

Review Article

Types, accuracy, and efficacy of salivary biomarkers in periodontal diagnosis

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ABSTRACT

Periodontal diseases primarily occur due, to infections and inflammation that affect the gums and bone structures supporting the teeth. In the stage, known as gingivitis the gums may become swollen turn red and bleed easily. These health issues not impact health but also have broader implications for overall well-being, including tooth loss, discomfort, bad breath and an increased vulnerability, to chronic illnesses. The main objective of this review is to examine aspects pertaining to diseases encompassing clinical indications, methods, for diagnosis, available treatment choices, and preventive strategies. This research meticulously examines the types of these diseases, their stages, and their causes. It also discusses the approaches and criteria used to diagnose these conditions. Additionally, the paper provides an evaluation of treatment alternatives and strategic frameworks, for managing pathologies. This includes both surgical approaches, well as supportive therapies. The paper emphasizes the importance of measures. Maintaining oral health through consistent dental hygiene practices, regular dental checkups, and necessary lifestyle adjustments. In conclusion, while periodontal diseases pose challenges in practice they can be controlled and prevented through collaboration, between dental practitioners, dental hygienists, and active patient participation.

Keywords: Accuracy, Biomarkers, Diagnosis, Efficacy, Periodontal disease

INTRODUCTION

Saliva contains molecules and microorganisms that can be found and used to diagnose or monitor oral and systemic diseases. One such disease is disease, a condition

characterized by inflammation in the tissues supporting the teeth caused by bacterial infection.¹ This condition can lead to tooth loss, difficulties in chewing, and an increased risk of disease, diabetes, and adverse pregnancy outcomes. Traditionally, diagnosing disease relied on radiographic

examinations like probing depth bleeding on probing, attachment loss, and bone loss. However, these methods have limitations; they are invasive, subjective time-consuming.^{2,3} It may not detect stages or active phases of the disease effectively. Therefore, there is a need for non-invasive diagnostic methods that provide objective information about patients at risk for periodontal disease while assessing its activity level and severity as well as evaluating treatment outcomes. Saliva proves to be a fluid for diagnostic purposes due to its ease of collection, storage convenience, and analytical feasibility.^{4,5} Saliva contains biomarkers that indicate the pathological conditions of both the oral cavity and the entire body. Salivary biomarkers can be grouped into four categories: agents, products, tissue degradation components of microbial origin, and modifiers of host response.⁶ Inflammatory substances are molecules that initiate and control the body's response to infection in relation to inflammation. This contains factors and enzyme, which includes cytokines, chemokines, and growth factors. Studies showed that any substance that is inflammatory in nature and is related to saliva is also related to periodontal disease. Certain substances play a role in this process by aiding the body's defense against infections and promoting wound healing.⁷ These include biomarkers that have demonstrated a connection with disease-related parameters. Demonstrate alterations after treatment. Tissue degradation products refer to molecules released as a result of the breakdown of the matrix and bone tissue during damage. In instances, collagen fragments, like pyridinoline linked telopeptide of type I collagen (ICTP) and C terminal telopeptide of type I collagen (CTX I) osteocalcin (OC) osteopontin (OPN) bone sialoprotein (BSP) and bone morphogenetic protein 2 (BMP 2) are used as examples. These biomarkers reflect the extent of tissue damage and bone resorption in disease, providing indicators for monitoring treatment effectiveness. Among several component examples, microbial components refer to microorganisms that are linked to the development of disease. They encompass DNA, RNA antigens, enzymes, toxins, and metabolic byproducts. On the other hand, host response modifiers are substances that impact. Alter how the host's immune system responds to bacterial infections. Additionally, there are complement components named C3a and C5a acute phase proteins like C reactive protein (CRP) and alpha one antitrypsin (AAT) antioxidants such as glutathione (GSH) and uric acid (UA) as hormones like cortisol and estrogen. These biomarkers provide insights into a person's vulnerability or resistance to disease.^{8,9} Various systemic factors, including stress, smoking, diabetes, and pregnancy, can influence their levels. The utilization of biomarkers for diagnosing disease offers several advantages compared to traditional methods. These benefits include being non-invasive, painless, cost-effective, quick, and accurate. However, there are some challenges and limitations to consider. These include variations in saliva flow rate and composition, the lack of validated tests, the necessity for more sensitive and specific biomarkers, as well as the complexities surrounding the interactions between multiple biomarkers.

Therefore, further research is required to discover reliable biomarkers.^{10,11} Research should also focus on establishing thresholds and predictive models while evaluating their clinical applicability and usefulness across different populations and settings. So, this study aims to review regarding the types, accuracy, and effectiveness of biomarkers in diagnosing periodontal disease.

METHODS

This study is based on an analysis of existing literature conducted on 17 September 2023, using the Medline and PubMed databases. We also searched on Google Scholar to find more journal paper. We utilized medical subject headings. Combined them with relevant keywords as outlined in the respective databases. Our search terms included "biomarkers," "diagnosis," as well as "accuracy" or "efficacy". Our focus was on studies involving participants and published in English. Additionally, we excluded any studies published before 2008. We carefully reviewed articles. Selected those that were directly applicable to our research objectives and met our inclusion criteria. The chosen articles were thoroughly examined in their entirety. In addition, we manually searched through the reference lists of these selected articles to identify any studies. From these articles, we extracted data that specifically addressed the types, accuracy, and effectiveness of biomarkers for diagnosis.

DISCUSSION

Salivary markers have become contenders for diagnosing disease. These markers, which include proteins, enzymes, and genetic material, offer benefits such as being noninvasive, easy to collect, and cost-effective. They hold the potential to transform detection techniques for diseases.

Types of salivary biomarkers

There is several research have undergone which identified biomarkers as a potentially relevant diagnosing tool for identifying periodontal diseases. Among all these biomarkers it contains several categories, including inflammatory, microbial, and genetic markers. There are several markers that mainly respond to bacteria for gum disease.¹² This may work as an inflammatory marker, which are cytokines including interleukin 1 β and tumor necrosis factor α , and it plays a significant role in this situation. When the levels of these markers are elevated in saliva, it indicates the presence of gum inflammation. Suggests the occurrence of a disease. Furthermore, saliva can be beneficial and can be utilized to detect DNA indicators of pathogens, like *Porphyromonas gingivitis* and *Treponema denticola*. Moreover, by examining markers, we can identify variations or polymorphisms that might increase an individual's susceptibility to diseases.¹³ Analyzing these factors in saliva helps us gain insight into an individual's predisposition towards experiencing issues.

Accuracy of salivary biomarkers

Salivary biomarkers represent molecular entities quantifiable within saliva, instrumental in the diagnosis and surveillance of periodontal maladies—a category encompassing enduring infections afflicting the gingival and bone structures that underpin our dentition. The accuracy of salivary biomarkers hinges upon a constellation of variables comprising the malady's evolutionary stage, the variegated array of biomarkers deployed, and the profound diversity intrinsic to individual salivary compositions.

An essential determinant influencing the accuracy of salivary biomarkers resides in the developmental stage of the associated periodontal disease.¹⁴ Salivary biomarkers exhibit heightened accuracy in the identification of incipient-stage periodontal afflictions marked by active inflammatory responses and elevated salivary biomarker concentrations. For instance, a research study examined the ability of saliva markers (MMP 8 and 9 along with TIMP 1) to distinguish between gums and both general periodontitis and stage 1 periodontitis. Nevertheless, as the malady advances into later stages marked by diminished inflammation and escalating tissue degradation, the precision of salivary biomarkers may undergo attenuation. For instance, another investigation revealed that salivary MMP-8 and -9 exhibited diminished sensitivity and specificity in distinguishing between asymptomatic individuals and those afflicted with stage 3 or 4 periodontitis.¹⁵ An additional facet exerting influence over the precision of salivary biomarkers pertains to the type and amalgamation of these biomarkers. Distinct biomarkers might encapsulate discrete facets of periodontal pathophysiology, spanning bacterial incursion, host response, tissue impairment, or systemic ramifications. Ergo, the judicious selection of biomarkers relevant to specific diagnostic purposes augments the veracity of salivary diagnostic modalities. Furthermore, amalgamating multiple biomarkers into a comprehensive panel augments diagnostic precision by furnishing supplementary information while concurrently mitigating the incidence of false-positive or false-negative outcomes. As an example, a study identified a tetrad of salivary biomarkers—MMP-8, MMP-9, osteoprotegerin, and interleukin-1 beta—wherein their amalgamation conferred superior diagnostic accuracy relative to any singular biomarker in prognosticating tooth loss resultant from periodontitis. Salivary biomarkers, as astute diagnostic agents, hold the potential to metamorphose the realm of periodontal disease diagnosis and monitoring. However, the practical value of these tests relies on a combination of factors. These factors include the stage at which the disease's, the choice of markers, and the personalized nature of saliva compositions.

As we delve deeper into the intricacies of these factors, we unveil the path toward harnessing the full potential of salivary biomarkers in the realm of periodontal care.

Efficacy of salivary biomarkers

Although salivary biomarkers provide significant importance compared to approaches for diagnosing and tracking periodontal disease, they have the ability to detect disease in its stages even before visible symptoms appear. This allows for prompt intervention and further tissue damage and tooth loss prevention. A study demonstrated that salivary levels of IL-1 β , MMP-8, and Pg. Patients with early-stage periodontitis showed levels of specific biomarkers compared to individuals with healthy gums.¹⁶ These biomarkers have the potential to predict the likelihood of deterioration in gum health. What's excellent about biomarkers is that they can be easily collected without any procedures like biopsies or radiation-exposing radiographs, which can be expensive and uncomfortable for patients. Simple devices like test strips or portable analyzers make it convenient for point-of-care testing and patient self-monitoring. Importantly, patients find salivary biomarkers acceptable since they don't cause any pain or discomfort during collection while allowing for monitoring of changes in gum health over time.

Clinical manifestations

Periodontal diseases encompass a variety of conditions that impact the gums and the underlying bone, which play a role in supporting the teeth. These conditions can vary from gum inflammation, commonly known as gingivitis, to cases involving infection and deterioration of tissues and bone, referred to as periodontitis. Having diseases can impact your health and well-being, leading to tooth loss, discomfort, bad breath, and an increased risk of chronic conditions. That is why it is crucial to be aware of the indications of these illnesses and actively seek assistance. Gingivitis represents the stage of the disease, which arises from the buildup of plaque—a sticky bacterial film—on teeth. This plaque can inflame gums, leading to redness, swelling, and tenderness.¹⁷ The gums may also bleed easily when brushing or flossing. Gingivitis is usually reversible with good oral hygiene and professional cleaning. If someone fails to take care of gingivitis, it may develop into a severe condition known as periodontitis. Periodontitis signifies an advanced stage of gum ailment characterized by the emergence of minuscule lacunae amidst the teeth and the gum tissue. These spaces can trap plaque and tartar, leading to infection. The bacteria in the pockets can produce toxins that damage the gum tissue and the bone that supports the teeth. This can lead to gingival recession, which exposes more of the tooth root and makes the teeth look longer. The teeth may also become loose or shift in position due to bone loss. Sometimes, infected fluid like pus may be discharged from the pockets, and this could indicate the presence of an abscess or a collection of pus in the tissue. Furthermore, Periodontitis may precipitate anguish, impediments in mastication, and even dental attrition. Myriad investigations have elucidated a nexus between periodontitis and an augmented susceptibility to maladies such as diabetes mellitus, respiratory afflictions, and rheumatoid arthritis, as well as untoward sequelae

during gestation.^{18,19} The clinical manifestations and indications of infirmities can manifest heterogeneously contingent upon variables encompassing the ailment's category, severity, scope, and persistence. Diverse morphologies of periodontitis exist, comprising the chronic, aggressive, necrotizing variants or those concomitant with comorbidities. Each phenotype possesses its own idiosyncratic attributes and predisposing factors. The stratification of periodontitis can be delineated into four phases contingent upon the degree of soft tissue and osseous forfeiture. The gradation of periodontitis may be further bifurcated into localized or generalized predicated upon the number of dentitions implicated. The temporal evolution of periodontitis can be gauged by quantifying the tempo of advancement and the responsiveness to therapeutic interventions.

Management

In order to manage periodontal diseases, there are multiple approach required that includes aspects such as prevention, diagnosis, treatment, and ongoing maintenance. The overarching objectives of this management endeavor revolve around the eradication of infection and inflammation, the arrest or deceleration of tissue and bone degradation, the restoration of both functional and aesthetic aspects of dental and gingival structures, and the proactive prevention of relapse and complications. It is crucial that the treatment of diseases is carried out as an effort involving the skills of the dentist, the dental hygienist, and the active participation of the patient. Prevention aims to reduce the chances of problems by strengthening the elements that safeguard gum health. One of the preventive measures is to maintain good oral hygiene by brushing and flossing daily. This helps remove plaque and tartar, which can harbor bacteria, causing damage to gums and underlying bone structures. Additional preventive strategies encompass abstaining from tobacco consumption, as its deleterious effects amplify both the susceptibility to and severity of periodontal afflictions. A well-balanced diet replete with essential nutrients conducive to gum health is also instrumental, alongside regular dental visits for professional cleanings and examinations, serving as early detection measures for timely intervention in the event of burgeoning periodontal diseases. The subsequent step in this comprehensive regimen is the pivotal aspect of diagnosis. Diagnosis entails a comprehensive oral examination aimed at assessing the symptomatic manifestations of periodontal diseases. The arsenal of diagnostic tools at the disposal of the dentist encompasses visual scrutiny, probing depth assessment, evaluation of bleeding upon probing, measurement of attachment levels, radiographic scrutiny, microbial analysis, genetic profiling, and biomarker evaluation. These modalities collectively facilitate the determination of disease type, severity, extent, and chronicity, ultimately guiding the formulation of tailored treatment strategies. Furthermore, it is essential to conduct an examination of the patient's medical background to uncover any underlying systemic

conditions or medications that may have an impact on their periodontal health. Treatment constitutes the subsequent juncture in the endeavor to manage periodontal diseases. The selection of the treatment approach depends on factors, including the type, severity, extent, and duration of the disease, as well as the patient's medical background and personal preferences.²⁰ There are options for treatment, such as nonsurgical methods, surgical procedures, additional therapies, and supportive treatments. Nonsurgical interventions assume primacy in managing most instances of periodontal diseases, encompassing procedures such as scaling and root planing to eliminate plaque and calculus deposits, administration of antibiotics or antimicrobials to curb bacterial proliferation, and the provision of oral hygiene instructions to empower patients in their plaque control endeavors.²¹ Surgical interventions come to the fore in cases marked by advanced or recalcitrant periodontal diseases. Procedures include flap or pocket reduction surgeries, bone grafting or guided tissue regeneration to restore lost bone and tissue, soft tissue grafting or gingival augmentation to conceal exposed tooth roots or augment thin gingival tissues, crown lengthening or gingivectomy to reshape excessive gum or bone tissue, and dental implantation to replace missing teeth with prosthetic crowns anchored by artificial roots. Adjunctive therapies may complement non-surgical or surgical interventions, including local or systemic antibiotic delivery systems, host modulation agents, laser therapy, photodynamic therapy, or the application of regenerative materials and growth factors to stimulate tissue regeneration.²² Vital to the overall management paradigm are supportive therapies that safeguard treatment outcomes. These entail maintenance care and recall visits for periodic monitoring of periodontal health, reinforcement of oral hygiene practices, smoking cessation counseling, nutritional guidance for gum health, and, when necessary, referral to specialists offering complex or interdisciplinary care. In the narrative of periodontal disease management, maintenance is a perpetual undertaking necessitating ongoing vigilance. In terms of these professional interventions, it is incumbent upon patients to diligently adhere to daily oral hygiene practices, encompassing regular brushing and flossing, to ensure sustained periodontal health. This regimen serves as a bulwark against the resurgence or progression of periodontal diseases, ensuring the enduring stability of periodontal well-being.

CONCLUSION

Periodontal disease stands as the prevailing affliction, impacting the gingival and bone tissues, and they are amenable to preemptive measures. The effective management of periodontal disorders necessitates a comprehensive strategy encompassing prophylactic initiatives, meticulous diagnosis, therapeutic interventions, and perpetual upkeep. The principal objectives of this therapeutic course encompass eradicating microbial infection and localized inflammation, attenuating or decelerating connective tissue and bone resorption, and

reinstating the form and functionality of dental and gingival structures. This comprehensive approach also takes into account the aspect of preventing relapses and complications. Successfully managing these conditions depends on the efforts of the dentist, dental hygienist, and the committed patient.

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