hepatology division of an university hospital, in Rio de Janeiro, Brazil. Exclusion criteria were: HIV, hepatitis B and hepatitis C, those with other etiologies for chronic liver diseases, those under steatogenic drugs (corticosteroids, amiodarone, and tamoxifen) or systemic chemotherapy; daily alcohol intake over 20 g; patients with less than 10 teeth present; smokers; patients who have used antibiotic medication in the last six months, anti-inflammatories or medications that potentially induce gingival hyperplasia (phenytoin, nifedipine and cyclosporine) in the last three months; patients who needs antibiotic prophylaxis for periodontal clinical approaches; patients undergoing periodontal treatment in the last six months; patients undergoing orthodontic treatment; and patients with any syndrome, except metabolic syndrome.

Individuals included in the study were submitted to clinical and laboratory evaluation and liver stiffness measurement (LSM) with controlled attenuation parameter (CAP) by vibration controlled transient elastography (VCTE) (FibroScan® Touch 502, Echosens,Fr). Laboratory data included alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, glycated hemoglobin and platelet count that were performed no more than 1 week before the VCTE evaluation.

Liver stiffness measurement results were expressed in kilopascals (kPa). The individuals were divided into two groups, GROUP 1 ≤ 7.9 kPa which might be related to those without advanced fibrosis e GROUP 2 > 7.9 kPa related to those with some higher odds of advanced fibrosis [15]. The CAP was simultaneously evaluated and was expressed in decibels per meter (dB/m). CAP results equal to or greater than 248 dB/m are defined as the presence of steatosis [16].

For bioimpedance assessment, an OMRON Body Composition Monitor was used to estimate body composition parameters through the bioelectrical impedance method. The following variables were

evaluated: body mass index (BMI), body fat percentage, visceral fat level, basal metabolic rate, body age, and skeletal muscle mass.

Blood samples and cytokine detection by multiplex: Blood samples were collected between using a peripheral vein. Plasma was collected by centrifugation at 500 g for 15 min, aliquoted and stored at -80°C until analysis. A multiplex cytokine kit (MIP 1β: Macrophage inflammatory protein 1 beta; IL-6: Interleukin 6; IFN γ: Interferon gamma; IL-5: Interleukin 5; GM-CSF: Granulocyte-Macrophage Colony-Stimulating Factor; TNF-α: Tumor necrosis factor; IL-1β: Interleukin 1 beta; IL-2: Interleukin 2; IL-13: Interleukin 13; IL-4: Interleukin 4; MCP-1: Monocyte Chemotactic Protein; IL-8: Interleukin 8; IL-10: Interleukin 10; GCSF: Granulocyte colony-stimulating factor; IL-7: Interleukin 7; IL-12: Interleukin 12; IL-17: Interleukin 17) was obtained and the assay performed in accordance with the manufacturer's instructions (Bio-Rad, Hercules, CA, USA).

Periodontal assessment: Full-mouth periodontal examination including measurements of probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), supragingival plaque (PL) and calculus (CA) was performed. The periodontal diagnosis was according to the classification proposed by the Workshop organized in 2017 by the American Academy of Periodontology (AAP) and the European Federation of Periodontology [17, 18].

Significance of differences between groups were sought by Chi-square, Student's T or the Mann-Whitney test. Correlation between variables were sought by correlation coefficients of Spearman or Person.

Ethical statements: The study protocol was approved by the Ethics Committees of Rio de Janeiro Federal University (UFRJ) School of Dentistry (protocol 6.066.467).

RESULTS

The total study population was composed of 58 patients from the Hepatology service at the Hospital Universitário Clementino Fraga Filho- HUCFF- UFRJ, who underwent intra-oral examination to evaluate their oral conditions. Of these, 26 individuals had less than 10 teeth or were edentulous (n=26) and 32 underwent complete periodontal examination and assessment of inflammatory mediators and liver assessment. (Figure 1)

Of the 32 individuals subjected to a complete dental evaluation and laboratory tests, 71.9% of the total were female, with 76.5% in GROUP 1 and 66.7% in GROUP 2 according to liver stiffness as previously described.

The average age of the total population was 59.72 years (SD ± 8.83), ranging from 31 to 71 years. The characteristics of the studied population are shown in TABLE 1, with no statistical difference between the two groups.

TABLE 1- Characteristics of the studied population (n=32):

Variables		All (n = 32)	Group 1 (n = 17)	Group 2 (n = 15)	p[1]
			≤ 7.9 kPa	> 7.9 kPa	
Age (mean ± SD)		59.72± 8.83	60.65± 5.61	58.67± 11.60	0.69
Woman (%)		71.9% (n=23)	76.5% (n=13)	66.7% (n=10)	0.70
Educational level (%)	Primary	21.9% (n=7)	29.4% (n=05)	13.3% (n=02)	0.59
	Secondary	46.9% (n=15)	41.2% (n=07)	53.3% (n=08)	
	Higher	31.3% (n=10)	29.4% (n=05)	33.3% (n=05)	
Income in minimum wage (%)	>1	16.1% (n=05)	23.5% (n=04)	7.1% (n=01)	0.64
	1-3	54.8% (n=17)	47.1% (n=08)	64.4% (n=09)	
	<3	19.4% (n=06)	17.6% (n=03)	21.4% (n=03)	

Reference minimum wage R$ 1.302.00. [1] Mann-Whitney U test; Fisher test

Considering the categorization of liver parameters based on LSM results from transient elastography, TABLE 2 presents a comparative analysis between GROUP 1 (control) and GROUP 2 (test). Regarding inflammatory biomarkers, no significant differences were observed between the groups for most of the parameters used. However, there was a difference for AST (U/L) and Platelets (thousand/mm³), showing lower values for GROUP 2, with p=0.026 and p=0.016, respectively.

TABLE 2- Comparative analysis of the studied population regarding clinical, laboratory, elastogralhy and cytokine profile(n=32):

Variables	All (n = 32)	Group 1 (n = 17) ≤ 7.9 kPa	Group 2 (n = 15) > 7.9 kPa	p[1]
BMI (Kg/m2)	31.3 (28.2-35.3)	31.2 (28.4-33.6)	33.5 (28.05-39.35)	0.53
AC (cm)	102 (96.5-111)	98.5 (95.7-102.2)	108 (104.5-115)	0.45
T2DM (%)	65.6% (n=21)	58.8% (n=10)	73.3% (n=11)	0.39
Systemic Arterial hypertension (%)	78.1 % (n=25)	76.5 % (n=13)	80.0% (n=12)	0.99
Dyslipidemia (%)	84.4% (n=27)	88.2% (n=15)	80.0% (n=12)	0.65
Metabolic Syndrome (%)	96.9% (n=31)	100% (n=17)	93.3% (n=14)	0.47
AST (U/L)	33,2 ± 30,2	34,1 ± 39,8	32,2 ± 14,3	0,026
CAP (dBm/m)	319.6 (50.1)	323.8 (46.4)	314.8 (57.5)	0.91
Visceral fat level	13.3± 4.7	12.7± 3.8	14.0± 5.7	0.69
Practice of physical activity (%)	59.4 % (n=19)	52.9 % (n=09)	66.6% (n=10)	0.72
Nutritional monitoring (%)	18.8% (n=06)	23.5% (n=04)	13.3% (n=02)	0.66
HDL (mg/dL)	48.3 ± 12.0	48.7 ± 10.5	48.0 ± 14.1	0.91
Triglycerides (mg/dL)	177.5 ± 106.8	171.4 ± 78.4	185.0 ± 136.6	0.69
CRP (mg/dL)	3.65 (2.0-5.8)	4.1 (2.0-5.4)	3.6 (2.5-8)	0.89
Platelet Count (mil/mm^3)	235.9 ±81.2	264.0 ± 60.3	204.2 ± 91.7	0.016*
Glycated hemoglobin (%)	6.65 (5.9-7.6)	6.2 (5.7-7.1)	7.2 (6.2-7.75)	0.86
TNF α (pg/ml)	55.9 (47.8-62.4)	55.9 (49.4-55.9)	55.9 (46.2-64.1)	0.62
IL-1β (pg/ml)	261.6 (212.2-298.7)	268.9 (212.2-298.7)	254.4 (240.1-329.2)	0.55
IL-6 (pg/ml)	34.7 (33.8-40.9)	35.6 (33.8-40.9)	33.8 (31.3-39.1)	0.63
MIP-1β (pg/ml)	906.6 (852.7-949.2)	913.0 (876.8-949.2)	900.9 (828.5-961.2)	0.25
IFN γ (pg/ml)	806.8 (668.3-978.4)	875.5 (529.2-944.2)	806.8 (668.6-1081)	0.98
IL-5	1031.5 (746.6-1230)	1031.5 (746.6-1215)	1031.5 (774-1215)	0.88

GM-CSF	63.6 (57.6-70.2)	65.6 (57.6-69.3)	61.6 (57.6-73.9)	0.77
IL-2	16.3 (15.1-17.6)	17.2 (15.5-19.6)	15.5 (13.5-17.2)	0.53
IL-13	48.1 (40.2-64.9)	48.1 (40.2-68.8)	42.9 (40.2-61.1	0.81
IL-4	16.6 (14.1-17.9)	16.6 (15.8-18.3)	14.9 (11.8-17.3)	0.85
MCP-1	44.7 (39.0-52.0)	44.7 (35.5-49.2)	47.0 (43.6-52.5)	0.64
IL-8	44.2(40.6-48.7)	47.8(44.2-51.4)	44.2 (38.8-46.0)	0.9
IL-10	257.7 (227.2-321.0)	257.8 (212.1-321.0)	257.8 (250.1-313)	0.69
G-CSF	18.7 (17.4-21.0)	18.7 (16.3-19.9)	18.7 (17.5-21.08)	0.8
IL-7	1444.8 (1315-1593)	1444.8 (1315-1711)	1444.8 (1315-1544)	0.8
IL-12	33.4 (7.5-33.4)	33.4 (7.5-33.4)	33.4 (18.2-33.4)	0.42
IL-17	129.2 (111.1-143.9)	129.2 (114.7-143.9)	128.2 (100.3-143.9)	0.8

The median LSM between the groups was 6.0 (4.8-6.9) for G1 and 10.4 (9.05-17.6) for G2 ($p<0.001$).

CAP: Controlled Attenuation Parameter; LSM: Liver Stiffness Measurement; BMI: Body Mass Index; AC: Abdominal circumference; T2DM: Type 2 Diabetes Mellitus; CRP: C-reactive protein; MIP-1β: Macrophage Inflammatory Protein 1 beta; IL-6: Interleukin 6; IFN-γ: Interferon gamma; IL-5: Interleukin 5; GM-CSF: Granulocyte-Macrophage Colony-Stimulating Factor; TNF-α: Tumor necrosis factor alpha; IL-1β: Interleukin 1 beta; IL-2: Interleukin 2; IL-13: Interleukin 13; IL-4: Interleukin 4; MCP-1: Monocyte Chemoattractant Protein 1; IL-8: Interleukin 8; IL-10: Interleukin 10; G-CSF: Granulocyte Colony-Stimulating Factor; IL-7: Interleukin 7; IL-12: Interleukin 12; IL-17: Interleukin 17.

Values are proportion for categorical data. mean (SD) for normally distributed data and medians (interquartile interval) for non-parametric data.

[1]Mann-Whitney U test

Regarding the analysis of periodontal clinical parameters, the evaluation of pocket depth (PD) and CAL showed no significant difference between the groups. The detailed results related to the periodontal clinical parameters are highlighted in TABLE 3.

TABLE 3- Comparison of oral clinical parameters between groups:

Variables	All (n = 32)	Group 1 (n = 17) ≤ 7.9 kPa	Group 2 (n = 15) > 7.9 kPa	p[1]
Periodontitis	81.3% (n=26)	70.6% (n=12)	93.3% (n=14)	0.13
PD 4-6mm	7.4%	7%	6%	0.43
PD ≥7mm	0.6%	0.7%	0.6%	0.76
CAL 1-2mm	36%	39%	32%	0.29
CAL 3-4mm	31%	30%	32%	0.68
CAL > 4mm	13%	11%	14%	0.45
BOP	31.1%	27.9%	34.6%	0.68
PI	50.1%	47.3%	53.5%	0.2
CI	31.1%	29.5%	33.1%	0.73
DMFT	17.5 (15-20.5)	19 (15-22)	17 (15-18.5)	0.24

PD: pocket depth; CAL: clinical attachment loss; BOP: bleeding on probing; PI: plaque index; CI: calculus index; DMFT: decayed, missing and filled teeth. Medians (interquartile interval) for non-parametric data.

[1]Mann-Whitney U test

Considering Spearman rho correlations between periodontal clinical parameters and inflammatory mediators, there was a positive correlation between IL-6 levels with sites showing greater clinical attachment loss, NCI > 7mm (p□0.0001).

DISCUSSION

This study demonstrated that the oral health of patients with MASLD (non-alcoholic fatty liver disease) is deficient. Additionally, the study aimed to provide evidence of an association between compromised oral conditions, such as dental caries, and periodontal clinical parameters, with the inflammatory state of individuals with MASLD. We found some correlations that will be discussed. Our results may differ from most of the few studies available in literature to date because the study population consisted entirely of individuals with different stages of MASLD regarding liver fibrosis evaluated by VCTE. Thus, the comparison was made between two groups with different severities of the disease, rather than including a true control group, without any hepatic condition. In this sense, this study presents a novel approach, showing similar results between groups with more advanced and milder stages of the disease.

The oral conditions of individuals with MASLD concerning dental caries demonstrated that this population showed poor oral health independently of the stage of liver disease. In MASLD some outcomes are more frequent in individuals with advanced fibrosis compared to those without such as

cardiovascular outcomes, Dental health does not seem to be related to the severity of liver disease itself but maybe to the inflammatory profile of both diseases. The DMFT for this population was 17.5, with an average of 7.2 teeth being lost. When compared with results from the southern region of Brazil, where the DMFT was 18.02 for the 20-64 age group, the results were consistent with our study [19].

Regarding the periodontal profile, only 9.4% of the studied individuals showed periodontal health, indicating a deficiency in the periodontal health condition of this population. The criterion for diagnosing periodontitis, based on the current Classification [18]. was the presence of attachment loss in 2 or more non-adjacent teeth with bleeding. Therefore, there was no difference between GROUPS 1 and 2 concerning the prevalence of Periodontitis (p=0.134).

Comparing with previous studies that investigated an association between Periodontitis and MASLD, it is possible to observe differences in the criteria used for both the diagnosis and definition of Periodontitis, as well as for MASLD, and conflicting results may be due to these differences [20]. Evidence so far of an association between Periodontitis and MASLD have been found in cross-sectional epidemiological studies in humans [21,22,23,24,25,26]. However, this association was not found in the cohort study by AKINKUGBE et al. (2017b) [27]. On the other hand, other cohort studies have found an association [5,28,29].

Alazawi et al. [30] and Pischke et al. [31], in different studies, obtained similar results where Periodontitis was more prevalent in the group of patients with significant fibrosis and hepatic stiffness values increased with the stage of Periodontitis. And also, Hicks [32] studying patients awaiting liver transplant, commonly showed generalized severe periodontal disease and periapical abscesses which would preclude the patient from undergoing transplant surgery.

Interestingly, Duseja et al. [33] , in a case-control study conducted in northern India, comparing 38 patients with MASLD, diagnosed through laboratory tests and transient elastography, using a cutoff of 7.0 kPa for group division, found no significant differences in inflammatory biomarkers such as TNF-α, IL-6, and C-reactive protein (CRP), despite higher averages in the group with more severe MASLD. The same finding was observed in our study, where, although there were no statistical differences in TNF-α and IL-6 levels, there was a higher average level in GROUP 2.

A systematic review focusing on the association between inflammatory cytokines and MASLD found significant associations depending on the degree of hepatic dysfunction. CRP, IL-1β, and TNF-α were significantly associated with different levels of MASLD and hepatic fibrosis; however, CRP, IL-1β, and IL-6 were not significant for steatosis [34]. Although CRP is an important biomarker in diagnosing periodontitis, hepatic dysfunction due to MASLD and/or bacteremia and endotoxemia can increase levels of this acute phase protein[6] and influence systemic interactions with Periodontitis. Furthermore, the variation and interpretation of this biomarker in patients with fatty liver disease and Periodontitis are still not well established, considering its variability over time.

On the other hand, IL-6 levels were positively correlated with sites showing greater clinical attachment loss (NCI > 7mm). Elevated circulating levels of IL-6 likely reflect the presence of chronic inflammation, and so far, studies are controversial regarding the hypothetical model in which IL-6 could be a cofactor for MASLD and increases the risk of Periodontitis[35].

When hepatic parameters and oral health status were compared between groups with and without advanced fibrosis, no significant difference was observed between the groups. However, considering the overall impairment of oral health of all patients was clearly noted.

Additionally, this work also has an important social impact since it improved the quality of life for people with MASLD and Periodontitis, advance scientific evidence in Periodontal Medicine, and strengthen the integration of Dentistry with other health fields. The main focus is to highlight the importance of, preventing, diagnosing and treating both oral health conditions and MASLD.

Given that the prevalence of MASLD is increasing worldwide and shares risk factors with periodontal disease, including obesity, diabetes, and metabolic syndrome, the oral-gut-liver axis is another emerging concept that highlights how alterations in the oral microbiota may influence the manifestations of liver disease. Comprehensive medical care approaches that integrate the treatment of both conditions could improve patient outcomes, underscoring the need for an interdisciplinary approach in patients with chronic diseases.

This study has some limitations that needs discussion. First, the sample size was rather small and this might precluded some associations to be demonstrated. Second, many patients were not included due to the restrict exclusion criteria tht we adopted in order to avoid bias in the study. Of note, almost 50% of the included individuals were edentulous, a finding that may probably be considered as an outcome of a periodontal disease. On the other hand, it is a study that included MASLD patients according to the new nomenclature who were evaluated with VCTE performed by the same experienced operator and had lab exams and citokines collection too closely to VCTE, which emphasizes the adequate and careful methodology of the present study.

Finally, growing evidence is showing associations between oral and systemic health. The link between MASLD and Periodontal Diseases is still uncertain, and various challenges are encountered, however, increasing studies are exploring this association and the hypothesis that improving periodontal health can impact the progression of MASLD and enhance patient outcomes [36]. There may be differences in the factors involving the relationship between Periodontitis and MASLD, such as risk factor profiles (lifestyle, diet...), genetics, and gut microbiome, which might vary in their associations. Furthermore, the variability in methodologies for defining hepatic impairment and Periodontal Disease found in literature hinders conclusions about this possible association and the causal link. The important finding of the impairment of the oral health of individuals in this sample, suggest that an interdisciplinary approach in patients with MASLD is crucial for their overall health.

CONCLUSION

This study showed poor oral health status in patients with MASLD. Additionally, considering that the MASLD sample was divided into two groups regarding liver stiffness measurement, the results were unable to demonstrate an association between dental caries, periodontal diseases, inflammatory profile, anthropometric assessment, and bioimpedance, related to severity of liver fibrosis in patients with MASLD.

Declarations

Ethical statements:

The study protocol was approved by the Ethics Committees of Rio de Janeiro Federal University (UFRJ) School of Dentistry (protocol 6.066.467).

FUNDING INFORMATION:

This study was financially supported, in part, by the Coordination for the Improvement of Higher Education Personnel (CAPES), Ministry of Education, Brasilia, Brazil.

CONFLICT OF I NTEREST STATEMENT: The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS APPROVAL: This study was approved by the Research Ethics Committee from the Dental School – FO-UFRJ (number 6.066.467); and all research participants signed the informed consent form.

References

1. Younossi Z, Stepanova M, Saverymuttu S, et al. Global burden of MASLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol. 2018;15(1):11-20. doi:10.1038/nrgastro.2017.103.
2. Barros F, Setúbal S, Martinho JM, Leite NC, Guaraná T, Monteiro ABS, Nogueira CAV. The correlation between obesity-related diseases and non-alcoholic fatty liver disease in women in the pre-operative evaluation for bariatric surgery assessed by transient hepatic elastography. Obes Surg. 2016;26(9):2089-2097. doi:10.1007/s11695-016-2290-5.
3. Wong VW, Vergniol J, Wong GL, Foucher J, Chan HL, Le Bail B, Choi PC, Kowo M, Chan AW, Merrouche W, Sung JJ, de Lédinghen V. Diagnosis of fibrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease. Hepatology. 2010;51(2):454-462. doi:10.1002/hep.23272.

4. Kuraji R, Ito H, Fujita M, Ishiguro H, Hashimoto S, Numabe Y. *Porphyromonas gingivalis* induced periodontitis exacerbates progression of non-alcoholic steatohepatitis in rats. Clin Exp Dent Res. 2016;2(3):216-225. doi:10.1002/cre2.60.
5. Kuroe K, Furuta M, Takeuchi K, Takeshita T, Suma S, Shinagawa T, Shimazaki Y, Yamashita Y. Association between periodontitis and fibrotic progression of non-alcoholic fatty liver among Japanese adults. J Clin Periodontol. 2021;48(3):368-377. doi:10.1111/jcpe.13447.
6. Yoneda M, Naka S, Nakano K, Wada K, Endo H, Mawatari H, Imajo K, Nomura R, Hokamura K, Ono M, Murata S, Tohai I, Sumida Y, Shima T, Kuboniwa M, Umemura K, Kamisaki Y, Amano A, Okanoue T, Ooshima T, Nakajima A. Involvement of a periodontal pathogen, *Porphyromonas gingivalis*, in the pathogenesis of non-alcoholic fatty liver disease. BMC Gastroenterol. 2012;12:16. doi:10.1186/1471-230X-12-16.
7. Papapanou PN, Wennström JL, Johnsson T. Extent and severity of periodontal destruction based on partial clinical assessments. Community Dent Oral Epidemiol. 1993;21(4):181-184. doi:10.1111/j.1600-0528.1993.tb00752.x
8. Petersen PE, Ogawa H. The global burden of periodontal disease: towards integration with chronic disease prevention and control. Periodontol 2000. 2012 Oct;60(1):15-39. doi: 10.1111/j.1600-0757.2011.00425.x.
9. Villoria GEM, Fischer RG, Tinoco, BEM, Meyle J, Loos BG. Periodontal disease: A systemic condition. Periodontology 2000. 2024; 96:7–19. doi: 10.1111/prd.12616
10. Pizzo G, Guiglia R, Lo Russo L, Campisi G. Dentistry and internal medicine: from the focal infection theory to the periodontal medicine concept. Eur J Intern Med. 2010;21(6):496-502. doi:10.1016/j.ejim.2010.07.011
11. Arimatsu K, Yamada H, Miyazawa H, et al. Oral pathobiont induces systemic inflammation and metabolic changes associated with alteration of gut microbiota. Sci Rep. 2014;4:4828. doi:10.1038/srep04828
12. Hajishengallis G. Interconnection of periodontal disease and comorbidities: Evidence, mechanisms, and implications. *Periodontol 2000*. 2022;89(1):9-18. doi:10.1111/prd.12430
13. Beck JD, Papapanou PN, Philips KH, Offenbacher S. Periodontal Medicine: 100 Years of Progress. J Dent Res. 2019;98(10):1053-1062. doi:10.1177/0022034519846113
14. Hajishengallis G. Periodontitis: from microbial immune subversion to systemic inflammation. *Nat Rev Immunol*. 2015;15(1):30-44. doi:10.1038/nri3785.
15. Kwok R, Tse YK, Wong GL, et al. Systematic review with meta-analysis: non-invasive assessment of non-alcoholic fatty liver disease--the role of transient elastography and plasma cytokeratin-18 fragments. Aliment Pharmacol Ther. 2014;39(3):254-269. doi:10.1111/apt.12569
16. Karlas T, Petroff D, Sasso M, et al. Individual patient data meta-analysis of controlled attenuation parameter (CAP) technology for assessing steatosis. *J Hepatol*. 2017;66(5):1022-1030. doi:10.1016/j.jhep.2016.12.022

17. Caton JG, Armitage G, Berglundh T, et al. A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key changes from the 1999 classification. J Clin Periodontol. 2018;45 Suppl 20:S1-S8. doi:10.1111/jcpe.12935
18. Papapanou PN, Sanz M, Buduneli N, et al. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol. 2018;89 Suppl 1:S173-S182. doi:10.1002/JPER.17-0721
19. Silva-Junior MF, Sousa ACCD, Batista MJ, Sousa MDLRD. Condição de saúde bucal e motivos para extração dentária entre uma população de adultos (20-64 anos). Ciência e Saúde coletiva. 2017;22(8):2693-2702. doi:10.1590/1413-81232017228.10312016.
20. Rinella ME, Lazarus, JV, Ratziue V et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology 2023 Dec 1;78(6):1966-1986. Epub 2023 Jun 24. doi: 10.1097/HEP.0000000000000520
21. Morita T, Yamazaki Y, Fujiharu C, et al. Serum γ-glutamyltransferase level is associated with periodontal disease independent of drinking habits in Japanese adults. Med Sci Monit. 2014;20:2109-2116. Published 2014 Oct 31. doi:10.12659/MSM.891204
22. 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. Published 2017 Dec 8. doi:10.1371/journal.pone.0185902
23. Iwasaki T, Hirose A, Azuma T, et al. Correlation between ultrasound-diagnosed non-alcoholic fatty liver and periodontal condition in a cross-sectional study in Japan. Sci Rep. 2018;8(1):7496. Published 2018 May 14. doi:10.1038/s41598-018-25857-z
24. Weintraub JA, Lopez Mitnik G, Dye BA. Oral Diseases Associated with Nonalcoholic Fatty Liver Disease in the United States. J Dent Res. 2019;98(11):1219-1226. doi:10.1177/0022034519866442.
25. Shin HS. Association between periodontal status and non-alcoholic fatty liver disease in a Korean adult population: A nationwide cross-sectional study. J Periodontol. 2020;91(4):524-532. doi:10.1002/JPER.19-0291
26. Sato S, Kamata Y, Kessoku T, et al. A cross-sectional study assessing the relationship between non-alcoholic fatty liver disease and periodontal disease. Sci Rep. 2022;12(1):13621. Published 2022 Aug 10. doi:10.1038/s41598-022-17917-2.
27. Akinkugbe AA, Slade GD, Barritt AS, et al. Periodontitis and Non-alcoholic Fatty Liver Disease, a population-based cohort investigation in the Study of Health in Pomerania. *J Clin Periodontol*. 2017;44(11):1077-1087. doi:10.1111/jcpe.12800
28. Helenius-Hietala J, Suominen AL, Ruokonen H, et al. Periodontitis is associated with incident chronic liver disease-A population-based cohort study. Liver Int. 2019;39(3):583-591. doi:10.1111/liv.13985
29. Shin HS, Hong MH, Moon JY, Sim SJ. Periodontal disease could be a potential risk factor for non-alcoholic fatty liver disease: An 11-year retrospective follow-up study. Clin Oral Investig. 2022;26(8):5503-5514. doi:10.1007/s00784-022-04518-6

30. 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. Published 2017 Dec 8. doi:10.1371/journal.pone.0185902
31. Pischke S, Shiprov A, Peters U, et al. High prevalence of periodontal disease in patients with NASH-possible association of poor dental health with NASH severity. Ann Hepatol. 2023;28(2):100887. doi:10.1016/j.aohep.2022.100887
32. Hicks JL. Oral care of the patient with liver failure, pretransplant—a retrospective study. Special Care Dentistry, 35(1) 2015. DOI: 10.1111/scd.12075
33. Duseja A, Chahal GS, Jain A, Mehta M, Ranjan A, Grover V. Association between nonalcoholic fatty liver disease and inflammatory periodontal disease: A case-control study. J Indian Soc Periodontol. 2021;25(1):47-54. doi:10.4103/jisp.jisp_45_20
34. Duan Y, Pan X, Luo J, et al. Association of Inflammatory Cytokines With Non-Alcoholic Fatty Liver Disease. *Front Immunol*. 2022;13:880298. Published 2022 May 6. doi:10.3389/fimmu.2022.880298
35. Khosravi R, Ka K, Huang T, et al. Tumor necrosis factor- α and interleukin-6: potential interorgan inflammatory mediators contributing to destructive periodontal disease in obesity or metabolic syndrome. *Mediators Inflamm*. 2013;2013:728987. doi:10.1155/2013/728987
36. Mousa N, Elmetwalli A,· Ahmed Abdel-Razik A et al. Periodontitis and Metabolic Dysfunction-Associated Steatotic Liver Disease: emphasizing the clinical interplay between hepatologists and dentists. Odontology. 2026; 114:378–389. doi: 10.1007/s10266-025-01184-4

Figures

I

FIGURE 1 - Flowchart of individuals in the study:

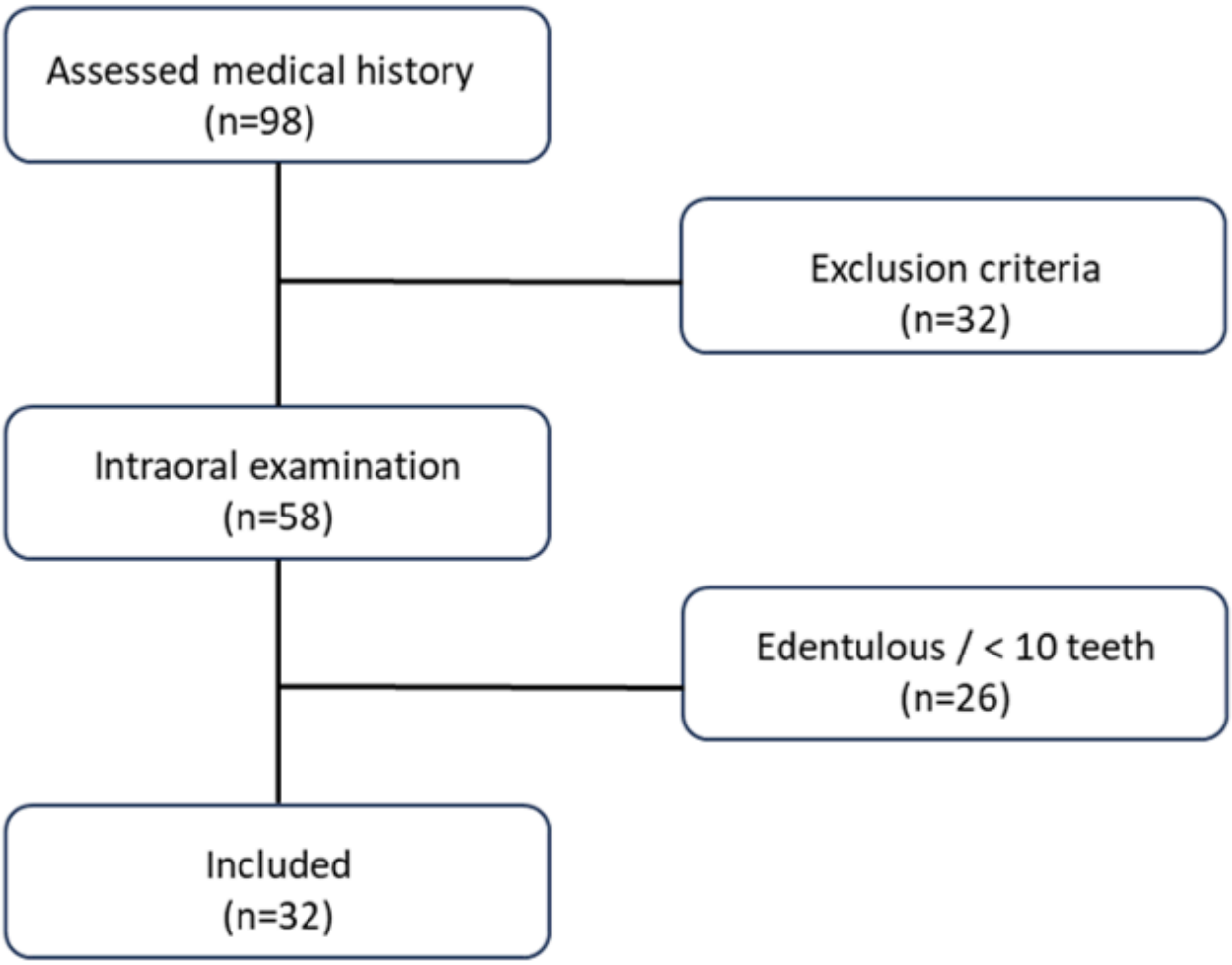


Figure 1

See image above for figure legend