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Early Diagnostic Potential of aMMP-8 POCT for Periodontitis in Type 2 Diabetes: A Narrative Review

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Abstract

Introduction: Approximately 589 million adults worldwide suffer from diabetes mellitus, with over 90% having type 2. One of its key oral manifestations is periodontitis, a chronic inflammatory disease that often remains unnoticed due to its silent progression, leading to late detection and poor prognosis. Early diagnosis and treatment of periodontitis are crucial, especially in high-risk groups such as diabetic patients. Active Matrix Metalloproteinase-8 (aMMP-8) has shown great potential as a biomarker with high precision for early diagnosis. aMMP-8 levels are measured non-invasively through various Point-of-Care Tests (POCT). This review aims to explore the early-diagnostic potential of aMMP-8 POCT in identifying periodontitis in patients with type 2 diabetes.

Method: An electronic search through PubMed/MEDLINE and EMBASE databases was conducted to identify clinical studies published within the past 10 years, without language or geographical restrictions. Additionally, relevant literature was also identified through WILEY. Search terms used included “periodontitis,” “type 2 diabetes mellitus,” and “aMMP-8,”.

Result: The reviewed studies suggested aMMP-8 POCT as an efficient, accurate and practical diagnostic tool for periodontitis, especially in high-risk groups such as patients with type 2 diabetes. Elevated aMMP-8 levels were strongly associated with periodontitis progression. Moreover, unlike conventional methods that often fail to detect early or asymptomatic cases, aMMP-8 POCT can detect ongoing periodontal breakdown chairside in clinical practice within approximately 5 minutes, thereby offering a significant advantage.

Conclusion: aMMP-8 POCT shows strong potential in detecting early periodontal tissue destruction in type 2 diabetes patients, enabling timely intervention, improving prognosis, and supporting integrated management between systemic and oral health.

Keywords: Periodontitis; Type 2 Diabetes Mellitus; aMMP-8 biomarker; Point-of-Care Test

1. Introduction

Diabetes mellitus is a non-communicable, chronic metabolic disorder characterized by persistently elevated glucose levels, known as hyperglycemia. This condition may arise from impaired secretion of insulin, resistance to insulin action, or both [1]. Diabetes mellitus poses a significant global health challenge, indicated by approximately 589 million adults aged 20-79 years worldwide suffering from the condition, which is predicted to skyrocket up to 853 million by 2050. In Indonesia, over 20 million adults suffer from this systemic disease, representing a prevalence rate of 11,3% [2]. Type 2

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diabetes mellitus (T2DM) accounts for over 90% of the global diabetes burden, making it the most prevalent form of the disease [2].

The progression of type 2 diabetes mellitus (T2DM) exerts adverse effects on multiple organ systems, leading to diverse complications. Type 2 diabetes is commonly associated with conditions of macroangiopathy, retinopathy, neuropathy, nephropathy, ulcers, and cardiovascular diseases [3]. In addition to systemic burdens, diabetes also causes a wide range of complications to the oral cavity, a few of which include dry mouth (xerostomia), dental caries, periapical lesions, periodontal disease, halitosis, oral candidiasis, delayed wound healing, and lichen planus [4]. One of the most notable oral complications arising from this metabolic disorder is periodontitis.

Periodontitis is a chronic inflammatory disease normally characterized by the destruction of the supporting structures of the tooth, namely the periodontium, which includes the periodontal ligament, gingiva, alveolar bone and cementum [5, 6]. This disease is initiated by polymicrobial biofilms on tooth surfaces as the primary causative factor. However, the severity and progression of periodontitis are heavily driven by the host's immune-inflammatory response [5]. In T2DM patients, hyperglycemic conditions, mainly caused by a mass of advanced glycation end-products (AGEs), upregulation of their receptors (RAGEs), and overexpression of pro-inflammatory cytokines, alter this physiological immune response. As a result, prolonged inflammation occurs, which disrupts tissue-repair processes and accelerates periodontal destruction [7, 8].

Various studies have established the bidirectional relationship of periodontitis and T2DM. However, despite the well-recognized relationship between the two chronic disorders, periodontitis often remains unnoticed in diabetic patients due to its asymptomatic progression. As a result, significant damage of the periodontal tissue may occur before properly addressed, making timely and effective treatment difficult, which leads to a poor prognosis [9, 10].

This diagnostic gap indicates the need for a more sensitive, rapid, and minimally-invasive tool to early-diagnose progressing periodontitis before significant tissue loss occurs. Recently, increased studies have found validated biomarkers to be a good indicator of real-time periodontal tissue breakdown. Among various biomarkers, one that has gained attention for its association to periodontal tissue breakdown is matrix metalloproteinase-8 (MMP-8) [11, 12]. This proteolytic enzyme is initially secreted as latent MMP-8, but is found to have better potential of diagnostic accuracy in its active form, known as active matrix metalloproteinase-8 (aMMP-8) [13]. aMMP-8, also known as active collagenase-2, indicates collagen breakdown in the periodontal tissues and therefore is related to the progression of periodontitis. Moreover, clinical signs of periodontitis were found in association with increased aMMP-8 levels in the oral cavity [14].

In recent years, aMMP-8 Point-of-Care Tests (POCT) have been developed, which act as a chairside, rapid, and non-invasive method to detect active periodontal tissue breakdown. Another advantage this approach offers is its ability to be easily integrated into both dental and non-dental medical settings. Such a tool may potentially be valuable for enabling earlier diagnosis of periodontitis in high-risk groups, such as T2DM patients [15].

This narrative review aims to explore the potential of aMMP-8 Point-of-Care Tests (POCT) as a rapid, non-invasive, and clinically efficient method for the early detection of periodontitis in individuals with type 2 diabetes, thus enabling timely intervention and improving patient prognosis.

2. Type 2 diabetes mellitus (t2dm) and periodontitis

Periodontitis and type 2 diabetes mellitus (T2DM) are prevalent chronic inflammatory diseases that often coexist and influence each other. The coexistence of both conditions indicates their high prevalence globally. Epidemiological research indicates that poorly managed diabetes significantly elevates the risk of periodontitis by about two to three times higher than in individuals with normal blood sugar levels. An epidemiological study in 2021 estimated the prevalence of adults living with diabetes at approximately 10.5% globally [16]. Similarly, the Global Burden of Disease (GBD) study in 2021 indicates the high prevalence of severe periodontitis in the worldwide population, reporting an age-standardized prevalence rate (ASPR) of 12,498.3 per 100,000 individuals in 2021 for a total of more than one billion people [17].

This global trend is also reflected in Indonesia, where the prevalence of both conditions is similarly concerning. The 2023 Indonesian Health Survey (SKI) reported that the prevalence of diabetes mellitus among individuals aged ≥15 years, based on blood glucose examinations, was 11.7% [18]. Additionally, the Basic Health Research (Riskesdas) in 2018 also found that the prevalence of periodontal disease in Indonesia reached 74.1% [19]. This high prevalence

underscores the need for integrated and attentive strategies from healthcare professionals to manage both conditions effectively.

The shared overlap incidence is significant for clinical populations as the two conditions affect each other in a bidirectional way, extending beyond oral health issues. Periodontitis leads to tooth loss, reduced life quality, and systemic inflammation, which can hinder glucose control and deteriorate overall health. Moreover, diabetes mellitus hastens periodontal destruction, resulting in increased attachment loss and alveolar bone resorption compared to non-diabetic individuals [20].

The mechanism via which T2DM causes periodontal degradation in periodontitis is a bidirectional link between the two diseases. In patients with T2DM, chronic hyperglycemia triggers a cascade of metabolic and immunological alterations that magnify the destructive processes in periodontal tissues. These occur through microbiota factors, inflammatory cytokines, immune response, oxidative stress, and periodontal tissue destruction [21, 22].

In the diabetes-mediated pathway to periodontitis, hyperglycemia and its downstream effects worsen the onset and progression. Hyperglycemia in those with T2DM modifies the periodontal microenvironment and the host response, resulting in the accumulation of advanced glycation end products (AGEs) in the periodontium that leads to periodontal tissue destruction. These AGEs induce oxidative stress, mitochondrial malfunction, and apoptosis of periodontal cells, hence the periodontium is more prone to degradation [21, 22].

By binding to their receptors, namely RAGEs, AGEs were found through numerous studies to affect all types of periodontal tissues, both directly and indirectly. This includes periodontal ligament stem cells (PDLSCs), gingival fibroblasts (GFs), periodontal ligament cells, and epithelial cells. In PDLSCs, AGE exposure inhibits osteogenic differentiation via activation of the Wnt/β-catenin pathway, thereby reducing bone regeneration capacity. Similarly, in gingival fibroblasts, AGEs enhance ICAM-1 and RAGE expression and increase oxidative stress by activating NF-κB and MAPK signaling, which amplifies the inflammatory cascade. In gingival epithelial cells, AGEs upregulate RAGEs and TLR2 through NF-κB, JNK, and p38 pathways, promoting calprotectin activation (S100A8/A9) and sustaining local inflammation. AGE/RAGE signaling in periodontal ligament cells additionally activates inflammasomes such as NLRP1 and NLRP3, further driving inflammatory mediator release. Collectively, these effects result in an exaggerated and persistent inflammatory response in periodontal tissues, coupled with enhanced ROS production and impaired tissue repair, thereby increasing the risk of periodontitis in diabetic patients [22, 23].

DM enhances the susceptibility to periodontitis by amplifying the inflammatory response to oral bacteria. Clinical studies reveal that levels of pro-inflammatory cytokines such as IL-1, IL-6, and TNF-α levels are significantly elevated in patients with both DM and periodontitis compared with only the periodontitis alone. This then aggravates periodontal destruction, demonstrated by increased TNF expression, greater leukocyte infiltration, increased levels of aMMP-8 and more extensive bone loss. At the cellular level, hyperglycemia and AGEs, further with *Porphyromonas gingivalis* lipopolysaccharide (LPS) act to modulate TLR expression, activate NF-κB signaling, and promote the production of pro-inflammatory cytokines [23].

Conversely, the relationship of periodontitis to diabetes starts when periodontal bacteria and their products disseminate into the bloodstream, triggering insulin resistance by inhibiting hepatic glycogen synthesis. Thus, this increases gluconeogenesis and interferes with insulin signaling via branched-chain amino acids (BCAA). In addition, *Porphyromonas gingivalis*-derived dipeptidyl peptidase-4 (Pg-DPP4) accelerates degradation of glucagon-like peptide-1 (GLP-1), reducing glucose-stimulated insulin secretion, while bacterial virulence factors may contribute to pancreatic β-cell dedifferentiation. Furthermore, periodontitis intensifies systemic inflammation, which can affect hepatic and adipose tissues, promoting the resistance of insulin. Additionally, swallowing periodontal bacteria can lead to gut dysbiosis, driving endotoxemia and altering the circulating metabolome, both of which negatively influence glucose regulation [23].

3. Challenges in early detection of periodontitis in t2dm patients

In the early stages of periodontitis in diabetic patients, there is often a lack of clear clinical manifestations. Although inflammation and tissue breakdown has progressed at a molecular and cellular level, periodontitis phases normally remain subclinical and undetected. This subclinical nature poses a major challenge, as the condition persists until irreversible damage of the periodontium becomes clinically evident. At this point, it is already too late to attempt restoring the physiological condition of the oral cavity, and management becomes focused on halting progression rather than reversing the disease. Thus, patients suffering from diabetes are often found with already severe periodontitis in clinical check-ups by dentists, often when bone loss or tooth mobility has already occurred [9].

A cross-sectional study testing the relationship between different progressions of periodontitis and the patient's glycemic control, which indicates whether the patient suffers from diabetes, found that the prevalence of severe periodontitis is the highest (97.9%) in participants with poor glycemic control. This underscores the close association between diabetes severity and periodontal breakdown. In other words, the majority of individuals suffering from T2DM are often diagnosed with periodontitis only in its advanced stages, when bone destruction and tooth mobility have already taken place [9]. This is because the elevation in HbA1c levels was more evident in patients with stage III and IV periodontitis. Thus, when the glycated levels show clear signs of an increase (like for example the HbA1c levels exceeding the threshold for diabetes diagnosis) that serves as cues to the person that he might be prone to periodontitis, the person would have already found out that he is already at the late stages of periodontitis, whereby treatment plans are more focused to slow down the progression of the disease and not to eliminate the disease in its early stages [24].

In fact, periodontitis was also found to be significantly associated with elevated glycated hemoglobin levels in patients not previously diagnosed with diabetes. This suggests that the early stages of periodontitis have a silent onset and are often asymptomatic. Subtle HbA1c increases may already signal periodontitis even before someone is formally diagnosed with diabetes with a HbA1c score of more than equal to 6.5% [22].

Furthermore, in stage IV periodontitis, patients with pCC (periodontal chief complaints) of mobility were observed the most. Interestingly, this finding noted that patients sought dental care primarily due to aesthetic reasons rather than functionality [25]. The chief complaints recorded include deposits, stains, bleeding gums, attrition, mobility, foul odour, cervical abrasion, hypersensitivity, food impaction, gingival enlargement, abscess and peri-coronitis [26]. Only 5 of them were considered periodontitis symptoms, highlighting the difficulty of relying on patient-reported symptoms for early detection since patients often seek care for cosmetic reasons rather than functional or inflammatory symptoms. Hence, subjective complaints are not able to act as indicators of early disease. In the context of the expectation that T2DM patients would seek care for periodontitis in its early detection, it is found that many patients tend to delay dental visits until pain, chewing difficulties, or tooth mobility occur, by which time the disease is already advanced [27].

4. aMMP-8 accuracy as a biomarker in periodontitis

Early detection and monitoring of periodontitis is crucial for preventing disease progression and improving treatment outcomes. Various biomarkers have been studied for periodontitis detection, including cytokines (e.g., IL-6), C-reactive protein, interferon gamma (IFN-γ), oxidative stress markers, and vitamin C. However, recent advances in salivary diagnostics have identified a specific biomarker that can facilitate early detection of periodontitis in a non-invasive manner. Among them, active Matrix Metalloproteinase-8 (aMMP-8) has emerged as one of the most reliable and well-studied markers [28].

aMMP-8 is the activated, collagenolytic form of MMP-8, also known as neutrophil collagenase, that breaks down type I, II and III collagen and is expressed, degranulated and activated when there are changes in the interaction between the host and microbial factors in oral fluids. This biomarker plays a pathogenic role in periodontal tissue destruction as elevated levels of active MMP-8 (aMMP-8), unlike total or latent MMP-8, signal ongoing collagen degradation. Its presence in oral fluids indicates patients' conditions strongly with active periodontal destruction process, making it a reliable biomarker for disease diagnosis prior to detectable clinical and radiographic change, as well as disease monitoring [11, 29]. Derived from a recent study, aMMP-8 remains the most accurate diagnostic biomarker in GCF and is also among the top five most promising salivary biomarkers for the diagnosis of periodontitis [28].

One key strength of aMMP-8 lies in its ability to discriminate between gingivitis and periodontitis. While inflammation occurs in both conditions, only periodontitis results in permanent destruction of the periodontal ligament and alveolar bone, while gingivitis does not involve ongoing tissue breakdown. Therefore, the rise of aMMP-8 levels in periodontitis is significant compared to that of gingivitis [11].

aMMP-8 is initially stored in neutrophil granules as pro-MMP-8 and becomes activated through host proteases (MMP-3, MMP-10) and bacterial proteases produced by key periodontal pathogens such as *Porphyromonas gingivalis* and *Treponema denticola*. In gingivitis, this activation is minimal because connective tissue destruction is limited. In contrast, periodontitis in characterized by persistent bacterial challenge and heightened inflammatory signaling (e.g., IL-1, IL-8, TNF-α, GM-CSF), which triggers massive neutrophil degranulation and activation of MMP-8, resulting in a pathological surge of aMMP-8 in saliva and GCF. This spike shows a strong correlation with clinical parameters, including bleeding on probing (BOP), probing pocket depth (PDD), and clinical attachment loss (CAL) [30]. Moreover, another study showed increased saliva aMMP-8 levels in individuals with periodontitis compared to gingivitis and healthy groups [31].

5. aMMP-8 Point-Of-Care Test (POCT)

As a biomarker, aMMP-8 is found to be more precise than total MMP-8, MMP-9, MMP-2, MMP-3, MMP-13, MMP-7, MMP-1, calprotectin, myeloperoxidase (MPO), human neutrophil elastase (HNE), tissue inhibitor of matrix metalloproteinase (TIMP)-1, and clinical diagnostic signs like bleeding on probing (BOP). Thus, this biomarker is used in Point-of-Care tests (POCT) in an attempt to help detect, classify, monitor and predict the course of periodontal diseases in a practical, inexpensive and non-invasive manner [32]. Moreover, aMMP-8 POCT is found to be able to detect the ongoing periodontal tissue breakdown cascade in approximately 5 minutes [11].

Traditionally, damage to the periodontal tissue is detected clinically utilizing periodontal probing, which shows loss of attachment of the tooth, or by radiographs that detect alveolar bone loss. These methods evaluate the damage caused by previous destruction episodes, resulting in a retrospective diagnosis. However, patients diagnosed with periodontitis using this method would already have gone past the early phases of periodontium breakdown, thus making recovery or treatment plans more difficult to carry out [33].

On the other hand, aMMP-8 POCT is a rapid chairside diagnostic assay designed to detect aMMP-8 levels in oral fluids, namely the gingival crevicular fluid and saliva. aMMP-8 POCT was found to predict alveolar bone loss in patients prior to visible radiographic or clinical signs due to its sensitivity and specificity[3]. Research has shown that lateral flow aMMP-8 POCT has a sensitivity of 75-85% and specificity of 80-90% in comparison to the catalytic protease activity assays for aMMP-8 [34].

POCT works through lateral flow immunoassay principles. Thus, during sample collection, a collection swab or strip is applied to collect the sample. It is then introduced into a test cassette containing monoclonal antibodies specific to aMMP-8. If present, aMMP-8 binds to these antibodies, forming complexes that migrate along a membrane by capillary action, where they are captured by immobilized antibodies, producing either a visible signal in qualitative kits or a measurable response when used in conjunction with a digital reader such as the ORALyzer®, which is a quantitative kit that provides a specific numerical value on its screen when the result exceeds its threshold value of 10 ng/mL. Meanwhile, PerioMarker® is an example of a qualitative kit that displays one line for negative results and two lines for positive results, indicating increased periodontitis risk [35].

Although diagnostic thresholds for periodontitis vary according to different manufacturers for the aMMP-8 POCT, they have been standardized at approximately 20-25 ng/mL, with values below this cut-off considered physiologically normal or indicative of periodontal stability. Conversely, concentrations above 20-25 ng/mL signal active collagenolysis and heightened risk for disease progression, even in the absence of overt clinical or radiographic findings [36]. Furthermore, two studies employed PerioMarker® with a threshold of 25 ng/mL for positive results [37, 38], while three studies used PerioSafe® with an ORALyzer® digital reader at a threshold of 20 ng/mL9,10,23. Under the 2017 classification of periodontal disease, interpretation of results follows a stratified model: levels below 6.46 ng/mL correspond to healthy or stable sites, values between 6.46-25 ng/mL suggest moderate activity or gingivitis, and concentrations ≥25 ng/mL reflect high tissue-destructive activity or periodontitis that warrants urgent intervention [39]. In this way, the aMMP-8 POCT offers diagnostic value at stages where conventional measures such as probing depth, bleeding on probing, or radiography may remain inconclusive [35].

The type of oral fluids in which aMMP-8 levels are measured affects the analysis. Oral fluids consist of saliva, mouthrinse, gingival crevicular, and peri-implant sulcular fluids [GCF/PISF], respectively. Among all these, mouth-rinse and GCF/PISF aMMP-8 analysis and testing were found to be more precise compared to that of salivary-based methods. This is because gingival crevicular fluid (GCF) has a higher on-site specificity to periodontitis compared to saliva as a diagnostic fluid. However, GCF is usually collected at a very slow speed and an easy-medium difficulty, and yields a very low volume of 1 microliter. GCF is also minimally invasive during collection, whereby saliva is non-invasive in nature [12, 40].

Offering similar levels of specificity to GCF, aMMP-8 POCT is also found to be highly valid and effective through mouthrinse. A study found that mouthrinse aMMP-8 POC tests offered more precise measurement results and displayed no false positives compared to salivary aMMP-8 immunofluorometric assay (IFMA) [41]. Another study has shown that the mouthrinse-based technology had a sensitivity of 96% in detecting poor oral hygiene, and 82.6% in bleeding on probing (BOP) [34]. This finding indicates that aMMP-8 POCT in mouthrinse is a non-invasive, quick, and patient-friendly diagnostic approach.

6. Discussion

The studies reviewed in this paper underscore the significant health burden posed by the coexistence of type 2 diabetes mellitus (T2DM) and periodontitis, and the complexity of their bidirectional relationship. Epidemiological data have proven the two conditions to be highly-prevalent with substantial overlap among affected individuals, both globally and nationally in Indonesia, indicating a self-perpetuating cycle of systemic and oral disease [2].

The high prevalence of both conditions is caused by a complex interplay of various factors, with one of the major challenges in current clinical practice being the early detection of periodontitis in diabetic patients. This difficulty arises mainly because patients typically only seek professional dental care when clinical signs are visible [9]. By this stage, significant periodontal tissue damage has occurred as periodontitis normally progresses silently in early stages. Moreover, patients' chief complaints, as shown in several studies, lean towards aesthetic-related reasons rather than functional [25]. Other than that, traditional diagnostic methods, including periodontal probing and radiographic assessment, have their limitations as they primarily focus on periodontal damage that has taken place rather than ongoing processes [35]. As a result, subclinical progression of periodontitis, specifically in high-risk groups such as T2DM patients, often goes undetected. Hence, this creates a gap in timely diagnosis and intervention. Consequently, the majority of diabetic patients seek care only after the disease has developed to late stages, where regenerative treatments are limited. This diagnostic delay highlights the demand for an accurate diagnostic tool capable of early-detecting periodontitis progression before clinical manifestations arise.

The introduction of active matrix metalloproteinase-8 (aMMP-8) as a promising biomarker addresses the limitations of conventional diagnostic tools, as aMMP-8 focuses on detecting active collagen breakdown in periodontal tissues rather than past clinical symptoms. Compared to other studied biomarkers, such as certain cytokines, C-reactive protein, and such, aMMP-8 possesses a superiority in specificity of local inflammation [32]. aMMP-8, specifically through tests with oral fluid samples, directly reflects disease progression locally in the periodontium. Moreover, this biomarker can also distinguish periodontitis from gingivitis, which indicates its specificity. Moreover, alignment of aMMP-8 levels with clinical parameters further reinforces its diagnostic accuracy [30]. As an addition, aMMP-8 as a biochemical marker minimizes the susceptibility to errors such as subjective interpretation of results and operator skills.

A major strength of aMMP-8 is its adaptability to be integrated to point-of-care tests (POCT). In recent years, chairside aMMP-8 POC tests through oral fluid-sampling have been developed to provide rapid and non-invasive diagnosis. These tests can deliver results within approximately 5 minutes, facilitating same-visit decision-making and eliminating the delay from conventional laboratory-based analyse [11]. This builds potential for rapid screening of periodontitis in high-risk groups such as individuals with T2DM, who may not seek evaluation of their periodontal health status routinely. aMMP-8 POCT also requires Moreover, in comparison to a traditional diagnostic method, namely bleeding on probing (BOP), which is occasionally subjective to the clinician's estimation, aMMP-8 POC/chairside test is a more objective measurement of local inflammation in the oral fluids [11].

aMMP-8 POCT brings advantages which extend beyond diagnostic accuracy. Unlike traditional diagnostic methods that focus primarily on detecting historical periodontal tissue destruction, aMMP-8 reflects ongoing and active tissue degradation, which allows early detection and diagnosis of subclinical periodontal disease [29]. Additionally, aMMP-8 POCT devices show rapid results and are done chairside and non-invasively. This immediacy increases the efficiency of the workflow of clinicians during rapid, mass screenings of high-risk groups, such as individuals suffering from T2DM.

Importantly, aMMP-8 POCT holds potential not only for diagnosis but also for monitoring therapeutic response [15]. As aMMP-8 is capable of reflecting real time active periodontal degradation, this technology is responsive to changes in disease activity. This dynamic monitoring ability benefits in allowing clinicians to give proper treatment and adjust required interventions.

Nevertheless, several considerations remain. Firstly, while the integration of aMMP-8 into POC/chairside test platforms demonstrates valuable potential, the most effective choice of oral fluid samples is to be considered based on the setting, as this influences specificity, accuracy and clinical applicability [34]. Given its ability to provide site-specific information on periodontal conditions and proximity to periodontal tissues, gingival cervical fluid (GCF) is often used for periodontal biomarkers. However, its sampling process is technically demanding, slow, and results in very small quantities, which may limit its practicality in large-scale screenings. Conversely, non-invasive and more time-efficient alternatives include salivary and oral rinse samplings. The two methods allow for assessment from multiple periodontal sites, and therefore are more feasible to be used routinely. However, multiple studies have shown mouthrinse-based aMMP-8 POCT to display both efficiency and accuracy, making them the more preferred choice of oral fluid sample in comparison to saliva [41].

The current evidence found supports the role of aMMP-8 biomarker as a robust diagnostic tool to detect and monitor periodontitis, particularly in T2DM groups both globally and nationally in Indonesia. The integration of aMMP-8 point-of-care testing (POCT) into the healthcare system represents an important translational step for clinical dentistry and interprofessional care. aMMP-8 POC/chairside tests have shown various advantages, presenting accurate and rapid results, executed in a non-invasive manner. Such advantages enable this technology to be integrated in primary dental and medical settings for routine screening of high-risk populations, including T2DM patients, and support personalized treatment planning. Furthermore, the early detection of periodontitis in T2DM patients may contribute to timely intervention, which affects treatment prognosis.

7. Conclusion

Active matrix metalloproteinase-8 (aMMP-8) point-of-care testing (POCT) is a rapid, non-invasive, and chairside diagnostic tool that can facilitate early detection of periodontitis and monitoring of disease progression in patients with type 2 diabetes mellitus (T2DM). The test can be performed using various oral fluid samples, including saliva, GCF, and oral rinse, each with its own advantages and limitations. For mass screenings, oral rinse serves as the most practical option due to its efficiency. However, in clinical dental practice, GCF sampling is preferable as it provides greater site-specific diagnostic accuracy. The applicability of aMMP-8 POCT is not limited to dental professionals, but also can be performed by non-dental medical practitioners as a primary screening method in T2DM patients, prior to dental referral. The integration of this technology in the healthcare system, including in Indonesia, offers a potential paradigm shift from reactive to proactive care by clinicians, thereby enabling earlier intervention and improving long-term prognosis.

Compliance with ethical standards

Disclosure of conflict of interest

All authors declare no conflicts of interest related to this manuscript, including any financial or non-financial relationships, funding, or collaboration involving PerioMarker®, PerioSafe®, ORALyzer®, or competing products.

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