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Review Article

Clinical Relevance of the Advanced Microbiologic and Biochemical Investigations in Periodontal Diagnosis: A Critical Analysis

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New approaches to periodontal diagnosis, including advanced microbiologic, biochemical, and genetic tests, have been shown to provide the clinician with the information not available by traditional means. The purpose of a diagnostic test is to confirm, exclude, classify, or monitor disease to guide treatment. Their clinical value depends on whether the information they provide leads to improved patient outcomes. This can be assessed by randomized trials, which compare patient outcomes from the new diagnostic test versus the old test strategy. Being nonmandatory for marketing approval, such trials are not always feasible because of large sample sizes requirements. So, many diagnostic tests enter the practice without being critically analysed for any additional benefits. Effective diagnosis is just as essential as the selection of effective treatments for the success of periodontal therapy. So, the current paper aims to focus on the practical utility of this rapidly emerging plethora of periodontal diagnostic tools, emphasizing the critical issues surrounding the clinical application of microbiologic and biochemical investigations, employed for periodontal diagnosis.

1. Introduction

"Periodontal diagnosis" is an important tag that a clinician ties on the periodontal disease condition of the patient, capturing all his past experience with the condition in question. The entire constellation of signs and symptoms, along with a detailed history, is elicited, documented, and interpreted to reach at a diagnosis. Most often an accurate diagnosis is the very first concrete step towards the planning and execution of an appropriate individualized treatment plan, contributing significantly towards the success of the therapy [1].

Clinical diagnostic parameters that were introduced more than half a century ago continue to function as the basic model for periodontal diagnosis in current clinical practice as well. A periodontal diagnostic tool, in general, provides pertinent information for differential diagnosis, localization of disease, and severity of infection. They include various disease characteristics such as probing pocket depths, bleeding on probing, clinical attachment levels, plaque index, and radiographs quantifying alveolar bone levels [2, 3]. Although there have been significant advances in the understanding of the etiopathogenesis of periodontal disease over the past 4-5 decades, the traditional methods by which clinicians diagnose periodontal disease have remained virtually unchanged [4].

These diagnostics were called in to question during the early 1980s, when longitudinal clinical studies demonstrated that long-held concepts concerning the natural history of periodontal disease required modification [5]. More recent paradigms for periodontitis diagnosis include the possibility of several disease types, based primarily on the rate of disease progression, the distribution of the disease within the mouth, and the chronological age of the patient as well as active and inactive stages of the disease. Since then, clinicians got to be interested in assessment tools that should give them information in the following three areas:

(i) diagnostic tests that could determine whether the periodontal disease process is currently active (progressive loss of attachment) with accuracy above what can be determined by traditional clinical indicators;

(ii) risk assessment, by which clinicians could identify patients or specific sites that are at higher risk for disease onset;

(iii) prognosis assessment, by which clinicians could predict the course of disease with or without treatment [6, 7].

Traditional clinical assessments do not enable a practitioner performing a single routine periodontal examination to determine whether active tissue destruction is occurring, for example, no definitive method to determine that gingival inflammation in a successfully treated case of periodontitis represents early recurrent disease or gingivitis on a stable but reduced periodontium [4, 8]. Albeit easy to use, cost-effective, and relatively noninvasive, clinical attachment loss evaluation using the periodontal probe measures damage from past episodes of destruction but requires a 2-3 mm threshold change before a site with significant breakdown can be identified. Demonstrating progressive loss of periodontal support requires longitudinal assessment. Current diagnostic methodologies do not enable us to accurately predict which periodontal sites, teeth, or individuals are susceptible to further periodontal breakdown [2, 9, 10]. Given the limitations of current diagnostic tools, researchers are continuously working to develop techniques that focus on the early detection, disease activity, and host susceptibility of disease [4, 8].

With the advent of so many new diagnostic tests developed in past few decades, we must not mislead ourselves to the belief that everything we can measure will always be helpful. Many traditionally taught methods have never been scrutinized for their precise benefits, and new tests are made available without any properly documented utility. To determine the diagnostic utility (the quality of being of practical use), detailed information is needed on how a test or diagnostic algorithm performs in a specific setting and what the consequences of a positive or negative test might be [8]. Detection of periodontal disease is seldom the principal problem in periodontics. One and the same test can have variable utility depending on the information already available before the test is done. The ideal diagnostic test should be [10, 11]

(i) highly specific,

(ii) highly sensitive,

(iii) reproducible,

(iv) quantitative,

(v) simple to perform,

(vi) rapid,

(vii) a one-stage or a two-stage procedure,

(viii) noninvasive,

(ix) versatile in terms of sample handling, storage, and transport,

(x) amenable to chairside use,

(xi) economical,

(xii) dependent upon simple and robust instrumentation.

The clinical value further largely depends on finding truly new information, any treatment alternative, cost effectiveness, and safety profile of the newly developed test protocol. Additional information (for, e.g., the cost of test, time taken, and patient acceptance) also should be sorted out to analyse the practical utility and actual impact of the test on the quality of care offered to the patient [8].

It is now worth taking a moment to critically analyse these newly emerged methods for their practical utility, with the purposes redefined. The diagnostic tests should not only provide details about the past disease activity but also be able to detect current disease status and predict the future susceptibility. The following section focuses on the microbiologic and biochemical investigations employed in periodontal diagnosis.

2. Microbiological Investigations

Recent developments in molecular biology techniques have enabled investigators to detect a much wider variety of bacterial species closely associated with periodontal disease [12–16]. Detailed information on the individual microbiologic techniques is beyond the scope of the present paper; an overview of the available techniques is summarized in Table 1 [17–22]. There are some issues which are certainly associated with these techniques in general and might affect their clinical applicability and limit the practical usefulness of the microbiologic diagnostic techniques.

2.1. The Uncultivables. The techniques in molecular biology have obviated the necessity for bacterial culture of dental plaque samples [22, 23]. Most predominant bacterial species in the oral cavity have been identified using culture-independent molecular methods based on sequence analysis of the 16S ribosomal RNA genes [24–37]. Collectively speaking, there are about 620 predominant oral bacterial species, of which about 35% have not yet been cultured in vitro [21]. The need for study of these uncultivables to understand their exact position in the oral ecology and in the pathogenesis of periodontal disease keeps us far from deciphering the complete scenario.

2.2. "What Is Being Measured?" The microbiologic tests that measure periodontal pathogens do not necessarily measure periodontal disease. Bacterial pathogens can be present even in high numbers in periodontal pockets without loss of connective tissue attachment or alveolar bone. Therefore, assays for periodontal pathogens are not, of themselves, diagnostic for periodontal disease [22]. Mere presence of the suspected pathogens cannot be directly interpreted as disease, as most of the putative periodontal pathogens are found colonizing the healthy gingival sulci as well. All identified isolates of a particular bacterial species are not necessarily equally pathogenic or detrimental, for example, *Aggregatibacter actinomycetemcomitans* (A.a) and *Porphyromonas gingivalis* (*P.*

Table 1: Various methods for identification of pathogens in periodontal infections.

Method	Description
Culture methods	
Selective	Can detect up to 104-105 species selectively and 103 species nonselectively, does not detect nonviable species, and takes approx. 1–3 weeks
Nonselective	
Immunological methods	
Particle concentration fluorescence immunoassay	Can detect up to 104 species, detects nonviable species, and takes approx. minutes to hours
DNA probe	Detects up to 102 species, detects nonviable species, and takes approx. 1–48 hours
Enzyme assay	
Benzoyl-DL-arginine-2-naphthylamide (BANA)	Detects 104 species, does not detect nonviable species, and takes approx. 15 minutes
Polymerase chain reaction	
Single target PCR	Detects specific species directly from oral clinical samples
Multiplex PCR	Expansion of single target PCR, detects multiple species simultaneously and detects up to 10–100 cells per PCR
Real-time PCR	Detects and quantifies multiple species
DNA-DNA hybridization	
Fluorescence in situ hybridization (FISH)	Quantify and determine special configuration and demonstrate the morphology of individual bacterial cell in complex natural communities
Checkerboard hybridization	Hybridization of 45 DNA samples against 30 DNA probes on a single support membrane
Reverse-capture checkerboard hybridization	16S ribosomal RNA based oligonucleotide checkerboard hybridization
Oligonucleotide microarray technology	A high sample-throughput, 16S ribosomal RNA-based technology allows the simultaneous detection of about 300 key and predominant bacterial species, including species that have not yet been cultured
Sequencing methods	
454 pyrosequencing	DNA is fragmented and amplified using special adaptors in an emulsion
SOLiD	PCR that binds to an agarose bead. Fragmented DNA is amplified on an agarose bead
Illumina/Solexa methodology	Utilises fragmented DNA and specialized adaptors attached to a slide

Adapted from [22].

gingivalis), and, lastly, a particular microorganism may not cause an identical disease in all infected hosts. So, the identified microorganisms represent only one aspect of this multifactorial disease [17].

2.3. Sampling. Information generated from microbiologic investigations is highly dependent on the sampling method employed. Assays for bacteria can only detect target species, that too when they are present in the patient sample. Since there may be over 100 different subgingival sample sites around a complete dentition, each harbouring a unique microbiologic profile, obtaining a representative sample poses another challenge. The findings suggest that different species of periodontal pathogens necessitate different sampling schemes [22]. The outcome of the analysis can further be affected by the method of sample collection [12, 19].

2.4. Information Provided. We now have microbiologic tools with the specificity and selectivity necessary to allow the investigator to determine the presence and the approximate proportion of a multitude of different subgingival species. An estimate of the proportion of a target species present is based on its contribution to the total number of bacterial species enumerated and not to total bacterial mass. So, such sort of variation can only give a clue about the proportion of the target species [12].

Even with the best of techniques available, we are yet unable to reliably state that we are aware of all bacterial species and taxa that are involved in the initiation and progression of periodontitis. Review of contemporary literature regarding the utility of microbial identification as an aid in the treatment planning of patients with periodontitis showed a limited number of studies, but the lack of appropriate controls, however, makes the interpretation of these results difficult and therefore the utility of microbial testing in developing specific treatment plans could not be ascertained. Similarly available evidence could not suggest a definitive benefit of microbiological testing as an indicator of healing or disease [12, 17, 19]. Although prospective studies monitoring patients after therapy would indicate that the use of microbial testing could aid in the selection of a more targeted therapy, mostly in patients with aggressive or recurrent periodontitis,

again, the lack of clinical trials with adequate controls prevents from demonstrating the real value of microbial diagnosis. Therefore, the available evidence does not fully prove the utility of microbiological testing in periodontitis patients.

Periodontal diseases are infections caused by microorganisms that colonize the tooth surface at or below the gingival margin and accumulate as dental plaque. The biofilms (dental plaque) that colonize the tooth surface are extremely complex and remarkably resistant to host defense mechanisms and antimicrobial agents. Therefore, the mechanical plaque control (i.e., removal of supra- and subgingival plaque) remains the cornerstone in periodontal therapy such as self-performed oral hygiene, scaling and root planning, or periodontal surgery [38]. So microbial analysis cannot be regarded as a routine first visit investigation for all patients, but it can be reserved for specific clinical situations, such as to identify (by knowing specific microbial profiles) for targeted and effective antimicrobial therapy for managing susceptible patients. Another evidence emphasizing the significance of microbial analysis in therapeutic management is now emerging. Papapanou et al. suggested that the microbial content of the periodontal pocket is a determinant of gene expression in the gingival tissues and can potentially identify susceptible sites in terms of additional periodontal breakdown or unfavorable response to therapy [39]. These findings can serve as basis of subsequent studies for exploring the role of microbial testing. At present, only the rationale usage of microbial diagnostic techniques might benefit our patients, by saving on the time, pain, labour, and cost of repeat mechanical therapy, antibiotic usage, and surgical trauma, if we are able to formulate a better tailored treatment plan which is based on the diagnostic information obtained.

3. Biochemical Analysis

Biomarkers, whether produced by normal healthy individuals or by individuals affected by specific systemic diseases, are tell-tale molecules that could be used to monitor health status, disease onset, treatment response, and outcome [2]. Informative biomarkers can serve as early sentinels of disease. A huge body of literature was generated in the 1990s on the utility and value of individual biomarkers of periodontal disease activity, measured within gingival crevicular fluid under the following categories:

(i) markers of the presence or absence of periodontal pathogens,

(ii) markers of gingival and periodontal inflammation,

(iii) markers of the host's inflammatory-immune response to certain pathogenic species,

(iv) markers of host tissue destruction [10].

The principal biological media within which biomarkers were sought including saliva, serum, subgingival plaque, tissue biopsies, and gingival crevicular fluid, mouth-rinse [40, 41]. Gingival crevicular fluid became the analytical fluid of choice as it was the most specific to the periodontal tissues, could be collected noninvasively, and allowed site-specific analyses. However, molecular analysis of GCF elution was time consuming and laboratory based, technically demanding collection of sample leading to a small volume of the fluid (1–5 μL). Despite these apparent diagnostic and technical disadvantages, GCF was still considered as a candidate potential oral fluid for the development of adjunctive noninvasive chair-side point-of-care diagnostic technology [42–44] especially because tissue destructive MMPs and their bioactive regulators can conveniently be measured by distinct catalytic and noncatalytic immunoassays from GCF [41, 45]. A plethora of biomarkers and diagnostic tests were developed thereafter, several of which demonstrated high levels of sensitivity, specificity, and diagnostic accuracy with respect to identifying and/or predicting disease activity at the site level [10, 46]. In particular, Loos and Tjoa [47] undertook a critical review of biomarkers in gingival crevicular fluid and found that only eight of 94 in the literature of the time fulfilled any of the criteria for biomarker status. These eight biomarkers were alkaline phosphatase [48–54], β-glucuronidase [52, 55–63], cathepsin B [64–69], MMP-8 and MMP-9 [52, 70–82], dipeptidyl peptidases II and IV [65, 66, 68, 83], and neutrophil elastase [46, 52, 61, 63–66, 76, 84–86].

A number of diagnostic kits emerged based upon individual biomarkers within gingival crevicular fluid, but market research had not been performed that actively and the tests did not popularize much among practicing dentists due to several reasons: (1) time-consuming and laborious to perform; (2) difficult to interpret and understand; (3) site specific and the choice of site being problematic; (4) the results not materializing to alterations in therapeutic intervention; (5) expensive for routine use. As compared to GCF, collection of salivary and mouth-rinse samples was considered more convenient, practical, rapid, and noninvasive and requires neither professional stuff nor specific materials. Saliva and mouth-rinse represented a pooled sample from all periodontal sites providing an overall assessment of periodontal disease and health at subject level [41]. Whilst it was firmly established that gingival crevicular fluid was the most appropriate diagnostic medium to use in analyses, it became clear that whole-mouth analysis was far more practical, simpler, and cheaper, and thus saliva became the medium of choice in the 21st century [87]. Saliva had many advantages as a diagnostic fluid in that it was simple to collect using noninvasive techniques and provides a whole-mouth summary analysis. Whole saliva could be affected by molecular constituents and cellular remnants from other oral niches, as well as systemic conditions [88, 89] which could have bearing on its diagnostic applications.

Principally it remains a surrogate fluid for gingival crevicular fluid and therefore assays need to be highly sensitive. In addition, saliva biochemistry varies with its origin (whole saliva or specific gland secretions), which are in turn affected by environmental and psychological stimuli. Therefore, it is not possible to fully quantify markers within saliva using chairside technologies, and qualitative analyses, or at best semiquantification, are all that can be reliably achieved [10].

MMP-8 or collagenase-2/neutrophil-collagenase was worked on extensively, being the major type of interstitial collagenase present in human periodontitis-affected gingival

Table 2: Five-phase approach for translating research on biomarker applications.

Process	Phases	Description
Discovery: biomarkers and pathway elucidation	PHASE1	Exploratory study to identify potentially useful biomarkers.
Validation: efficacy in 2% population	PHASE2	To determine their capacity for distinguishing between cases with disease and those without.
Cohort and longitudinal validation: efficacy in an at-risk population	PHASE3	To determine the capacity of a biomarker to detect preclinical disease.
	PHASE4	Prospective screening studies.
Clinical use: diagnosis and prognosis	PHASE5	Large-scale population studies that evaluate overall impact of screening on the population.

Adopted from [109].

tissue, gingival crevicular fluid, peri-implant sulcular fluid, saliva, and mouth-rinse samples [43]. Antibodies applied in the immunoassays for the detection of MMPs and their regulators affected the measurement outcomes [45, 90, 91]. Nevertheless, particularly MMP-8 immunoassays and activity assays targeting PMN-type MMP-8 isoenzyme species in oral fluids have been found to be useful to differentiate periodontitis/peri-implantitis and gingivitis sites/patients as well as healthy sites/subjects [44, 45, 90, 92]. These researchers utilized selective antibodies for detection of active MMP-8 in oral fluids for developing adjunctive diagnostic point-of-care/chair-side tests identifying sites susceptible for periodontitis progression and periodontitis affected patients [41]. Smoking has been found in several studies to decrease MMP-8 levels in GCF because of the effects on local blood circulation and lowered signs of inflammation [93, 94]. However, Mäntylä et al. [92] suggested that it cannot be regarded categorically that all smoking periodontitis patients have lower levels of MMP-8 in GCF and further in oral rinse sample as they detected the highest MMP-8 GCF levels in smoking subjects with poor response to conventional periodontal treatment (scaling and root planning, SRP). Simultaneous analysis of MMP-8 and TIMP-1 proved beneficial [90]. Also the effect of MMP-8 inhibiting SDD medication could be monitored by analyzing the salivary and oral rinse MMP-8 levels to find out when a possible break in medication would be possible or when the medication should be taken again [95, 96]. The point-of-care MMP-8 immunotechnologies from oral fluids and serum/plasma could be well adapted for monitoring of systemic inflammation [41, 89, 97].

On the basis of our current understanding of the complexity of periodontitis, the identification of one single diagnostic marker for all forms of periodontal disease seems illusionary [47]. Several excellent reviews discuss these samples for targeted approaches to biomarker discovery [86, 87, 98–100]. As Bensalah et al. [101] have recently documented, six different types of biomarker can be differentiated as follows:

(i) early detection of disease,

(ii) diagnosis of presence or absence of disease,

(iii) prognosis of disease outcome and possible patient stratification for those at elevated risk of disease recurrence,

(iv) prediction of treatment outcome,

(v) identification of patients who will respond well to a particular treatment,

(vi) surrogate end-points.

The proteomic era has made multiple biomarker analyses an achievable goal and advances in modern diagnostic technologies have made delivery at the point-of-care a realistic proposition. A multitude of biomarkers will improve sensitivity, specificity, and the diagnostic accuracy of tests, and early studies involving combinations of biomarkers in so-called lab-on-a-chip platforms have shown promising results [2, 47, 102]. In addition, for a biomarker or a panel of biomarkers to be successfully employed within the clinical environment, they must also be objective, reproducible, easy to use, cheaper, and with greater sensitivity, specificity, and diagnostic accuracy than existing tests. Also in parallel to drug discovery is the process of validation through which biomarkers should pass through before appearing in clinical practice (Table 2) [46, 103]. Validation of periodontal diagnostics will need to be benchmarked with existing gold standards of disease, including alveolar bone height and clinical attachment levels [40].

There is definitely an urgent need for a more sophisticated and precise predictor for periodontal disease. If a marker is capable of identifying the onset of disease activity or characterizing the transition between gingivitis and periodontitis (either by its simple presence or by being present at a certain concentration threshold), then we would potentially have a diagnostic tool that could become the standard of care in delivering periodontal treatment. This deficiency in knowledge about the initiation of disease activity at the subclinical level may not lie with the technical ability to identify biomarkers in saliva but may actually reside in what biomarkers to look for. In other words, we must focus to better understand the pathogenesis of periodontitis. It may well be that different sets of markers exist for initiating the disease process and associated with the presence of established inflammation. It may also be that markers that characterize the inflammatory process in individuals who develop periodontitis are different from those who present with chronic gingivitis (and never develop periodontitis) and lastly that markers of inflammation are not specific enough to predict the development of periodontitis [2].

Table 3: Earlier and recent diagnostic biomarker kits available.

	Commercial kit	Details	Source	References
Earlier diagnostic kits	BANA periodontal test (Ora Tec Corporation Manassas, USA)	It utilizes the BANA test for bacterial trypsin like proteases.	Subgingival plaque sample	[110]
	Evalusite test (Kodak, Eastman company, Switzerland)	Immunological detection of antigens of *Aggregatibacter actinomycetemcomitans, P. intermedia, and P. gingivalis* using antibodies	GCF	[111]
	Periocheck (ASTech) (CollaGenex Pharmaceuticals, Newtown, PA)	Detects presence of neutral proteinases, that is, collagenase	GCF	[110, 112]
	Perioscan (Oral B Laboratories)	Detects enzymatic activity of *Aggregatibacter actinomycetemcomitans, T. forsythus, and P. gingivalis*	Subgingival plaque sample	[110]
	Prognostik (Dentsply)	Aids in detection of serine proteinases and elastases	GCF	[112]
	Biolise (SLT-Labinstruments, Crailsheim, Germany)	Aids in detection of elastase	GCF	[84]
	Periogard (Colgate)	Detects the presence of aspartate aminotransferase	GCF	[113, 114]
	Pocket watch (SteriOss, San Diego, CA, USA)	Detects aspartate aminotransferase through colorimetric detection	GCF	[115]
	TOPAS (Affinity Labelling Technologies, USA)	Detects toxins derived from anaerobic metabolism and measures GCF protein level	GCF	[114]
Recent diagnostic kits	MMP dipstick method	Helps in detection of MMPs	GCF	[44]
	Oral Fluid NanoSensor Test (OFNASET)	Simultaneous and precise detection of multiple salivary proteins and nucleic acids. It analyzes saliva for the presence of four salivary mRNA biomarkers (SAT, ODZ, IL-8, and IL-1b) and two salivary proteomic biomarkers (thioredoxin and IL-8)	Saliva	[116]
	Electronic Taste Chips	Detects multiple biomarkers for early diagnosis of periodontal disease	Saliva	[117]
	Integrated Microfluidic Platform For Oral Diagnostics (IMPOD)	For Oral Diagnostics rapidly (3–10 min) measures the concentrations of MMP-8 and other biomarkers in small amounts (10 mL) of saliva	Saliva	[118]
	Salivary diagnostic and research assay kits (Salimeterics)	Helps in the estimation of cytokines including interleukins, MMPs and so forth and various hormones including cortisol, cortinine, DHEA, testosterone, estradiol, progesterone, estriol in saliva	Saliva	[119]

The key challenge is to elucidate a panel of biomarkers that differentiate health from periodontitis and, more importantly, gingivitis from periodontitis. This calls for performing studies in which gingivitis and periodontitis are induced experimentally in animal models. All markers that are potentially associated with initiating the disease process are monitored longitudinally (form health to the full-blown disease state) by salivary genomics, proteomics, and other state-of-the-art diagnostic techniques. A similar methodology could be adopted to analyse the treatment of disease, correlating periodontal healing and stability with the absence of such markers. The complexity of the associated microflora and the critical role of the host further heighten the issues for conducting the research regarding specific biomarkers for periodontal disease and might point towards exploring novel simulated animal models for studying these specific investigations. In human trials, for prospective investigations a combination of surrogate endpoints can be analysed for enhancing specificity while evaluating the biomarker.

It is highly unlikely that a single biomarker may prove to be a stand-alone measure for predicting periodontal disease activity. A combined analysis of proteomic, genomic, microbial, and other indicators is required to identify the set of biomarkers with the most favourable combination of sensitivity, specificity, reproducibility, and correlations with established disease diagnostic criteria. Emerging clinical applications of lab-on-a-chip (LOC) technologies as point-of-care (POC) diagnostics developed for systemic diseases are now being readily applied to periodontology. Many diagnostic kits have been commercialized and are being marketed (Table 3). The field of periodontology is now able to detect a panel of salivary biomarkers to predict disease, including matrix metalloproteinase-8 (MMP-8), microbial factors, and proinflammatory cytokines such as IL-1 beta [40]. These salivary biomarker detectors can be used in the office of a dentist or another healthcare provider for point-of-care disease screening and detection. The dental community is not generally familiar with mass screening of populations for oral and systemic diseases [40]. If more efficient periodontal therapy can be delivered, clinicians will be more likely to utilize new diagnostic approaches. Dentists will have greater involvement in the identification monitoring of oral and systemic disorders in the not too distant future.

Prospective healthcare is a new approach that incorporates all the power of current disease-oriented medicine but is based on the concept of strategic health planning, a proactive, prospective approach to care. In this system, individuals are evaluated to determine their baseline risk for a specific disease, their current health status, and their likelihood of developing specific clinical problems given their risks [102, 104, 105]. As mentioned before, allocation of resources to prevent periodontitis/peri-implantitis would be optimized and may help to reduce costs if diagnostic information would assist in identifying susceptible patients and help providing more specific prevention/treatment strategies for high-risk and low-risk patients. Saliva as a diagnostic and/or prognostic tool can improve and ease treatment planning in periodontics and implant dentistry, thus resulting in more predictable treatment outcomes and cost savings [2, 106]. Periodontal oral POC devices will also enable masses to be screened; particularly underserved communities and resource limited areas as in developing nations may be accessed more efficiently. such applications might serve better for identification of at-risk groups and increase access to treatment for those most in need, improving public health in periodontology and the oral health field in general [40].

A careful analysis is mandatory, before adopting any newly emerged diagnostic test in the current clinical protocol. The novel test must be weighed against the conventional criteria of diagnosis in its sensitivity, specificity, validity, and reliability [107]. The benefit of having a particular piece of diagnostic information must not only outweigh the effort to obtain it on the level of each individual; however, the impact of a new diagnostic procedure should also be evaluated at a more global level, to maximize the overall benefit of the total investment in health care [8]. Adequate guidelines for the use of diagnostic routines should be issued and implemented from regulatory bodies in health care. Nevertheless, as new procedures are introduced in periodontology during these times of cost containment in health care, practitioners must use caution in deciding which particular patients would benefit from a comprehensive evaluation [8, 108].

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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