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Adipokines and Inflammatory Biomarkers Linking Obesity and Periodontitis: A PRISMA-Guided Systematic Review

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 March 2026 and was last updated on 25 March 2026.

INTRODUCTION

Review question / Objective Among adults with obesity or obesity-related phenotypes and periodontitis, what systemic and local inflammatory biomarkers, adipokines, and directly assessed omics signals are reported, and how do these markers change after non-surgical periodontal therapy (NSPT)?

Rationale Obesity and periodontitis frequently coexist and may be linked by reciprocal inflammatory and metabolic pathways. Obesity is characterized by chronic low-grade inflammation and altered adipokine signaling, whereas periodontitis may increase systemic inflammatory burden through recurrent bacteremia, endotoxemia, and dissemination of inflammatory mediators. Although epidemiologic associations are reported, the biological mediators underlying the obesity-periodontitis axis remain incompletely defined, and evidence specific to biomarker changes after periodontal therapy in people with obesity is inconsistent. A focused synthesis of human biomarker evidence is therefore needed.

Condition being studied The condition being studied is the coexistence of obesity or obesity-related phenotypes and periodontitis in adults, with emphasis on systemic and local inflammatory mediators, adipokines, and directly assessed omics-derived signals relevant to host immune and metabolic dysregulation.

METHODS

Search strategy We will search PubMed/MEDLINE, Scopus, Embase, and Web of Science from January 2000 to 26 November 2024 using controlled vocabulary and free-text terms related to obesity/adiposity, periodontitis, and biomarkers/omics. The core strategy will combine terms such as (obesity OR adiposity OR body mass index) AND (periodontitis OR periodontal disease OR

gum disease) AND (biomarker* OR cytokine* OR adipokine* OR proteom* OR transcriptom* OR genetic* OR epigenetic*). Search strings will be adapted for each database. Reference lists of included studies and relevant reviews will also be screened.

Participant or population Adults with obesity or obesity-related phenotypes (typically BMI >= 30 kg/m^2, morbid obesity, bariatric surgery candidacy, or metabolic syndrome with central adiposity) and a clinical diagnosis of periodontitis. Studies including comparator groups without obesity and/or without periodontitis will also be eligible if the obese-periodontitis phenotype can be ascertained.

Intervention For interventional evidence, non-surgical periodontal therapy (NSPT), scaling and root planing, intensive periodontal treatment, or adjunctive periodontal therapy delivered in adults with obesity or obesity-related phenotypes and periodontitis. For observational studies, the exposure of interest is the coexistence of obesity and periodontitis.

Comparator No intervention comparator is required for observational studies. When reported, eligible comparators will include normal-weight or non-obese participants, obese participants without periodontitis, lean participants with periodontitis, pre-treatment versus post-treatment comparisons, or minimal/control periodontal treatment.

Study designs to be included Randomized controlled trials, controlled clinical trials, non-randomized interventional studies, cohort studies, case-control studies, longitudinal studies, and cross-sectional studies conducted in humans.

Eligibility criteria We will include peer-reviewed human clinical studies published in English between January 2000 and November 2024. Eligible studies must report at least one systemic (serum/plasma) or local (gingival crevicular fluid or saliva) biomarker relevant to inflammation or adipose-immune signaling, such as C-reactive protein, high-sensitivity C-reactive protein, IL-6, TNF-alpha, IL-1beta, leptin, adiponectin, resistin, or visfatin, or must report a directly assessed omics-derived signal (e.g., proteomics or genetic variation) in cohorts characterized for both obesity and periodontitis. We will exclude animal and in vitro studies, narrative reviews and meta-analyses, conference abstracts without extractable data, pediatric studies, and studies in which obesity or periodontitis status cannot be ascertained.

Information sources Electronic databases (PubMed/MEDLINE, Scopus, Embase, and Web of Science) and backward citation screening of included studies and relevant reviews. We will use full-text articles as the primary information source; conference abstracts without extractable data will not be included.

Main outcome(s) The main outcomes are systemic and local biomarker levels and/or between-group differences in inflammatory biomarkers and adipokines associated with obesity and periodontitis, including C-reactive protein/high-sensitivity C-reactive protein, IL-6, TNF-alpha, IL-1beta, leptin, adiponectin, resistin, visfatin, and related mediators measured in serum, plasma, gingival crevicular fluid, or saliva. For interventional studies, post-NSPT biomarker changes at reported follow-up time points will be extracted. Effect measures will be summarized as reported by the primary studies (e.g., means and standard deviations, medians and ranges, change from baseline, adjusted associations, or p-values).

Additional outcome(s) Additional outcomes will include periodontal clinical measures (e.g., probing depth, clinical attachment loss, bleeding on probing, plaque indices), metabolic or cardiometabolic markers reported alongside biomarker outcomes (e.g., lipid profile, glucose, insulin, HOMA-IR), obesity-related parameters, and directly assessed omics signatures such as salivary proteomic patterns or gene-environment interactions relevant to periodontitis progression.

Data management Search results will be exported from each database and deduplicated. Two reviewers will independently screen titles/abstracts and full texts, extract data using a standardized extraction form, and resolve disagreements through discussion with involvement of a third reviewer when necessary. Extracted items will include study design, setting, participant characteristics, obesity and periodontitis definitions, follow-up, biospecimen, analytical methods, biomarker panel, and main findings. When multiple reports describe the same cohort, the most complete dataset will be prioritized and companion publications will be noted.

Quality assessment / Risk of bias analysis Risk of bias will be assessed independently by two reviewers. The Cochrane Risk of Bias 2 tool will be used for randomized trials, ROBINS-I for non-randomized interventional studies, and the Newcastle-Ottawa Scale for observational studies. Disagreements will be resolved by consensus.

Strategy of data synthesis Because substantial heterogeneity is anticipated across study design, obesity phenotype, periodontal case definition, biospecimen, biomarker panel, and analytical methodology, quantitative pooling is not planned a priori. Findings will therefore be synthesized narratively and grouped into systemic inflammatory biomarkers, adipokines, local mediators (gingival crevicular fluid/saliva), and omics-derived signals. Interventional studies will be summarized separately from observational studies.

Subgroup analysis Where data permit, results will be narratively subgrouped by study design (interventional versus observational), biospecimen (serum/plasma versus gingival crevicular fluid/saliva), obesity phenotype (BMI-defined obesity, morbid obesity/bariatric candidates, or metabolic syndrome/central adiposity), periodontal case definition/severity, biomarker family, and type/intensity of periodontal therapy.

Sensitivity analysis A formal sensitivity analysis is not planned because a meta-analysis is not anticipated. If a sufficiently homogeneous subset of studies becomes available, sensitivity analyses excluding studies at high/serious risk of bias or special populations (e.g., pregnancy or bariatric surgery candidates) would be considered.

Language restriction English.

Country(ies) involved Romania.

Keywords obesity; periodontitis; periodontal therapy; adipokines; inflammatory biomarkers; proteomics; genetic variation; systematic review.

Contributions of each author

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