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INTEGRATING LABORATORY BIOMARKERS AND DENTAL IMAGING FOR THE DIAGNOSIS AND MONITORING OF ORAL DISEASES: A SYSTEMATIC REVIEW

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Abstract

Background: Oral diseases are traditionally diagnosed and monitored using clinical assessment supported by dental imaging. Imaging primarily reflects structural change and may lag behind early inflammatory or metabolic activity. Laboratory biomarkers from saliva, gingival crevicular fluid, and blood have been proposed to complement imaging, potentially improving early detection, risk stratification, and treatment monitoring. **Objective:** To evaluate the data on integrated use of laboratory biomarkers and dental imaging for diagnosing and monitoring major oral diseases. **Methods:** We systematically searched open access databases with emphasis on PubMed Central and Scopus, for original human studies assessing at least one laboratory biomarker alongside dental imaging outcomes. Studies addressing periodontitis, peri implant conditions, and apical periodontitis were prioritized. Two reviewers independently screened titles, abstracts, assessed full texts, and extracted study characteristics and key findings. Risk of bias was evaluated using appropriate tools for observational and clinical studies. **Results:** Eight eligible studies were included. In periodontitis, salivary inflammatory and bone turnover markers (IL 1β, IL 6, MMP 8, ICTP, HGF, osteonectin) were associated with radiographic alveolar bone loss and improved discrimination in disease states when used in panels. Studies in implant dentistry suggested that serum vitamin D status may relate to marginal, crestal bone levels assessed radiographically or by CBCT. In apical periodontitis, systemic inflammatory markers appeared to vary with baseline radiolucency size and treatment response.

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Conclusion: Available data supports a complementary role for biomarkers with imaging, but heterogeneity and limited longitudinal data prevent firm clinical thresholds.

Keywords: Oral Diseases; Biomarkers; Saliva; Vitamin D; Periodontitis; Dental Implants; CBCT; Radiography; Apical Periodontitis.

INTRODUCTION

Dental imaging, periapical radiographs, panoramic imaging, and cone beam computed tomography (CBCT), is central to diagnosing and monitoring oral diseases, especially when bone involvement is suspected. Yet imaging primarily captures established structural change, while early inflammatory or metabolic activity may not be visually apparent. This gap has driven interest in laboratory biomarkers that reflect host response, tissue breakdown, and bone remodeling.

Periodontitis is a prototypical condition where combining biomarkers with imaging may add value. Classical diagnosis is based on clinical measures and radiographic bone loss, but early detection and prognostic refinement remain challenging. Salivary biomarkers such as interleukin 1β (IL 1β), interleukin 6 (IL 6), matrix metalloproteinase 8 (MMP 8), and bone turnover markers have been repeatedly explored as adjuncts.

The premise is that inflammatory cytokines and collagenases may reflect active tissue destruction and help distinguish health, gingivitis, and periodontitis beyond what a single clinical or imaging snapshot can capture.

Large observational work linking salivary analytes to radiographic outcomes provides an important bridge between “lab” and “image.” For example, earlier cross-sectional data associated radiographic alveolar bone loss with salivary inflammatory and bone turnover markers, supporting the concept that saliva could mirror underlying bone pathology.

A related prospective signal suggested that baseline salivary hepatocyte growth factor (HGF), IL 1β, and osteonectin may help predict future radiographic bone loss in at risk populations.

In implant dentistry, marginal or crestal bone level changes are routinely monitored radiographically. Vitamin D, given its role in bone metabolism, has emerged as a candidate systemic biomarker potentially associated with osseointegration and peri implant bone maintenance.

Recent open access clinical studies and summaries indicate that vitamin D deficiency may be linked to less favorable radiographic bone outcomes, though data is mixed and heterogeneous.

Apical periodontitis provides another model for integration. Lesion size and healing are often evaluated on radiographs or CBCT, while systemic or local inflammatory markers may track disease burden and response to endodontic or surgical interventions.

Studies exploring these relationships suggest a biologically plausible, clinically relevant synergy. This systematic review synthesizes original data on combined biomarker imaging approaches in key oral disease categories.

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METHODS

This systematic review was conducted in accordance with PRISMA 2020 principles. The protocol conceptually predefined the research question, eligibility criteria, outcomes of interest, and analytical approach before study selection.

Eligibility Criteria: We included original human studies evaluating at least one laboratory biomarker (saliva, gingival crevicular fluid, or blood) alongside a dental imaging outcome for the diagnosis or monitoring of oral diseases.

Target conditions included periodontitis, gingivitis with radiographic alveolar bone loss, peri implant outcomes measured by radiographs or CBCT, and apical periodontitis assessed by radiographic, CBCT lesion characteristics.

Both observational and interventional designs were eligible. We excluded animal studies, in vitro only reports, narrative reviews, conference abstracts without full data, and studies lacking an imaging outcome.

Information Sources and Search Strategy: We searched PubMed Central and other open access sources for studies published up to 2025, using combinations of keywords and MeSH terms related to oral disease, periodontitis, apical periodontitis, dental implants, salivary biomarkers, serum biomarkers, radiography, and CBCT.

Reference lists of relevant open access articles were also screened to identify additional eligible studies.

Study Selection: Two reviewers screened titles and abstracts, then assessed full texts for eligibility. Discrepancies were resolved through discussion. Studies were grouped by disease domain (periodontal, peri implant, endodontic, apical) to facilitate structured synthesis.

Data Extraction: We extracted author, year, setting, study design, sample size, participant characteristics, oral condition, biomarker type and assay method, imaging modality and outcome definition, and principal findings linking biomarkers to imaging measures.

We prioritized results that explicitly connected biomarker levels with radiographic, CBCT bone or lesion parameters, or that used imaging as part of validated disease classification.

Risk of Bias Assessment: Observational studies were appraised using domain-based criteria aligned with STROBE principles and common risk of bias considerations (selection, measurement, confounding).

Interventional studies, when applicable, were assessed for randomization, allocation concealment, and outcome measurement transparency.

Due to heterogeneity in biomarkers, imaging outcomes, and study designs, a narrative synthesis was performed rather than meta-analysis.

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RESULTS

Study selection and overview

The search identified a focused body of open access literature where laboratory biomarkers were directly evaluated alongside imaging outcomes in oral disease. Eight studies met eligibility criteria and were included in qualitative synthesis. The data clustered into three domains: periodontal disease with radiographic alveolar bone loss, peri implant bone outcomes linked to systemic bone related biomarkers, and apical periodontitis with imaging defined lesion size and systemic inflammatory measures.

Table 1: Characteristics of included studies

Study (Author, Year)	Condition	Biomarker source, targets	Imaging modality, outcome	Design, sample	Key integrated finding
Ng et al. 2007	Periodontiti, bone loss	Saliva: IL 1β, TNF α, IL 6, PGE2, ICTP, osteocalcin, osteonectin	Intra oral radiographs assessing alveolar bone loss	Cross sectional; 110 untreated dental patients	Multiple salivary inflammatory and bone turnover markers associated with radiographic bone loss.
Scannapieco et al. 2007	Future alveolar bone loss risk	Saliva: HGF, IL 1β, osteonectin	Intra oral X rays; future bone loss assessment	Prospective signal in postmenopausal cohort	Baseline salivary HGF and IL 1β positively, osteonectin negatively associated with later radiographic bone loss.
Zhang et al. 2021	Gingivitis, periodontitis diagnosis	Saliva: IL 1β, MMP 8, ICTP, *P. gingivalis*	Radiographic, clinical reference standard	Diagnostic model study	Panels (IL 1β + ICTP + Pg) improved discrimination in health, gingivitis, periodontitis.
Reddahi et al. 2022	Periodontitis	Saliva: IL 1β, IL 6, MMP 8, IL 10	Radiographic + clinical periodontal diagnosis context	Pilot case control; 40 participants	IL 1β and IL 6 higher in periodontitis; authors emphasize biomarkers as complements to radiographic, clinical assessment.
Mohammed et al. 2022	Periodontal diagnosis, staging	Saliva: MMP 8, MMP 9, TIMP 1; ratios	Standard periodontal diagnostic framework (includes imaging)	Diagnostic accuracy study	Biomarkers and especially ratios showed strong discrimination between periodontal health and periodontitis.

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Singh et al. 2023	Dental implants	Serum vitamin D	CBCT based crestal bone level	Retrospective clinical study	Serum vitamin D correlated with CBCT measured crestal bone status post implant.
Tabrizi et al. 2022	Dental implants	Serum vitamin D sufficiency vs insufficiency	Long cone periapical radiographs; 12-month marginal bone loss	Prospective cohort	Vitamin D status evaluated against radiographic marginal bone loss over follow up.
Bakhsh et al. 2022	Apical periodontitis	Serum inflammatory markers	Radiographic apical radiolucency size + treatment outcome	Prospective, clinical interventional comparison	Systemic marker levels related to baseline radiolucency size and changes after retreatment or surgery.

Periodontal Disease: Biomarkers Aligned with Radiographic Bone Loss

Two landmark 2007 investigations provide direct data that salivary analytes reflect radiographic alveolar bone changes. Ng et al. evaluated untreated patients and reported associations between radiographic data of bone loss and salivary inflammatory mediators and bone turnover markers, including IL 1β and ICTP. This bridges biologic activity with structural imaging and supports saliva as a noninvasive adjunct for risk stratification. Scannapieco et al. extended this concept by suggesting predictive utility: baseline HGF and IL 1β showed positive, while osteonectin showed negative relationships with future radiographic bone loss in a postmenopausal cohort. Although the design and population limit generalizability, this study reinforces the possibility that biomarkers could forecast imaging detectable progression.

More recent diagnostic studies emphasize that single markers may be less reliable than multi marker panels. Zhang et al. found salivary IL 1β, MMP 8, ICTP, and *Porphyromonas gingivalis* to be effective for periodontal disease diagnosis, with combinations improving discrimination between health, gingivitis, and periodontitis. Reddahi et al. similarly reported higher IL 1β and IL 6 in periodontitis and highlighted the ongoing reliance on radiographic and clinical examinations, positioning biomarkers as complementary tools rather than replacements.

Collectively, these studies suggest a consistent direction of effect: inflammatory cytokines and collagen, bone degradation markers in saliva tend to increase with greater disease burden that is ultimately confirmed by radiographic bone loss.

Peri Implant Outcomes: Systemic Bone Related Biomarkers with Imaging

Two implant focused studies investigated vitamin D as a systemic biomarker linked to radiographic outcomes. Singh et al. used CBCT to evaluate crestal bone level and correlated these measurements with serum vitamin D status. Tabrizi et al. followed patients with periapical radiographs at loading and 12 months, comparing marginal bone

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loss in vitamin D sufficiency categories. While both studies support biologic plausibility, differences in design, follow up intervals, and imaging metrics limit direct comparability. Moreover, open access summaries of the broader literature note heterogeneity in outcomes and supplementation strategies.

Apical Periodontitis: Lesion Size and Systemic Inflammation

Bakhsh et al. provided relevant integrated data by measuring serum inflammatory markers in patients treated for apical periodontitis and linking these levels to baseline radiographic radiolucency size and long-term outcomes. This reinforces the concept that imaging defined lesion burden may carry systemic inflammatory correlates that evolve with successful treatment.

DISCUSSION

This review synthesized open access original data supporting a complementary relationship between laboratory biomarkers and dental imaging in the diagnosis and monitoring of oral diseases. The most coherent integration was observed in periodontitis, where salivary inflammatory and bone turnover markers aligned with radiographic alveolar bone loss and improved diagnostic discrimination when used in panels. The early cross-sectional framework by Ng et al. is mainly informative because it used radiographic bone loss as an anchor outcome while measuring a broad salivary inflammatory and bone remodeling profile. The prospective signal from Scannapieco et al. adds an important longitudinal perspective, suggesting that baseline biomarker patterns might anticipate later structural change visible on imaging. Even if future studies refine these findings, the concept is clinically attractive: a rapid salivary panel could flag high risk patients before substantial radiographic progression is evident. More contemporary biomarker panels, such as those involving IL 1β, MMP 8, ICTP, and microbial markers, suggest improved performance over single markers in differentiating health, gingivitis, and periodontitis. This aligns with the multifactorial pathophysiology of periodontal disease, where host and microbial signals jointly influence tissue breakdown and bone loss.

In implant dentistry, vitamin D represents a plausible systemic biomarker affecting osseointegration and peri implant bone stability. The included studies used CBCT or standardized radiographs to quantify crestal, marginal bone changes, providing a tangible imaging outcome linked to serum status. However, open access data summaries indicate that deficiency thresholds, supplementation timing, and confounders (smoking, diabetes, bone quality) vary widely in studies, limiting the adoption of definitive clinical cutoffs. For apical periodontitis, the association between systemic inflammatory markers and radiographic lesion size, treatment outcome suggests that endodontic disease can extend beyond a purely local process. This supports a broader model of oral systemic interplay in which imaging provides structural quantification while biomarkers reflect biologic activity and systemic burden. Despite encouraging signals, several limitations apply. First, the included body of literature is heterogeneous in biomarkers, assays, imaging modalities, and disease classification standards.

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Second, many studies are observational, increasing susceptibility to confounding. Third, the broad concept of “oral diseases” means that data strength is uneven in conditions; periodontal and implant contexts are more developed than other domains, such as MRONJ or oral mucosal disease within this specific integration framework. Future research should prioritize standardized biomarker panels, harmonized imaging outcomes (including CBCT quantitative metrics where appropriate), and well-designed longitudinal cohorts to define clinically actionable thresholds.

CONCLUSION

Integrated use of laboratory biomarkers and dental imaging shows promise for improving the diagnosis and monitoring of oral diseases. The strongest data exists in periodontitis, where salivary inflammatory and bone turnover markers align with radiographic alveolar bone loss and where multi marker panels improve discrimination in disease states. Implant studies suggest that systemic vitamin D status may relate to radiographic or CBCT assessed peri implant bone outcomes. In apical periodontitis, systemic inflammatory markers appear to correlate with radiographic lesion burden and response to therapy.

Reference

1) Bakhsh A, Moyes D, Proctor G, Mannocci F, Niazi SA. The impact of apical periodontitis, non-surgical root canal retreatment and periapical surgery on serum inflammatory biomarkers. Int Endod J. 2022 Sep;55(9):923-937. doi: 10.1111/iej.13786. Epub 2022 Jun 27. PMID: 35707939; PMCID: PMC9540413.

2) Mohammed HA, Abdulkareem AA, Zardawi FM, Gul SS. Determination of the accuracy of salivary biomarkers for periodontal diagnosis. Diagnostics (Basel). 2022; 12:2485.

3) Ng PYB, Donley M, Hausmann E, Hutson AD, Rossomando EF, Scannapieco FA. Candidate salivary biomarkers associated with alveolar bone loss: cross sectional and in vitro studies. Ann N Y Acad Sci. 2007. PMCID: PMC2258090.

4) Reddahi S, et al. Salivary biomarkers in periodontitis patients: a pilot study. [Journal details in PMC] 2022. PMCID: PMC8970949.

5) Scannapieco FA, Ng PYB, Hovey K, Hausmann E, Hutson A, Wactawski Wende J. Salivary biomarkers associated with alveolar bone loss. J Dent Res. 2007. PMCID: PMC2254505.

6) Singh S, Dhawan P, Kaur H. Correlation of serum vitamin D with crestal bone level in dental implant patients using CBCT: a clinical retrospective study. J Contemp Dent Pract. 2023.

7) Sun J, et al. Association between C reactive protein and periodontitis in population data. BMC Oral Health. 2023. (SpringerLink)

8) Tabrizi R, Mohajerani H, Jafari S, Tümer MK. Does the serum level of vitamin D affect marginal bone loss around dental implants? Int J Oral Maxillofac Surg. 2022 Jun;51(6):832-836. doi: 10.1016/j.ijom.2021.11.006. Epub 2021 Dec 3. PMID: 34872836.

9) Tallon E, et al. Can vitamin D levels influence bone metabolism and dental implant outcomes? Healthcare. 2024.

10) Zhang Y, et al. Evaluation of salivary biomarkers for the diagnosis of periodontal disease. PMC (2021. PMCID: PMC813017).