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Doença periodontal e estado redox: insights sobre o impacto da obesidade no equilíbrio oxidativo sistêmico

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Dissertação apresentada ao Programa Pós-Graduação em Ciências Aplicadas à Saúde da Universidade Federal de Juiz de Fora, como requisito parcial à obtenção do título de Mestre em Ciências da Saúde. Área de concentração: Biociências.

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RESUMO

A doença periodontal (DP) é uma condição que pode levar à perda de estruturas de suporte e proteção dentária devido à sua natureza inflamatória. A DP apresenta um perfil inflamatório sistêmico crônico e de baixo grau e pode estar associada a alterações nos níveis oxidativos sistêmicos, os quais podem estar ligados ao desenvolvimento de outras doenças. A obesidade é outra condição prevalente na população que também apresenta caráter inflamatório e afeta o estado redox do organismo. Portanto, é essencial investigar essas doenças em relação ao equilíbrio oxidativo sistêmico de indivíduos com diferentes estados nutricionais e periodontais. Neste estudo transversal, 18 indivíduos passaram por avaliações periodontais e antropométricas e foram agrupados de acordo com o IMC e o estado periodontal: I) NHP: peso normal + periodontalmente saudável; II) NG: peso normal + gengivite; III) OBG: obesidade + gengivite; IV) OBP: obesidade + periodontite. Amostras de sangue também foram coletadas para análise de marcadores de estresse oxidativo sistêmico no plasma e eritrócitos (TBARS, capacidade antioxidante total, SOD, CAT). Em relação aos parâmetros periodontais, o grupo OBP apresentou valores de BOP (sangramento à sondagem) maiores do que os grupos não obesos. Não houve diferença significativa entre as medidas de BOP nos grupos com obesidade ou entre indivíduos com gengivite. O grupo OBP apresentou valores de nível clínico de inserção (CAL) maiores do que os outros grupos ($p < 0,05$). OBG e OBP apresentaram maior IMC, massa gorda e circunferência da cintura ($p < 0,001$). O grupo OBP apresentou níveis plasmáticos de TBARS mais altos ($p < 0,05$) em comparação ao grupo NHP, maior atividade de SOD ($p < 0,05$) em comparação aos grupos de peso normal e menor CAT ($p < 0,05$). A carbonilação de proteínas aumentou significativamente no grupo OBG ($p < 0,05$) em comparação aos outros grupos. Observou-se correlações positivas entre os níveis plasmáticos de TBARS e a profundidade de sondagem ($r = 0,527$; $p < 0,04$) e entre as proteínas carbonilas e o índice de placa ($r = 0,416$; $p < 0,05$). CAT e SOD apresentaram correlações negativas com os parâmetros inflamatórios periodontais, especialmente entre os participantes com obesidade. Embora o estudo não permita deduções sobre causalidade, observou-se completamente os parâmetros do estado periodontal, antropométrico e bioquímico desses indivíduos, o que permite uma melhoria na abordagem clínica de pacientes com obesidade e periodontite.

Palavras-chave: Obesidade. Doença periodontal. Estresse oxidativo. Espécies Reativas de Oxigênio

ABSTRACT

Periodontal disease (PD) is a condition that can lead to the loss of dental supportive and protective structures due to its inflammatory nature. PD exhibits a chronic, low-grade systemic inflammatory profile and may be associated with alterations in systemic oxidative levels, which in turn can be linked to the development of other diseases. Obesity is another prevalent condition in the population that also carries an inflammatory character and affects the organism's redox state. Therefore, it is essential to investigate these diseases in relation to the systemic oxidative balance of individuals with different nutritional and periodontal statuses. In this cross-sectional study, 18 individuals underwent periodontal and anthropometric evaluations and were grouped according to BMI and periodontal status: I) NHP: normal weight + periodontally healthy; II) NG: normal weight + gingivitis; III) OBG: obesity + gingivitis; IV) OBP: obesity + periodontitis. In addition to these evaluations, blood samples were collected for the analysis of systemic oxidative stress markers in plasma and erythrocytes (TBARS, total antioxidant capacity, SOD, CAT). Regarding periodontal parameters, the OBP group presented higher BOP (bleeding on probing) values than the non-obese groups. However, there was no significant difference between BOP measurements in the obese groups or among individuals with gingivitis. Furthermore, the OBP group presented higher clinical attachment level (CAL) values than the other groups ($p < 0.05$). OBG and OBP had higher BMI, fat mass, and waist circumference ($p < 0.001$). The OBP group presented higher plasma TBARS levels ($p < 0.05$) compared to the NHP group, higher SOD activity ($p < 0.05$) compared to the normal weight groups, and lower CAT ($p < 0.05$). Protein carbonylation increased significantly in the OBG group ($p < 0.05$) compared to the other groups. Positive correlations were observed between plasma TBARS and probing depth ($r=0.527$; $p<0.04$) and between protein carbonyls and plaque index ($r=0.416$; $p<0.05$). CAT and SOD showed negative correlations with periodontal inflammatory parameters, especially among obese participants. Although the study does not allow for deductions about causality, it was possible to fully analyze the parameters of the periodontal, anthropometric, and biochemical status of these individuals, which allows for an improvement in the clinical approach to patients with obesity and periodontitis.

Keywords: Obesity. Periodontal Disease. Oxidative Stress. Reactive Oxygen Species

LISTA DE ABREVIATURAS E SIGLAS

BFI	Body Fat Index
BOP	Bleeding on Probing
BSA	Bovine serum albumin
CAL	Clinical Insertion Level
CAT	Catalase
CID	Classificação Internacional de Doenças
DNPH	2,4-dinitrophenylhydrazine
DP	Doença periodontal
EO	Estresse Oxidativo
ERO	Espécies Reativas de Oxigênio
FRAP	Ferric reducing antioxidant power
IMC	Body Mass Index
MDA	Malondialdehyde
NG	Normal Weight Health
NHP	Normal Weight with periodontally healthy status
OBG	Obesity with gingivitis
OBP	Obesity with periodontitis
PD	Probing Depth
ROS	Reactive Oxygen Species
SOD	Superoxide dismutase
TAC	Total antioxidant capacity
TBARS	Thiobarbituric acid-reactive substances
WC	Waist Circumference
WHO	World Health Organization

SUMÁRIO

1 INTRODUÇÃO

A influência da saúde bucal sobre a saúde sistêmica tem sido amplamente reconhecida, refletindo diretamente na qualidade de vida e na esfera social dos indivíduos (FIORILLO, 2019). Ao longo dos anos, o estado bucal pode sofrer alterações que impactam funções essenciais como alimentação, respiração e fala, além de afetar aspectos psicossociais, especialmente no que se refere à autoestima e às interações interpessoais (WHO, 2023).

Estima-se que cerca de 3,5 bilhões de pessoas em todo o mundo sejam acometidas por algum tipo de doença bucal, sendo a cárie dentária e a doença periodontal as condições mais prevalentes (WHO,2022). A gengivite, forma inicial e reversível da doença periodontal, é caracterizada por inflamação aguda da gengiva, sem perda de inserção. Quando não tratada, pode evoluir para periodontite, uma condição inflamatória crônica marcada pela destruição dos tecidos de suporte do dente (CATON et al., 2018; PAPAPANOUS et al., 2018). De acordo com o Relatório Global sobre o estado da Saúde Bucal, publicado pela Organização Mundial de Saúde em 2022, cerca de 1 bilhão de pessoas são afetadas pela periodontite, uma das principais causas de perda dentária em nível mundial (WHO, 2022).

A periodontite está associada a várias doenças sistêmicas, como diabetes *mellitus* tipo 2, doenças cardiovasculares e nefropatias. Essa associação é devido ao fato da periodontite ser caracterizada por aumento de marcadores inflamatórios sistêmicos derivados da resposta imune exacerbada pela doença periodontal (LOSS, 2005; PAPAPANOU et al., 2018; PARASKEVAS; HUIZINGA & LOOS, 2008; FISHER et al., 2020; BHUYAN et al., 2022; PAMUK & KANTARCI, 2022).

A fisiopatologia da periodontite envolve um aumento na produção de espécies reativas de oxigênio (ERO), principalmente por neutrófilos hiperativados. Quando não adequadamente neutralizadas por mecanismos antioxidantes, essas ERO causam estresse oxidativo, que resulta em danos teciduais irreversíveis. Na periodontite há excesso de ERO não balanceados local e sistemicamente, gerando peroxidação lipídica, danos a proteínas e ao DNA, com capacidade antioxidante alterada e insuficiente para manter o balanço oxidativo (WANG; ANDRUKHOV,

RAUSCH-FAN, 2017; HUSSAIN et al., 2016). Esse estresse oxidativo intensifica a inflamação, ampliando os efeitos sistêmicos da periodontite. Além disso, o estresse oxidativo parece ser um elo entre periodontite e outras condições crônicas inflamatórias, como a obesidade . (NIELSEN et al., 2023; ZHAO; XU & LEUNG, 2022, PAMUK & KANTARCI, 2022).

A obesidade (CID: E66) é reconhecida como uma doença crônica, complexa e de impacto global (WHO, 2025). Em 2022, 43% dos adultos apresentavam sobrepeso, sendo 16% com obesidade, com projeções de que mais da metade da população adulta mundial estará acima do peso até 2050, o que reflete a repercussão dessa condição, além de contribuir também para impactos econômicos (WHO, 2022; COX; WEST & CRIPPS, 2014). A obesidade acarreta um estado inflamatório crônico de baixo grau, predispondo ao desenvolvimento de diabetes tipo 2, hipertensão e doenças cardiovasculares (KOPELMAN, 2000; ZAGO et al., 2013; HAJISHENGALLIS, 2022).

Sabe-se que a obesidade e a doença periodontal causam prejuízos sistêmicos, apresentam um caráter inflamatório relacionado a esses efeitos no organismo e proporcionam um desequilíbrio no estado redox sistemicamente (ZHAO; XU & LEUNG, 2022). Pesquisadores observaram maiores concentrações de marcadores de estresse oxidativo em fluido gengival de pacientes com obesidade de acordo com a severidade periodontal (ATABAY et al., 2017). Essa análise, localmente, foi um importante achado para que outras pesquisas investiguem esses marcadores de modo sistêmico nesses indivíduos com obesidade e doença periodontal. Assim, o objetivo do presente estudo foi avaliar a associação entre parâmetros clínicos periodontais e marcadores do estado redox sistêmico em indivíduos com diferentes condições nutricionais (eutróficos e com obesidade).

1 ARTIGO CIENTÍFICO

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Periodontal disease and redox status: insights into the impact of obesity on systemic oxidative balance

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ABSTRACT

Objective: To investigate the association between clinical periodontal parameters and systemic redox status markers in individuals with different nutritional and periodontal conditions.

Materials and Methods: Eighteen adults were included and allocated into four groups: normal weight with healthy periodontium (NHP, n=4), normal weight with gingivitis (NG, n=4), obesity with gingivitis (OBG, n=4), and obesity with periodontitis (OBP, n=6). Periodontal examination and body composition assessment were performed. Oxidative stress markers were analyzed in plasma and erythrocytes, including TBARS, protein carbonyls, SOD and CAT enzymatic activity, and total antioxidant capacity (TAC).

Results: The OBP group presented worse periodontal parameters, and the clinical attachment level (CAL) was significantly higher than the other groups ($p < 0.05$). Obese individuals had higher BMI, fat mass, and waist-specific fat mass ($p < 0.001$). The OBP group had higher plasma TBARS levels ($p < 0.05$) compared to the NHP group, higher SOD activity ($p < 0.05$) compared to the normal weight groups, and lower CAT ($p < 0.05$). Protein carbonylation increased significantly in the OBG group ($p < 0.05$) compared to NHP and NG groups. Positive correlations were observed between plasma TBARS and probing depth ($r = 0.527$; $p < 0.04$) and between protein carbonyls and plaque index ($r = 0.416$; $p < 0.05$). CAT and SOD showed negative correlation levels with periodontal inflammatory disruptions, especially among obese participants.

Conclusion: This study suggests that obesity may exacerbate systemic redox imbalance associated with periodontal inflammation.

Keywords: Periodontal Diseases, Gingivitis, Obesity, Oxidative Stress, Antioxidants

1. INTRODUCTION

Periodontal disease (PD) encompasses a spectrum of inflammatory conditions affecting the supporting dental tissues, including gingivitis — the initial and reversible form of the disease — and periodontitis, a more advanced stage that involves irreversible tissue destruction (Papapanou et al., 2018; Kinane, Stathopoulou & Papapanou, 2017). Both share common pathophysiological mechanisms, such as activation of the host immune response to microbial dysbiosis in the subgingival biofilm, culminating in the excessive production of inflammatory mediators and reactive oxygen species (ROS) (Neurath & Kesting, 2024; Wang, Andrukhov & Rausch-Fan, 2017).

Although gingivitis is generally considered a mild local condition, there is evidence that gingival inflammation can trigger measurable systemic changes, especially in individuals with greater immunological susceptibility or underlying inflammatory conditions (Neurath & Kesting, 2024). Oxidative stress, defined as an imbalance between ROS and antioxidant mechanisms such as superoxide dismutase (SOD) and catalase (CAT), plays a central role in PD progression, from early stages to its relationship with systemic conditions (Deng et al, 2024; Kumar et al., 2017; Wang, Andrukhov & Rausch-Fan, 2017).

Obesity, in turn, is a chronic low-grade inflammatory condition associated with the persistent production of ROS and proinflammatory cytokines (Kawai, Autieri & Scalia, 2021). This systemic oxidative environment can enhance the inflammatory effects of PD, even in its early stages, as suggested by some studies showing increased lipid peroxidation in patients with gingivitis (Atabay et al., 2017).

The literature acknowledges the interrelation between obesity, oxidative stress, and periodontitis (Zhao, Xu & Leung, 2022), but studies assessing gingivitis in this context remain scarce. Systematic reviews and previous case-control studies — such as those by Toy et al. (2023) and Ahmadi-Motamayel et al. (2017) — have predominantly focused on periodontitis samples or local parameters, without adequately exploring systemic effects in the initial stages of the disease.

Thus, the present study aimed to investigate the association between clinical markers of periodontal disease and biochemical parameters of systemic

redox status in individuals with different nutritional profiles, contributing to expanding the understanding of the relationship between oral inflammation and circulating oxidative stress.

2. MATERIALS AND METHODS

2.1 Study design and sample

This cross-sectional study was conducted at the Federal University of Juiz de Fora – Governador Valadares campus, between April 2024 and June 2025. The study was approved by the Research Ethics Committee of the Federal University of Juiz de Fora (Protocol No. 77963324.3.0000.5147) and carried out in accordance with the principles of the Declaration of Helsinki (2013). A total of 18 participants underwent anthropometric assessment, body composition analysis, clinical periodontal examination, and evaluation of systemic biomarkers related to redox status. Participants were grouped according to their nutritional status and periodontal condition.

To be eligible for participation, individuals had to meet the following criteria: (I) be between 18 and 60 years of age; (II) have not undergone periodontal treatment within the last 6 months; (III) not present with systemic conditions such as neoplasms, rheumatoid arthritis, diabetes *mellitus*, osteoporosis, autoimmune diseases, immunosuppressive conditions, hypersensitivity disorders, acute or infectious diseases; (IV) not be using anti-inflammatory, antimicrobial, antioxidant, immunosuppressive therapy, or medications interfering with metabolism in the past 6 months; (V) have a minimum of 10 natural teeth, excluding third molars; (VI) present a diagnosis compatible with periodontal health, localized or generalized gingivitis, or periodontitis stage III or IV (Papapanou et al., 2018; Caton et al., 2018); (VII) have no history of smoking; (VIII) not be pregnant or lactating.

For nutritional classification, the body mass index (BMI) was used, calculated as the ratio of body weight to the square of height (kg/m²). Individuals with a BMI < 25 kg/m² were classified as having normal weight, whereas those with a BMI ≥ 30 kg/m², combined with a waist circumference (WC) > 88 cm for women or > 102 cm for men, were classified as obese. Body composition was assessed by

bioelectrical impedance analysis using the InBody 270 analyzer (InBody Co. Ltd, Republic of Korea), which provided data on body fat percentage, fat mass, and visceral fat level. For bioelectrical impedance analysis, patients were required to follow the following protocol: a minimum fasting period of 4 hours; no alcohol consumption in the 24 hours preceding the assessment; no physical exercise within the previous 12 hours; bladder emptying; and, for female participants, assessment could not occur during menstruation. Additionally, waist circumference was measured at the midpoint between the lower margin of the last rib and the iliac crest. The body fat index (BFI) was calculated as the ratio of fat mass to the square of height.

2.2 Periodontal Clinical Assessment

The periodontal clinical examination was performed at six sites per tooth (distobuccal, buccal, mesiobuccal, distolingual, lingual/palatal, and midlingual) on all teeth except third molars, using a Williams periodontal probe (Hu-Friedy, Chicago, IL, USA). The following clinical parameters were assessed: visible plaque index (VPI; Ainamo & Bay, 1975), probing depth (PD), bleeding on probing (BOP), and clinical attachment level (CAL).

Participants were classified according to their clinical periodontal profile (Caton et al., 2018) and allocated into the following groups:

-Periodontally healthy: PD ≤ 3 mm at all sites, BOP < 10% of sites, with possible presence of attachment loss and/or radiographic bone loss.

-Gingivitis: PD ≤ 3 mm at all sites, BOP ≥ 10% of sites, with possible presence of attachment loss and/or radiographic bone loss.

-Periodontitis: PD ≥ 6 mm, with clinical attachment loss ≥ 5 mm and bleeding on probing at a minimum of two non-adjacent interproximal sites. Radiographic bone loss involving more than 50% of the root or extending to the apical third. Presence or absence of tooth loss due to periodontitis.

Thus, the study participants were grouped according to body mass index and periodontal status as follows: normal weight with periodontally healthy status (NHP), normal weight with gingivitis (NG), obesity with gingivitis (OBG), and obesity with periodontitis (OBP).

2.3 Blood collection and processing

Blood samples (8 mL) were collected from the antecubital vein after an 8-hour fast (7–9 AM) in EDTA tubes. Plasma and erythrocytes were separated by centrifugation (4°C, 1500g, 10 min). Plasma was stored at −20°C for TBARS and protein carbonyl assays. Erythrocytes were hemolyzed according to Glass and Gerson (1981) and used for the assessment of TBARS, total antioxidant capacity (TAC), and antioxidant enzymes (superoxide dismutase [SOD] and catalase [CAT]).

2.3.1*Redox status assessment*

The content of thiobarbituric acid-reactive substances (TBARS) in plasma and lysed erythrocytes was evaluated as described by Donnan (1950). Briefly, following an acid-heating reaction, TBARS concentrations were determined at 532 nm based on a standard curve using known concentrations of malondialdehyde (MDA) (1,1,3,3-tetramethoxypropane) (Sigma, MO, USA), reflecting the lipid peroxidation status. The amount of MDA produced was interpreted as TBARS concentration.

Protein carbonyls in plasma, as markers of oxidative protein damage, were quantified as previously described (Levine et al., 1994) and adapted by Pereira et al. (2024), based on the reaction with 2,4-dinitrophenylhydrazine (DNPH). Briefly, proteins in the samples were precipitated with 10% trichloroacetic acid and then incubated in the dark at room temperature with DNPH (10 mM) in 2 mM HCl for 30 minutes. The protein precipitate was washed twice with ethanol/ethyl acetate (1:1) and dissolved in 6% sodium dodecyl sulfate. Samples were centrifuged (10,000 g, 10 minutes, 4 °C) and the supernatant was measured at 370 nm, considering the DNPH molar extinction coefficient of 22,000 M^{-1} cm^{-1}.

Superoxide dismutase (SOD; EC 1.15.1.1) activity was determined according to Marklund and Marklund's method (Marklund & Marklund, 1974) and adapted by Castro et al. (2024), using an assay based on the inhibition of pyrogallol autoxidation, which was spectrophotometrically monitored at 420 nm for 4 minutes at 37 °C. Catalase (CAT; EC 1.11.1.6) activity was estimated as described by Nelson and Kiesow (1972). The decomposition of H_2O_2 was monitored for 1 minute at 240 nm (ΔE), using a spectrophotometer at 25°C (Costa et al., 2022).

Total antioxidant capacity (TAC) was estimated by the ferric reducing antioxidant power (FRAP) assay (Benzie & Strain, 1996), adapted by Castro et al. (2024). Briefly, the reduction of the ferric-tripyridyltriazine (Fe^{3+} -TPTZ) complex to

the ferrous form (Fe^{2+} -TPTZ) at acidic pH by non-enzymatic antioxidants in the sample determines the antioxidant capacity. The assay was performed following protocols that preserve enzymatic activity (Costa et al., 2022).

Protein concentration in the samples was determined by the Bradford method (Bradford, 1976), using bovine serum albumin (BSA) (1 mg/mL) as the standard.
All assays were performed in triplicate under blinded conditions..

2.4 Statistical analyses

The data were analyzed using GraphPad Prism version 8.0 (GraphPad Software, San Diego, CA, USA). Results were presented as mean ± standard deviation. The Shapiro–Wilk test was used to assess data normality. One-way ANOVA followed by Tukey's post hoc test was applied for group comparisons. Associations between clinical periodontal parameters and redox status markers were evaluated using Pearson's correlation test. Differences were considered statistically significant when $p < 0.05$.

3. RESULTS

A total of 18 participants were included in the study and distributed into four groups according to nutritional status and periodontal condition: normal weight with healthy periodontium (NHP, n=4), normal weight with gingivitis (NG, n=4), obesity with gingivitis (OBG, n=4), and obesity with periodontitis (OBP, n=6). The distribution of sexes varied across groups, but without statistically significant differences. Age was significantly higher in the OBP group compared to the OBG group ($p < 0.05$).

Descriptive data for clinical, anthropometric, and body composition parameters are presented in Table 1. Individuals with obesity (OBG and OBP) exhibited significantly higher values of BMI ($p < 0.0001$), body fat percentage ($p < 0.0001$), fat mass ($p < 0.0001$), visceral fat ($p < 0.001$), waist circumference (WC) ($p < 0.001$), and body fat index (BFI) ($p < 0.001$) compared to normal-weight groups (NHP and NG) ($p< 0.05$), as expected for this population. The OBP group presented the worst periodontal clinical indicators, including greater probing depth (PD), clinical attachment loss (CAL), bleeding on probing (BOP), and visible plaque index (VPI).

Gingival inflammation, assessed by bleeding on probing (BOP), was

significantly higher in the OBP group compared to the NHP and NG groups ($p < 0.02$); the OBG group also exhibited higher BOP compared to the NHP group ($p < 0.01$). No differences in BOP were observed between the obese groups or between individuals with gingivitis. Similarly, clinical attachment loss (CAL) was greater in the OBP group ($p < 0.03$), significantly differing from the other groups (Table 1), as expected.

Regarding periodontal diagnosis, within the OBP group, 50% presented generalized periodontitis and 50% localized periodontitis. In the OBG group, 50% had localized gingivitis and 50% generalized gingivitis. In the NG group, 75% exhibited localized gingivitis and 25% generalized gingivitis.

Results related to oxidative damage and antioxidant capacity are summarized in Figures 1 and 2.

Figure 1 illustrates markers of oxidative damage to lipids (A) and proteins (B) in the plasma of participants. Plasma TBARS levels were higher in the OBP group compared to the NHP group ($p < 0.05$), with intermediate values observed in the OBG and NG groups. Protein carbonyl derivatives (Figure 1B) showed a significant increase in the OBG group compared to the NHP and NG groups ($p < 0.05$).

Regarding erythrocyte and antioxidant markers (Figure 2), the OBP and OBG groups exhibited significantly higher levels of TBARS compared to the NHP and NG groups (Figure 2A). Superoxide dismutase (SOD) activity was significantly elevated in the OBP group relative to the normal-weight groups (Figure 2B), whereas no differences were observed between the normal-weight groups themselves. Catalase (CAT) activity showed no differences among groups (Figure 2C). Non-enzymatic total antioxidant capacity (TAC) levels (Figure 2D) were lower in the NG, OBG, and OBP groups compared to the periodontally healthy normal-weight group ($p < 0.05$), suggesting impairment of the antioxidant system in both obesity and gingivitis.

Correlation analyses were conducted separately for normal-weight and obese individuals to investigate potential associations between clinical periodontal parameters (visible plaque index [VPI], bleeding on probing [BOP], probing depth [PD], and clinical attachment level [CAL]) and systemic markers of oxidative stress.

Among obese individuals, a significant positive correlation was observed between plasma TBARS levels and probing depth ($r = 0.527$; $p < 0.04$), suggesting that higher levels of plasma lipid damage are associated with greater severity of periodontal inflammation. Erythrocyte TBARS correlated positively with plaque index ($r = 0.520$; $p < 0.02$) and bleeding on probing (BOP) ($r = 0.492$; $p < 0.05$), indicating

an association between biofilm accumulation and cellular oxidative damage. Additionally, protein carbonyl content showed a positive correlation with plaque index ($r = 0.416$; $p < 0.05$), reinforcing the role of protein oxidative stress in the local inflammatory response.

Regarding antioxidant markers in the obese group, significant negative correlations were observed between non-enzymatic total antioxidant capacity and bleeding on probing (BOP) ($r = –0.643$; $p < 0.01$), as well as between SOD activity and BOP ($r = –0.426$; $p < 0.05$) and probing depth (PD) ($r = –0.575$; $p < 0.05$). These findings indicate that reduced antioxidant defense is associated with increased inflammatory activity and periodontal destruction in these individuals (Table 2).

In the normal-weight group, a significant positive correlation was observed between erythrocyte TBARS and bleeding on probing (BOP) ($r = 0.534$; $p < 0.04$), indicating a possible association between oxidative damage and gingival inflammation even in individuals without excess body fat. Additionally, significant negative correlations were found between total antioxidant capacity (TAC) ($r = –0.797$; $p < 0.05$) and SOD activity ($r = –0.666$; $p < 0.01$) with BOP, suggesting that reduced antioxidant levels are also associated with increased gingival bleeding in this group. No significant correlations were observed between other markers and clinical parameters in normal- weight individuals.

4. DISCUSSION

This study analyzed the systemic redox profile in individuals with different nutritional statuses and periodontal conditions, aiming to understand how obesity and periodontal disease interact at both systemic redox and clinical levels. The anthropometric and body composition findings observed among the study groups were consistent with expectations, based on the nutritional classification criteria applied. From a periodontal clinical perspective, inflammatory parameters (including VPI, PD, BOP and CAL) also followed the expected trend, showing progressive worsening of periodontal condition in the gingivitis and periodontitis groups, respectively. Furthermore, no patients with obesity and periodontal heatlth were found, that is, all obese patients in the sample had some level of periodontal inflammation (gingivitis or periodontitis), which may suggest a greater propensity for imbalance in the local inflammatory response of obese patients.

The findings demonstrated that individuals with obesity generally exhibited higher levels of oxidative damage markers in plasma and erythrocytes, alongside significant reductions in antioxidant defense indicators (TAC and SOD), as previously reported (Furukawa et al., 2004). Individuals with obesity and periodontitis showed an intensification of these results compared to normal-weight individuals with periodontal health (plasma TBARS and SOD), while the lipid peroxidation marker in erythrocytes proved sensitive to obesity status in both gingivitis and periodontitis. This redox imbalance was directly associated with more severe clinical periodontal parameters, such as higher percentages of BOP, PD, and VPI, suggesting an exacerbation of local and systemic inflammatory responses in these patients.

Previous studies have demonstrated that obesity is associated with a chronic low-grade inflammatory state characterized by increased production of reactive oxygen species, inflammatory cytokines, and reduced antioxidant enzyme activity (Repetto et al., 2021; Furukawa et al., 2004; Atabek et al., 2006; Kolyva et al., 2014). This imbalance promotes a systemic pro-oxidative environment that may influence tissue responses to infections, including periodontitis. As described by Furukawa et al. (2004), hypertrophied adipose tissue releases large amounts of reactive oxygen species (ROS) and pro-inflammatory adipokines, which contribute to endothelial dysfunction and amplify the innate immune response. Our data support this view by demonstrating that individuals with obesity and periodontitis exhibited increased plasma and erythrocyte TBARS levels, which were directly associated with clinical markers of gingival inflammation, suggesting an exacerbation of systemic inflammatory response in these individuals.

Negative correlations between TAC/SOD and periodontal inflammation further support the link between antioxidant depletion and disease severity (Atabay et al, 2017; Toy et al., 2023). Additionally, the reduction in total antioxidant activity may be explained by the progressive consumption of protective molecules in response to the increased oxidative burden generated by chronic inflammation, both systemic and periodontal, while the increased enzymatic activity represented by SOD may suggest an attempt to regulate the redox imbalance (Chapple & Matthews, 2000).

Although associations between oxidative stress and gingival inflammation were also observed in normal-weight individuals, they were less consistent, reinforcing the role of obesity as a modulator of redox imbalance and periodontal severity. Similarly, Toy et al. (2023) reported that obese patients show reduced

clinical response to periodontal therapy and persistent oxidative and inflammatory markers in gingival crevicular fluid. In line with our results, Baltacıoğlu et al. (2014) also found negative correlations between non-enzymatic antioxidant levels in serum and saliva and periodontal parameters, such as plaque index and probing depth, in individuals with and without periodontitis.

Previous studies, even in non-obese populations, reported similar redox disturbances in periodontitis (Ahmadi-Motamayel et al., 2017; Panjamurthy et al., 2005), supporting the contribution of local inflammation. However, our data suggest that obesity amplifies this effect through synergistic ROS release from both adipose and periodontal tissues (Repetto et al., 2021).

Recent studies reinforce the hypothesis that periodontal inflammation acts as a “peripheral trigger” in individuals with obesity, activating systemic inflammatory and metabolic pathways through Toll-like receptors. According to findings compiled by Toy et al. (2023), obesity is not only associated with increased periodontitis severity but also modifies the response to periodontal treatment, potentially due to the pro-inflammatory profile sustained by adipokines and oxidative stress markers, both locally and systemically. Furthermore, research using experimental and human models indicates that lipopolysaccharides from Porphyromonas gingivalis can activate TLR4 receptors in adipose tissues, amplifying reactive oxygen species (ROS) release, hepatic inflammation, and metabolic alterations such as insulin resistance (Cani et al., 2007; Wallet, Puri & Gibson, 2018). These mechanisms help explain how obesity potentiates the systemic effects of periodontitis, creating a bidirectional pathway between metabolic disorders and periodontal disease—consistent with the findings of the present study, which demonstrated significant correlations between clinical periodontal parameters and systemic oxidative stress markers in obese individuals.

A relevant aspect of the present study is the assessment of oxidative stress and antioxidant defense markers at the systemic level through plasma and erythrocyte samples. This is particularly important in the context of chronic diseases, as sustained oxidative stress contributes to endothelial dysfunction, insulin resistance, and other metabolic comorbidities (Forbes & Cooper, 2013; Furukawa et al., 2004). Furthermore, this approach broadens the understanding of the clinical impact of periodontitis beyond the oral environment, positioning it as an inflammatory condition with metabolic effects of wider systemic reach. Previous studies, such as Atabay et al.

(2017), demonstrated increased MDA levels, protein carbonylation, and alterations in the total non-enzymatic antioxidant profile in individuals with periodontitis; however, these data were predominantly obtained from gingival crevicular fluid. Although such measurements provide important insights into the periodontal microenvironment, they do not necessarily reflect the systemic impact of oral inflammation. Thus, the present study is relevant as it addresses these markers at the systemic level.

Among the limitations of this study are the relatively small sample size and the absence of individuals with normal weight and periodontitis, as well as those with obesity and periodontal health. Nevertheless, established redox markers were employed, and the significant correlations support the relevance of the findings. Concerning the study groups, the results are consistent with epidemiological data showing a high prevalence of periodontal disease among overweight and obese individuals (Kassebaum et al., 2017).Conversely,the exclusion of classic risk factors—such as smoking, diabetes, and previous periodontal disease—helped ensure homogeneity among the groups (Kinane, Stathopoulou, & Papapanou, 2017).

Another important factor to consider in this study is the age difference between groups, with higher values observed in the obesity and periodontitis group. Aging is a well-recognized non-modifiable risk factor for the development and progression of periodontitis, and its severity increases with age (Eke et al., 2012; Kinane, Stathopoulou & Papapanou, 2017). In this context, the higher mean age in the group with greater disease severity aligns with expected epidemiological patterns. Although this age difference may have influenced the findings, the interpretation of the results should take this factor into account alongside the other clinical and biochemical variables assessed.

It is important to consider that the cross-sectional design of the study does not allow for the establishment of causal relationships. On the other hand, a major strength of the study lies in its integrated approach, combining clinical, anthropometric, and biochemical variables, which provides a broader understanding of the interactions between obesity, periodontitis, and oxidative stress.

In this exploratory study sample, the findings suggest that obesity may act as a relevant modulator of periodontal inflammation and systemic redox status.The associations observed between clinical periodontal parameters and oxidative stress markers, particularly in individuals with obesity, support the hypothesis that excess

adiposity exacerbates the systemic impact of oral inflammation. Thus, the present study provides preliminary evidence to guide future research with larger and more diverse samples, including these comparison groups, which are necessary to better clarify the interactions between therapeutic strategies. Furthermore, this study supports a differentiated clinical approach for patients with obesity and periodontitis by taking into account the impact of systemic inflammatory response and redox status in individuals affected by both conditions.

5. CONCLUSION

This exploratory study suggests that obesity may enhance the systemic effects of periodontal inflammation, as reflected by changes in circulating redox status. Further studies with larger samples and broader comparison groups are needed to confirm these findings and deepen our understanding of this relationship.

Authors' Contributions

Conceptualization and project administration: Karine Beatriz Costa, Fernanda de Oliveira Bello Corrêa, Pollyana Pereira Luciano de Souza, Etel Rocha Vieira and Marcelo Henrique Fernandes Ottoni.

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Visualization, writing – review & editing: All authors. All authors have read and approved the final version of the manuscript.

Ethics Statement

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Research Ethics Committee of the responsible institution Federal University of Juiz de Fora (Protocol No. 77963324.3.0000.5147).

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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TABLE 1- Periodontal, Anthropometric, and Body Composition Parameters in Participants Stratified by Nutritional and Periodontal Status

Clinical, anthropometric and body composition parameters	Study groups			
	NHP	NG	OBG	OBP
Age (years)	42.75 ± 9.81^{ab}	48.75 ± 3.50^{ab}	37.00 ± 14.31^{b}	54.67 ± 3.50^{a}
Sex (M/F)	2/2	0/4	1/3	2/4
BMI (kg/m^2)	22.87 ± 2.30^{a}	20.49 ± 1.33^{a}	38.63 ± 5.98^{b}	33.69 ± 2.47^{b}
Body fat (%)	26.48 ± 5.39^{a}	27.28 ± 4.67^{a}	48.08 ± 5.05^{b}	45.18 ± 5.78^{b}
Fat mass (kg)	17.50 ± 4.68^{a}	15.15 ± 3.86^{a}	52.95 ± 11.75^{b}	40.42 ± 7.24^{b}
Visceral fat level	7.00 ± 2.16^{a}	5.75 ± 2.06^{a}	22.0 ± 4.16^{b}	19.4 ± 4.39^{b}
WC (cm)	79.15 ± 11.03^{a}	69.00 ± 2.63^{a}	114.30 ± 6.92^{b}	102.10 ± 9.30^{b}
BFI (kg/m^2)	6.05 ± 1.59^{a}	5.76 ± 1.31^{a}	19.11 ± 4.77^{b}	15.62 ± 2.88^{b}
VPI	15.95 ± 5.75^{a}	20.32 ± 12.6^{a}	21.58 ± 14.7^{a}	36.54 ± 22.9^{a}
BOP (%)	5.69 ± 3.54^{a}	22.62 ± 8.59^{ac}	35.8 ± 14.19^{bc}	45.13 ± 13.3^{b}
PD (mm)	1.72 ± 0.38^{a}	1.94 ± 0.26^{ab}	1.96 ± 0.19^{ab}	2.73 ± 0.50^{b}
CAL (mm)	0.07 ± 0.06^{a}	0.22 ± 0.31^{a}	0.16 ± 0.30^{a}	2.13 ± 1.64^{b}

Data expressed as mean ± SD. $p < 0.05$ are represented by different superscript letters, one-way ANOVA, Tukey's post-hoc. BFI, body fat index; BMI, body mass index; BOP, bleeding on probing; CAL, clinical attachment level; f, female; GI, gingival index; m, male; NHP, normal weight + periodontally healthy; NG, normal weight + gingivitis; OBG, obesity + gingivitis; OBP, obesity + periodontitis; PD, probing depth; VPI, visible plaque index; WC, waist circumference.

TABLE 2- Correlation Between Clinical Periodontal Parameters and Systemic Redox Status Markers in Individuals with obesity.

	Clinical Parameters			
Systemic oxidative state markers	VPI	BOP	PD	CAL
Oxidative damage markers				
TBARS plasma	0.375	0.019	0.527*	0.496
TBARS erytrocytes	0.520*	0.492*	0.267	0.472
Protein carbonil content	0.416*	0.369	0.321	0.293
Antioxidants markers				
TAC	-0.124	-0.643*	-0.115	-0.217
SOD	-0.006	-0.426*	-0.575*	-0.429
CAT	-0.244	-0.062	-0.337	-0.348

Pearson's correlation coefficients between clinical periodontal parameters (visible plaque index – VPI, bleeding on probing – BOP, probing depth – PD, and clinical attachment level – CAL) and systemic oxidative stress biomarkers (TBARS, protein carbonyls, SOD, CAT, and TAC) in individuals with obesity. Values of r and p are presented. *$p < 0.05$.

TABLE 3 - Correlation between clinical periodontal parameters and systemic redox status markers in normal-weight individuals.

	Clinical Parameters			
Systemic oxidative state markers	VPI	BOP	PD	CAL
Oxidative damage markers				
TBARS plasma	0.062	0.179	0.385	0.058
TBARS erytrocytes	0.224	0.534*	0.425	-0.411
Protein carbonil content	0.281	-0.065	-0.0796	0.325
Antioxidants markers				
TAC	-0.317	-0.797*	-0.602	-0.406
SOD	-0.308	-0.666*	-0.330	0.062
CAT	-0.320	-0.295	-0.482	-0.068

Pearson's correlation coefficients between clinical periodontal parameters (visible plaque index – VPI, bleeding on probing – BOP, probing depth – PD, and clinical attachment level – CAL) and systemic oxidative stress biomarkers (TBARS, protein carbonyls, SOD, CAT, and TAC) in individuals with obesity. Values of r and p are presented. *$p < 0.05$.

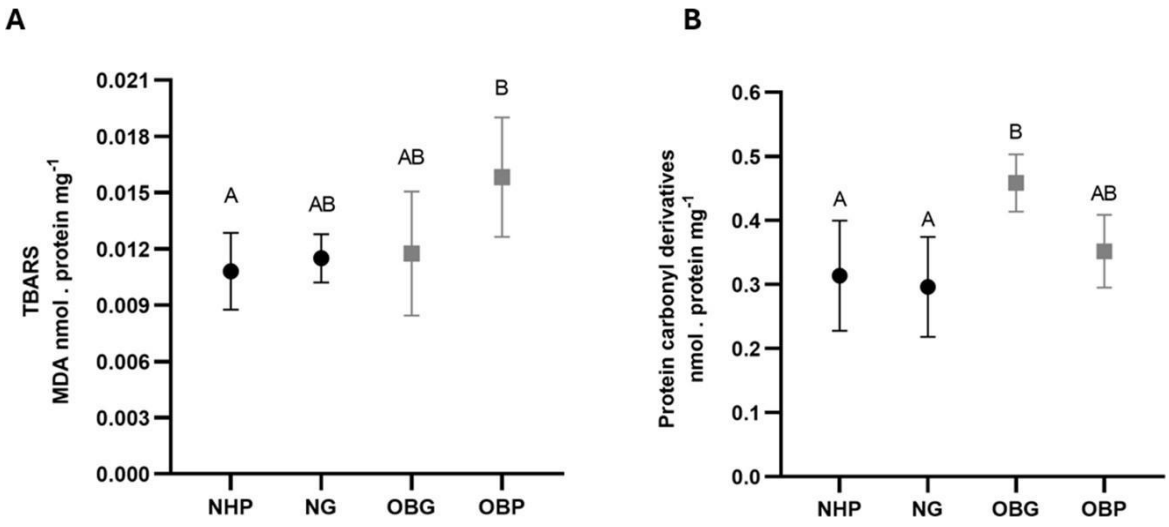

Figure 1 - Plasma oxidative damage markers in individuals with different periodontal and nutritional statuses. (A) Thiobarbituric acid reactive substances (TBARS) – marker of lipid peroxidation. (B) Protein carbonyl content – marker of protein oxidation. Data are expressed as mean ± standard deviation. Different lowercase letters indicate statistically significant differences between groups ($p < 0.05$; one-way ANOVA followed by Tukey's post hoc test). NHP: normal-weight periodontally healthy; NG: normal-weight with gingivitis; OBG: obese with gingivitis; OBP: obese with periodontitis.

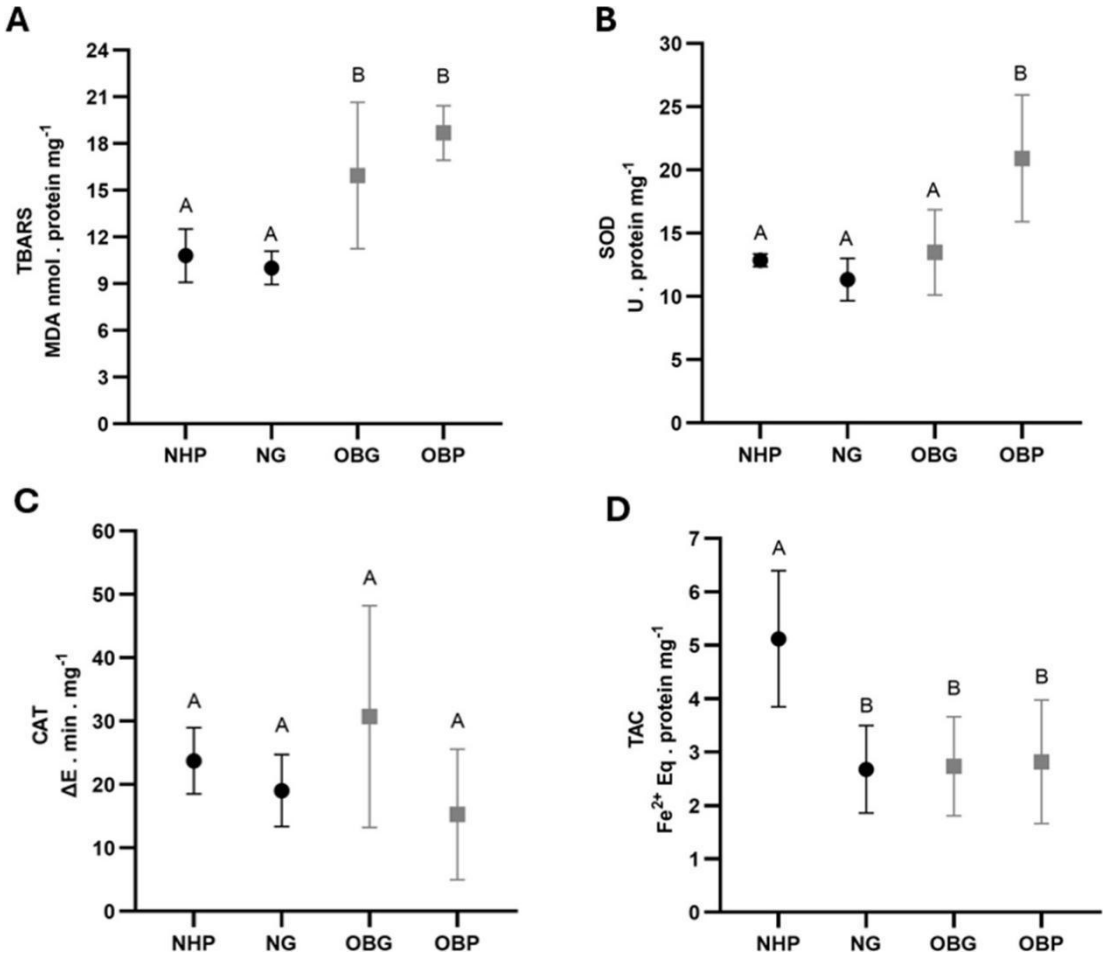

Figure 2- Oxidative damage and antioxidant activity in erythrocytes from individuals with different periodontal and nutritional statuses. (A) TBARS – marker of lipid peroxidation. (B) Superoxide dismutase (SOD) activity. (C) Catalase (CAT) activity. (D) total non-enzymatic antioxidant capacity (TAC). Data are presented as mean ± standard deviation. Different lowercase letters indicate statistically significant differences between groups ($p < 0.05$; one-way ANOVA followed by Tukey's post hoc test). NHP: normal-weight periodontally healthy; NG: normal-weight with gingivitis; OBG: obese with gingivitis; OBP: obese with periodontitis.

3. CONCLUSÃO GERAL

Este estudo exploratório sugere que a obesidade pode intensificar os efeitos sistêmicos da inflamação periodontal, refletidos por alterações no estado redox circulante. As correlações observadas entre marcadores clínicos periodontais e biomarcadores de estresse oxidativo indicam uma possível interação entre condição nutricional e resposta inflamatória. Novas investigações com amostras maiores e grupos comparativos mais amplos são necessárias para confirmar esses achados e aprofundar sua compreensão.

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APÊNDICE A – Normas e orientações da Revista

As orientações e normas para submissão do artigo referente ao capítulo 1 na revista Journal Clinical of Periodontology, podem ser encontradas no link abaixo: https://onlinelibrary.wiley.com/page/journal/1600051x/homepage/forauthors.html