International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435 (Online) Volume 15, Issue 07, July 2026)

Emerging Point of Care Diagnostics and Biosensor Technologies in Periodontal Disease

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I. Introduction

Periodontal disease is a chronic, multifactorial inflammatory condition affecting the supporting structures of the teeth and remains a leading cause of tooth loss in adults worldwide [1]. Beyond its local oral impact, periodontal disease has been strongly associated with several systemic diseases, including diabetes mellitus, cardiovascular disorders, and adverse pregnancy outcomes [2]. Conventional diagnostic methods such as probing depth measurement, clinical attachment loss, and radiographic assessment are retrospective in nature and reflect past tissue destruction rather than current disease activity [3]. Consequently, there is a growing need for advanced diagnostic tools that can identify active disease at an early stage and enable timely intervention [4].

Recent developments in molecular biology have highlighted the crucial role of biomarkers as indicators of periodontal health and disease progression. These biomarkers, measurable in biological fluids such as saliva, gingival crevicular fluid (GCF), serum, and subgingival plaque, provide real-time insight into inflammatory and tissue-destructive processes [5,6]. The integration of biomarkers with biosensor technology has led to innovative diagnostic approaches that offer high sensitivity, specificity, and rapid detection at the point of care [7]. Emerging platforms such as lab-on-a-chip, microfluidic, and paper-based biosensors have made chairside analysis feasible, supporting the paradigm shift from conventional laboratory diagnostics to point-of-care testing (POCT) in periodontology [8,9].

This transformation represents a new era in periodontal diagnostics one that combines biotechnology, nanomaterials, and digital sensing to deliver personalized and preventive oral healthcare. This review aims to explore the evolving landscape of point-of-care diagnostics and biosensors in periodontal disease, highlighting recent advancements, biomarker identification, and their potential to revolutionize clinical practice.

II. Aim

The aim of this review is to comprehensively analyze the current developments, potential applications, and future prospects of point-of-care diagnostic technologies and biosensors in the detection and management of periodontal disease

III. Objectives

1. *To review* the role of biomarkers in the pathogenesis and diagnosis of periodontal disease.
2. *To explain* the fundamental principles and working mechanisms of biosensors and point-of-care (POC) diagnostic devices.
3. *To explore* recent technological advancements in biosensor-based periodontal diagnostics.
4. *To analyze* various biosensor platforms, including electrochemical, optical, and microfluidic systems, used for periodontal disease detection.
5. *To discuss* the integration of nanotechnology in enhancing biosensor sensitivity and miniaturization.
6. *To evaluate* the emerging role of smartphone-based and AI-enabled diagnostic tools in periodontal disease management.
7. *To examine* the clinical applications, advantages, and limitations of POC diagnostics in current periodontal practice.
8. *To identify* ongoing research trends, challenges, and future directions in biosensor and POC technology for personalized periodontal care.

IV. Review Of Literature

Periodontal Disease Biomarkers

Biomarkers are measurable indicators that reflect physiological or pathological conditions, providing valuable insights into a patient's overall health status [10].

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In the context of periodontal disease, biomarkers help in identifying disease activity, monitoring progression, and evaluating treatment response. These biomarkers can be detected in various biological media such as saliva, serum, and gingival crevicular fluid (GCF). However, since periodontal disease is a multifactorial condition, a single biomarker may not be sufficient to predict disease activity or severity. Therefore, a combination of multiple biomarkers is often utilized to enhance diagnostic accuracy and assess disease progression more comprehensively [11].

Based on their biological roles, periodontal disease biomarkers are classified into several categories

- *Enzymatic biomarkers* such as α-glucuronidase, acid phosphatase, alkaline phosphatase, elastase, and carboxytelopeptidase type-I indicate tissue destruction and cellular activity associated with inflammation.
- *Antimicrobial and immune response markers* like cystatins, lactoferrin, immunoglobulin M (IgM), and platelet-activating factor reflect the host's immune defense mechanisms against periodontal pathogens.
- *Matrix metalloproteinases (MMPs)* including MMP-8 (neutrophil collagenase), MMP-9 (gelatinase B), and MMP-13 (collagenase 3) serve as key tissue degradation markers that break down extracellular matrix components during periodontal breakdown.
- *Bone and tissue metabolism markers* such as osteocalcin and osteopontin are associated with alveolar bone turnover and remodeling.
- *Growth and repair factors* including epidermal growth factor (EGF) and platelet-derived growth factor (PDGF) play a crucial role in tissue healing and regeneration following periodontal destruction.

Together, these biomarkers provide a comprehensive understanding of the dynamic interactions between microbial challenge, host immune response, and tissue remodeling in periodontal disease [10].

V. Principle Of Biosensors And Point-Of-Care (POC) Devices

The integration of biosensor and point-of-care (POC) diagnostic technologies represents a major advancement in the detection and monitoring of periodontal biomarkers. A biosensor is an analytical device that couples a biological recognition element with a transducer to generate a measurable signal corresponding to the concentration of an analyte [12].

The biorecognition element which may be an enzyme, antibody, nucleic acid probe, or aptamer—selectively interacts with the target biomarker, while the transducer converts this biorecognition event into a quantifiable electrical, optical, or mechanical signal [13]. The signal is subsequently processed and displayed in an interpretable format, enabling rapid and accurate measurement [14].

In the context of periodontal diagnostics, biosensors offer a promising alternative to traditional laboratory assays by enabling real-time and chair-side detection of disease-specific biomarkers in easily accessible biological fluids such as saliva, serum, or gingival crevicular fluid (GCF) [15]. For instance, antibody-based biosensors for salivary Matrix Metalloproteinase-8 (MMP-8) have demonstrated high sensitivity and specificity, comparable to conventional enzyme-linked immunosorbent assays (ELISA), for distinguishing periodontitis from healthy conditions [16]. These devices provide rapid results, minimize the need for invasive sampling, and allow continuous monitoring of disease activity.

The **operational principle** of biosensors is based on three essential components:

1. *Bioreceptor:* Recognizes and binds the target analyte (e.g., MMP-8, osteopontin, lactoferrin).
2. *Transducer:* Converts the biological interaction into a measurable signal (electrochemical, optical, or piezoelectric).
3. *Signal Processor and Display Unit:* Amplifies, interprets, and presents the signal in a user-readable format [17].

The **electrochemical biosensors** are the most widely explored in periodontal applications because of their high sensitivity, portability, and low cost [18]. Optical biosensors, on the other hand, provide rapid and label-free detection with minimal sample preparation [19].

VI. Application Of Biosensors In Periodontal Disease

Periodontal disease progression involves complex interactions between microbial pathogens and host immune responses, leading to the release of multiple biomarkers such as matrix metalloproteinases, cytokines, and bone metabolism markers. Biosensors are particularly suitable for detecting such analytes due to their ability to **quantify small biomolecular changes** in real time.

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Several recent studies have reported the successful detection of MMP-8, interleukin-1β (IL-1β), and osteocalcin using electrochemical and microfluidic biosensors, supporting their clinical relevance in monitoring disease activity [20,21]. The **use of multiple biomarkers** rather than a single indicator enhances diagnostic accuracy. Advanced biosensor platforms now enable **multiplex detection**, allowing simultaneous measurement of different classes of biomarkers—enzymatic, immune, and metabolic—thereby providing a more comprehensive assessment of periodontal status [22].

Point-of-Care Diagnostic Devices

POC devices are miniaturized systems designed for diagnostic testing near or at the site of patient care, eliminating the need for central laboratory analysis [23]. These devices utilize biosensor technology to enable rapid, affordable, and user-friendly detection of periodontal biomarkers from saliva or GCF. According to the World Health Organization's ASSURED criteria (Affordable, Sensitive, Specific, User-friendly, Rapid, Equipment-free, and Deliverable to end users), ideal POC devices must combine analytical performance with clinical practicality [24]. In periodontal diagnostics, POC systems facilitate early detection, disease progression monitoring, and treatment evaluation. Microfluidic "lab-on-a-chip" and paper-based analytical platforms are under active development for this purpose [25]. Such technologies hold potential to revolutionize periodontal care by enabling clinicians to make evidence-based decisions chair-side, thereby improving personalized treatment outcomes.

VII. Recent Technological Advances In Periodontal Biosensing

Electrochemical Biosensors

Electrochemical biosensors remain the most widely explored platform for periodontal biomarker detection due to their high analytical sensitivity, simplicity, low cost, and ease of miniaturization for chair-side use. Recent advances have incorporated antibody and molecularly imprinted polymer (MIP) recognition layers onto modified electrodes such as graphene, gold nanostructures, and screen-printed carbon electrodes. These designs have enabled sensitive detection of biomarkers including MMP-8, IL-1β, and enzymatic activity markers in saliva and gingival crevicular fluid (GCF), often achieving detection limits in the low nanogram-per-millilitre range. Several prototypes have demonstrated analytical performance comparable to conventional laboratory-based ELISAs, while offering faster readouts suitable for point-of-care (POC) applications [26, 27].

Optical Biosensors

Optical biosensors, employing techniques such as surface plasmon resonance (SPR), fluorescence, surface-acoustic-wave (SAW), and colorimetric detection, provide label-free and highly specific analysis of periodontal biomarkers. These systems offer the advantage of real-time and multiplex detection, making them suitable for chair-side or home-based diagnostic use. Miniaturized SPR and SAW platforms have been developed for the detection of salivary biomarkers such as MMP-8 and cytokines, achieving rapid and reliable quantification with minimal sample preparation. Such optical configurations also support integration with microfluidic and smartphone-based systems for portable, visual-based diagnostics [28].

Microfluidic (Lab-on-a-Chip) Platforms

Microfluidic lab-on-a-chip technologies have revolutionized biosensing by integrating sample handling, separation, and multiplexed detection within a single miniaturized platform. These systems require only microlitre volumes, making them ideal for biological fluids like GCF and saliva. Recent "oral-chip" and "organ-on-chip" systems have demonstrated the simultaneous measurement of MMPs, IL-1β, and microbial DNA, facilitating rapid diagnosis and improved reproducibility. Furthermore, automated fluid control and sensor integration minimize operator variability and enhance assay precision, making these platforms promising candidates for chair-side diagnostics and personalized periodontal care [29].

Nanotechnology Integration

Nanotechnology has significantly enhanced biosensor performance through the incorporation of gold and silver nanoparticles, carbon nanotubes, graphene derivatives, quantum dots, and nanozymes. These nanomaterials increase the active surface area for biomolecular interactions, improve signal amplification, and enhance bioreceptor immobilization. Nanozyme-enhanced electrochemical and optical biosensors have achieved lower limits of detection, faster response times, and reliable detection even in complex oral matrices. Despite these advantages, challenges remain regarding long-term stability, biocompatibility, and prevention of biofouling, which are the focus of ongoing investigations [30].

Smartphone and AI-Enabled Diagnostics

Recent progress in smartphone-based biosensing has enabled real-time monitoring of salivary biomarkers using portable electrochemical and optical devices. Integration with wireless communication and cloud-based data storage facilitates remote patient monitoring and data sharing with clinicians.

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Concurrently, machine learning (ML) and artificial intelligence (AI) algorithms are being employed to interpret biosensor signals, enhance noise reduction, and identify disease patterns. These intelligent systems have shown potential to distinguish between periodontal health, gingivitis, and periodontitis based on biomarker signatures, paving the way for personalized and predictive periodontal diagnostics [32].

Clinical Applications and Current Research

Recent clinical research has focused on validating biosensor platforms for early diagnosis and monitoring of periodontitis. Both electrochemical and optical biosensors have been evaluated in pilot clinical trials for the quantification of biomarkers such as MMP-8, IL-6, and osteocalcin, demonstrating strong correlations with conventional clinical parameters including probing depth and bleeding on probing. Smartphone-compatible biosensors have enabled remote follow-up and post-treatment monitoring, enhancing patient compliance and accessibility to care. Ongoing research aims to standardize biomarker thresholds, expand multiplexing capabilities, and incorporate AI-driven predictive analytics to improve diagnostic accuracy and clinical decision support [33, 34, 35].

VIII. Discussion

Recent advances in point-of-care (POC) diagnostics and biosensor technologies have significantly transformed periodontal disease detection, enabling rapid, minimally invasive, and highly specific chairside testing. Traditional diagnostic tools, such as probing and radiographic evaluation, provide retrospective and operator-dependent assessments [2,3]. In contrast, biosensor-based systems now deliver real-time and quantitative information on disease activity through the detection of salivary and gingival crevicular fluid biomarkers such as MMP-8, IL-1β, and CRP [16,33].

Electrochemical biosensors are among the most extensively explored platforms in periodontal diagnostics due to their high sensitivity, low cost, and potential for miniaturization. Recent developments using graphene-based, gold-nanostructured, or screen-printed electrodes have achieved detection limits in the low nanogram per milliliter range for inflammatory markers [18,27,33]. Incorporation of nanomaterials such as gold nanoparticles, carbon nanotubes, and nanozymes enhances signal transduction efficiency and bioreceptor stability [22,31].

Optical biosensors including surface plasmon resonance (SPR), fluorescence, and colorimetric systems offer label-free and highly visual detection modes that are ideal for multiplexed salivary biomarker assays [19,29]. Miniaturized SPR and SAW-based platforms have achieved near real-time detection of salivary MMP-8 and cytokines, demonstrating promising accuracy for clinical application [29,35].

Microfluidic lab-on-a-chip and organ-on-chip systems integrate sample handling, immunoassay, and multiplex detection within a single miniaturized cartridge, enabling standardized and reproducible measurements with microliter-scale samples [20,30]. These systems allow simultaneous analysis of host and microbial biomarkers, providing deeper insight into disease pathogenesis and progression.

The emergence of AI-enabled and smartphone-integrated biosensors marks a major step toward digital periodontology. Machine learning algorithms can analyze biosensor outputs for biomarker pattern recognition and disease classification, improving diagnostic precision and real-time monitoring [32,34,35]. Smartphone interfaces allow remote data acquisition and cloud-based analytics, supporting teledentistry and patient-driven periodontal health monitoring [15,32].

However, challenges remain. Biological variability of saliva, biosensor calibration stability, and standardization across devices still limit clinical translation [4,7,23]. Adherence to the World Health Organization's ASSURED criteria—Affordable, Sensitive, Specific, User-friendly, Rapid, Equipment-free, and Deliverable—remains essential for ensuring accessibility and reliability of future biosensor platforms [24].

IX. Future Directions

The future of periodontal diagnostics lies **in** fully integrated, multi-analyte POC systems capable of simultaneously detecting biomarkers, staging disease, and monitoring therapeutic outcomes. Hybrid biosensors combining electrochemical and optical modalities may enhance analytical performance and multiplexing capability [19,21].

Nanotechnology-based innovations, such as nanozyme-enhanced and field-effect transistor (FET) biosensors, promise ultra-low detection limits and fast response times for early disease prediction [26,27,31]. Integration of AI and machine learning will enable predictive diagnostics by analyzing longitudinal biomarker and clinical datasets, advancing personalized treatment planning [34,35].

Microfluidic organ-on-chip systems offer physiologically relevant in vitro platforms for periodontal tissue simulation, allowing high-throughput biomarker validation and drug testing [20,30]. Meanwhile, smartphone-linked biosensors with cloud connectivity could extend diagnostic access to underserved regions, supporting portable, real-time disease surveillance [15,32].

Future research should focus on addressing device calibration, standardization, long-term stability, and large-scale clinical validation. Moreover, harmonization of regulatory frameworks and cross-disciplinary collaboration among clinicians, engineers, and data scientists will be essential for successful clinical translation of these technologies [1,4,23].

X. Conclusion

Emerging POC biosensor technologies are reshaping the diagnostic paradigm for periodontal disease, moving from conventional invasive assessments toward objective, real-time, and personalized diagnostic approaches. Progress in electrochemical, optical, microfluidic, and nanotechnology-based biosensors, coupled with AI and smartphone integration, has enhanced sensitivity, portability, and clinical applicability [5,8,18,19,32].

These systems offer unprecedented opportunities for early detection, disease monitoring, and treatment evaluation, contributing to the development of precision periodontology. However, clinical translation requires rigorous validation, affordability assessments, and adherence to WHO's ASSURED framework [24]. Continued collaboration among dental professionals, material scientists, and data engineers will drive the next generation of intelligent biosensors, ultimately enabling accessible and preventive periodontal care for all populations [1,4,27,34]

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Website: www.ijrdet.com (ISSN 2347-6435 (Online) Volume 15, Issue 07, July 2026)

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