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Original Article

Interaction of periodontal clinical indicators in metabolic syndrome and nonalcoholic fatty liver disease: Implications for preventive interventions

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ABSTRACT

Introduction: The behavior of periodontal clinical indicators in metabolic syndrome (MetS) and fatty liver disease (NAFLD) are not clearly defined. It's even considered that high-risk cases for NAFLD are currently underreported or not identified in a timely manner. The aim of the study is to elucidate the interaction of periodontal clinical indicators in MetS and NAFLD. *Materials and methods*: 336 patients were eligible because they met the diagnostic criteria for metabolic *syn*-drome and nonalcoholic fatty liver disease. Those selected were randomly selected for a cross-sectional study. Metabolic status and non-alcoholic fatty liver disease were measured using the MetS Metabolic Syndrome Diagnostic Criteria (NCEP/ATP-III) and laboratory tests, respectively. In addition, periodontal clinical indicators were evaluated: probing depth, clinical attachment, plaque index and gingival bleeding.
Results: The association for NAFLD and probing depth was p = 0.736. The association for MetS and probing depth was p = 0.598. For NAFLD and clinical attachment loss, the association was p = 0.751. For MetS and clinical attachment loss, the association was p = 0.435. The plaque index for MetS was p = 0.238. The plaque index for NAFLD was p = 0.269. The gingival bleeding association for NAFLD was p = 0.673 and for MetS was p = 0.522.
Conclusions: Periodontal clinical indicators of metabolic syndrome were as-sociated with elevated serum levels of low-density lipoproteins (LDL), HDL-cholesterol, and triglycerides. However, when comparing the values in NAFLD and MetS, a greater significance is evident in the first study group.

1. Introduction

Periodontal disease is characterized by the destruction of the connective tissue of the periodontium. The periodontal symptoms include gingival recession, edema, erythema among other characteristics. At present, the systemic pathologies may be associated with periodontal disease. Periodontal pathologies affect 11.2 % of the world's population. In some regions, the prevalence of periodontal disease is up to 52.5 % of the population (Valenzuela et al., 2021).

Metabolic syndrome (MetS) includes metabolic abnormalities that would lead to an increased risk of diabetes mellitus and cardiovascular disease. The key features of the metabolic syndrome include hypertension, obesity, hypertriglyceridemia, high-density lipoprotein HDL, and hyperglycemia. On the other hand, non-alcoholic fatty liver disease (NAFLD) is considered the most common liver problem, affecting between 15 % and 40 % of the world's general population.[2] NAFLD ranges from simple steatosis to steatohepatitis, cirrhosis, and advanced fibrosis (Zhu et al., 2016).

The evidence of the interaction of periodontal clinical indicators in MetS and NAFLD is not clearly defined. Currently, there are no studies that indicate the behavioral patterns of periodontal clinical indicators for MetS and NAFLD. The aim of our study was to identify the interaction of periodontal clinical indicators in metabolic syndrome and non-alcoholic fatty liver disease and compare their implications for corresponding preventive interventions.

2. Materials and methods

2.1. Participants

A total of 1604 participants were assessed for eligibility in the study. Of them, 336 participants were randomly selected according to the sample inclusion criteria. 252 patients were diagnosed with metabolic syndrome (MetS) and 84 patients were diagnosed with nonalcoholic

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fatty liver disease (NAFLD) (Fig. 1). The cross-sectional study was conducted over a period of five years according to the principles outlined in the Declaration of Helsinki for medical research according to the STROBE guidelines. The study protocol was approved by the Institutional Review Board to which the investigators are affiliated (MH04320064). All patients provided written informed consent.

2.2. Measurements

The diagnosis of MetS and NAFLD was made by a specialist gastroenterologist through different tests that were performed on the study participants. Diagnosis for MetS parameters comprised identification of the presence of three or more components of the NCEP/ATP-III metabolic syndrome diagnostic criteria (Table 1). The diagnosis of NAFLD was made through clinical analysis. Waist circumference was measured between the lowest rib and the iliac crest. Systolic and diastolic blood pressure was recorded in the left arm of each patient using a sphygmomanometer. Laboratory tests were performed under international standards in the institution's clinical laboratory. Plasma glucose was measured by the glucose-peroxidase method with a sensitivity of 5 mg/dL. Serum cholesterol and triglycerides of all participants were measured after 12 h of fasting with the colorimetric method with a sensitivity of 5 mg/dL (Table 1).

Periodontal status was assessed by a periodontics specialist using periodontal clinical indicators: probing depth, clinical attachment, plaque index and gingival bleeding (Tables 2 and 3).

2.3. Statistical analysis

The analysis of the relationship between MetS and NAFLD was performed through the Chi-Square test. The mean and standard deviation (SD) were used to analyze the quantitative data, and the differences between two groups were studied using two independent samples t-tests ($p < 0.001$).

3. Results

Considering the study criteria, 252 participants were diagnosed with MetS, and 84 participants were diagnosed with NAFLD (Fig. 1). The study included 116 men (34.5%) and 220 women (65.5%). The mean age was 55.38 ± 10.2 years.

The interaction of periodontal clinical indicators for probing depth in MetS corresponded to significant values for probing depth of 1–3 mm ($p < 0.001$) compared to NAFLD, which showed significant values for probing depth of 4–6 mm ($p < 0.001$) and >6 mm ($p < 0.001$). For clinical attachment loss, it was shown that MetS had the most significant values for the 1–3 mm group ($p < 0.001$). While in NAFLD the most significant values were shown for the 4–6 mm ($p < 0.001$) and >6 mm ($p < 0.001$) group. The association for NAFLD and probing depth was p = 0,736. The association for MetS and probing depth was p = 0.598. For NAFLD and clinical attachment loss, the association was p = 0.751. For MetS and clinical attachment loss, the association was p = 0.435 (Table 2). The plaque index for MetS was p = 0.238. The plaque index for NAFLD was p = 0,269. The gingival bleeding association for NAFLD was p = 0.673 and for MetS was p = 0.522 (Table 3).

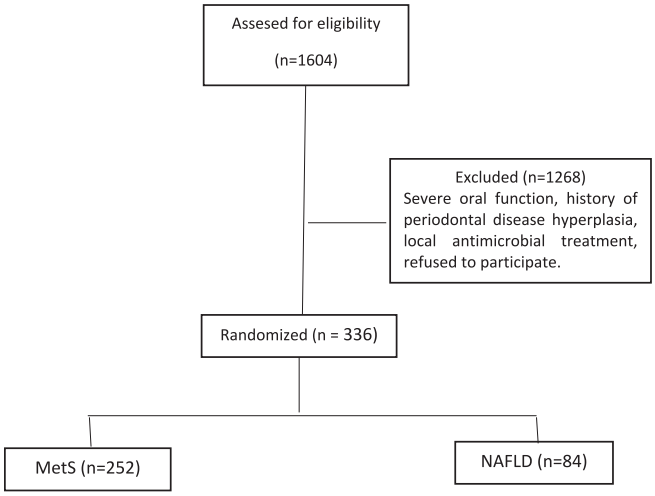

Fig. 1. Participant selection diagram.

Table 1
MetS and NAFLD diagnostic criteria.

Measures	MetS Mean ± SD	NAFLD Mean ± SD
Waist circumference	86.22 ± 13.44	92.13 ± 14.11
Triglycerides	122.09 ± 105.87	135.44 ± 102.68
HDL-cholesterol	44.9 ± 10.1	46.1 ± 10.3
Blood pressure	115.45 ± 15.13	120.68 ± 19.36
Fasting glucose (mg/dL)	73.07 ± 11.05	76.09 ± 11.36
Participants	92.56 ± 23.75	97.99 ± 25.12
	252	84

MetS: metabolic syndrome; NAFLD: non-alcoholic fatty liver disease.

Table 2
Probing deep and clinical attachment para MetS y NAFLD.

Groups	MetS			NAFLD		
	1–3 mm	4–6 mm	>6mm	1–3 mm	4–6 mm	>6mm
Probing deep	59.68 ± 4.03 %*	34.93 ± 3.01 %	5.39 ± 2.96 %	44.71 ± 4.03 %	45.67 ± 4.47 %*	9.62 ± 1.50 %*
Clinical Attachment	60.74 ± 4.48 %*	34.19 ± 4.41 %	5.07 ± 1.11 %	39.08 ± 4.87 %	49.23 ± 4.01 %*	11.69 ± 1.12 %*

*$p < 0.001$; Probing deep NAFLD: p = 0.736; Probing deep MetS: p = 0.598; clinical attachment NAFLD: p = 0.751 clinical attachment NAFLD: p = 0.431.

Table 3
Plaque index and gingival bleeding in MetS and NAFLD.

Groups	MetS	NAFLD
Plaque index	26.88 ± 4.88 %	27.41 ± 3.12 %
Gingival bleeding	11.14 ± 3.90 %	12.29 ± 3.92 %*

*$p < 0.001$; Plaque index MetS p = 0.238; Plaque index NAFLD p = 0.269; Gingival bleeding MetS p = 0.522. Gingival bleeding NAFLD p = 0.673.

4. Discussion

The immune response is related to the metabolism whose dysfunction can lead to chronic metabolic-inflammatory disorders such as metabolic syndrome and fatty liver disease. It is possible to consider that there may be chronic inflammation in these pathologies (Norata et al., 2015), therefore, it could be affirmed that the inflammatory processes in the tissues of the oral cavity, as in the case of periodontal tissues, would affect the inflammatory metabolic conditions (Schenkein et al., 2020). In this sense, it is important to know the behavior of periodontal clinical indicators in relation to the serum levels of triglycerides, and high-density lipoproteins (HDL). In a study, it was found that metabolic syndrome (MetS) and non-alcoholic fatty liver disease (NAFLD) presented certain clinical characteristics that show their association (Valenzuela et al., 2023). However, considering this finding, we are interested in identifying the behavior of these pathologies in relation to the clinical indicator's periodontal disease.

Through a report, the possibility that periodontal treatment in

simulated hyperlipidemic models reduced triglyceride levels (D'Aiuto et al., 2018). In our study we found triglycerides values of 135.44 mg/dL for NAFLD and 122.09 mg/ dL for MetS. For HDL-cholesterol values we found NAFLD values of 46.1 mg/dL and 44.9 for MetS mg/dL. The association for NAFLD and probing depth was $p = 0.736$. The association for MetS and probing depth was $p = 0.598$. For NAFLD and clinical attachment loss, the association was $p = 0.751$. For MetS and clinical attachment loss, the association was $p = 0.435$. In this sense, according to what was reported in our study, it is possible that the periodontal clinical indicators of metabolic syndrome are associated with elevated serum levels of HDL-cholesterol, and triglycerides. However, when comparing the values in the NAFLD and MetS groups, a greater significance is evident in the first study group.

According to studies, the host's immune response is integrated with metabolism, and dysfunction of this system can lead to chronic metabolic-inflammatory disorders, such as obesity and related pathologies, including metabolic syndrome and non-fatty liver disease alcoholic (Valenzuela et al., 2023).Chronic inflammation is a feature of these disorders. Therefore, it is possible that inflammatory processes in periodontal tissues trigger inflammatory conditions (Türer et al., 2017), including increased serum levels of acute phase proteins and inflammatory cytokines, as observed in an experimental model (O'Boyle et al., 2020).

A study demonstrated that adequate periodontal treatment reduces systemic inflammatory markers, favorably influencing the reduction of plasma glucose concentrations. There would be a high probability that periodontal treatment will improve vascular and endothelial function (Orlandi et al., 2020; Kitamoto et al., 2020).

In the oral cavity, it is necessary to identify periodontal pathogens that induce bone loss in addition to producing localized inflammation, which would promote steatosis and alteration of fatty acid metabolism. (Nakahara et al., 2018; Nagasaki et al., 2020; Quin et al., 2014). Hyperglycemia and insulin resistance can activate proinflammatory receptors that produce metabolic disorders, influencing vascular inflammation (Valenzuela et al., 2023; Acharya et al., 2017).

Systemic inflammation mediated by the presence of oral bacteria would cause intestinal dysbiosis and increased intestinal permeability, which produces endotoxemia and systemic inflammation (Potempa et al., 2017). In this sense, a study reported that some species of oral bacteria found in the intestinal microbiome are associated with liver cirrhosis (Qin et al., 2014). It is important to elucidate the behavior of bacterial translocation from the oral cavity to the intestine, as a cause of the defective secretion of gastric acid and bile salts, which are clinical characteristics in patients with cirrhosis. Vascular damage induces inflammatory cytokines, promoting atherosclerosis. Although this pattern is not well defined in humans (Potempa et al., 2017; Lamont et al., 2018).

Our study shows the plaque index for MetS was $p = 0.238$. The plaque index for NAFLD was $p = 0.269$. The gingival bleeding association for NAFLD was $p = 0.673$ and for MetS was $p = 0.522$. In this sense, according to what was reported in our study, it is possible that the oral clinical indicators of metabolic syndrome are associated with elevated serum levels of HDL-cholesterol, and triglycerides. However, when comparing the values in the NAFLD and MetS groups, a greater significance is evident in the first study group. There were no significant variations between the groups analyzed by gender and age.

The host's immune response is closely related to metabolism. Dysfunction of this integrated system would induce chronic metabolic-inflammatory disorders. In our study, periodontal clinical indicators were associated with elevated serum levels of HDL-cholesterol and triglycerides.

The implications for preventive actions lead us to recommend in the case of patients affected with NAFLD and MetS, to undergo a timely periodontal clinical evaluation, in whom early and adequate periodontal treatment should be planned. Periodontal treatment may reduce systemic inflammatory markers, favorably influencing metabolic status. Periodontal preventive actions and patient education will positively influence the reduction of LDL and triglyceride levels and the improvement of oral clinical indicators in metabolic syndrome and non-alcoholic fatty liver disease.

5. Conclusion

In our study, periodontal clinical indicators in patients with metabolic syndrome interacted and were related to elevated serum levels of HDL cholesterol and triglycerides. However, when comparing the behavior of periodontal clinical indicators in the NAFLD and MetS groups, greater significance is evident in the first study group. The implications for preventive actions lead us to recommend, in the case of patients affected with NAFLD and MetS, to promptly undergo an evaluation of periodontal clinical indicators, for the implementation of a planned periodontal treatment.

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Informed Consent Statement

Informed consent was obtained from all subjects involved in the study and the consent to publish this paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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