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Review Article

CURRENT DIAGNOSTIC TRENDS IN PERIODONTICS- A REVIEW

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ABSTRACT

Periodontitis is a chronic disease with a multi-factorial etiology. To arrive at the accurate diagnosis, one that will help establish the prognosis and guide the treatment plan, requires a multi-faceted clinical and laboratory investigations. With the improvement in our knowledge of the etiopathogenesis of periodontal diseases and advances in technology, we have overcome the limitations of the traditional diagnostic methods. This article aims to review all the advanced diagnostic aids available at the disposal of the present-day clinician.

IINTRODUCTION

"*Diagnosis is not the end, but the beginning of practice "*

This quote by Dr. Martin H Fischer explains the crucial nature of arriving at the right diagnosis. For it is the diagnosis that guides the treatment plan for the diseased and ultimately determines the benefit the patient has derived from it. But, establishing the right diagnosis might prove to be tricky, especially in chronic diseases that have a multifactorial etiology; such as Periodontitis.

The group of inflammatory diseases that affect the connective tissue attachment and bone around the tooth are collectively called as Periodontitis. If left untreated, this disease leads to destruction of collagen fibers leading to apical migration of the Junctional Epithelium (JE), loss of attachment from the cemental surface with progressive bone destruction leading to tooth mobility and consequent tooth loss. Although, bacteriae are considered the primary etiological factor for periodontitis, the host response to the pathogenic infection is also critical in disease progression.

Hence, to arrive at a perfect diagnosis in case of a periodontal disease, the clinician can rely on 3 factors: His/her knowledge on etiopathogenesis of the disease, clinical signs and symptoms and adjunctive laboratory investigations. Thus, in the present article we will discuss the use of relevant lab tests based on the valid etiopathogenesis that will help in early detection and management of the periodontal disease.

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Etiopathogenesis of periodontitis

The composition of oral microbiome differs from one intraoral site to another, reflecting in part of host-response and immune capacity of the individual. Several theories have debated and discussed how the dental plaque induces periodontal destruction since 1900s. Beginning with the Non-Specific Plaque Hypothesis proposing that the overall activity of the total plaque microflora was responsible for the disease process. This was later contradicted by the Specific Plaque Hypothesis, 1976 that held only certain few bacterial species responsible for periodontal destruction. However, in 1994 another hypothesis was put forth combining the former two propositions and explained periodontitis pathogenesis as being caused due to imbalance in the microbiota as a result of ecological stress. This was called the Ecological Plaque Hypothesis.

Theory	Year	Author
Non-Specific Plaque Hypothesis	1990	Miller
Specific Plaque Hypothesis	1976	Loesche
Ecological Plaque Hypothesis	1994	Philip D. Marsh
Keystone Pathogen Hypothesis	2012	Hajishengallis and Lamont
Polymicrobial Synergy And Dysbiosis Model	2012	Hajishengallis and Lamont

Currently, there are two most widely accepted theories that explain the pathogenesis of periodontal disease. They are the Keystone Pathogen Hypothesis and Polymicrobial Synergy and Dysbiosis Model. This model proposes that periodontitis is initiated by a dysbiotic microbial community, rather than by selective periodontal pathogens, within which different microbes and specific gene combinations have a synergistic role to shape microbiota that causes disease.

Why do we need advanced diagnostic aids?

Periodontitis does not progress in a continuous manner. Infact, the presence of an active destructive phase & a latent phase that's devoid of destruction is the characteristic feature of periodontal diseases. Today, despite our increased understanding of the etiology and pathogenesis, to arrive at a periodontal diagnosis, the dentist must rely on the traditional methods of clinical & radiographic assessments. (Pajnigara NG *et al*, 2016)

However, these traditional diagnostic tests display various shortcomings such as they are markers of past periodontal destruction rather than the current status, they also do not provide any information about the host responses to the periodontal pathogens. Infact a study conducted by I. B. Lamster and J. T. Grbic in 1995 concluded that "eventually a combination of tests involving different aspects of the host response and the microbial challenge may ultimately provide a useful strategy for identifying patients at risk for progressive periodontal disease."

Also according to all the hypotheses mentioned previously, periodontal disease can be detected as early as in the subclinical stage. In addition, the new lab tests have made it possible for the clinician to predict the susceptibility of an individual to develop periodontitis in the future. Appropriate use of these investigations will not only help prevent the disease progression rather it could prevent disease initiation in itself. Thus, eliminating all the demerits associated with the traditional diagnostics.

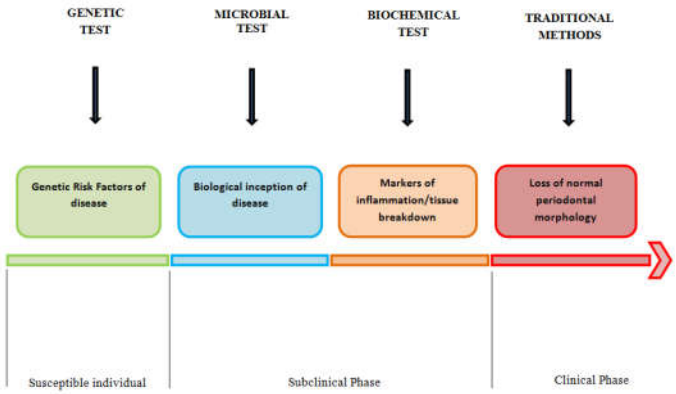


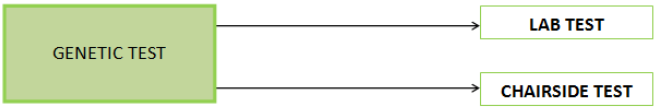
Figure 1 Schematic Representation of Co-Relation Between Advanced Lab Tests And Stage of Periodontitis Progression. (Bolerázska B *et al*, 2016)

Assessment of a Susceptible Individual

It is evident that periodontal disease is a consequence of the complex interactions between host factors and the environment. Genetic factors play an important role in moderating an individual's interaction with the environmental agents, including biofilm, to determine his/her susceptibility to periodontitis. This role of genetics in periodontal pathogenesis is researched via twin studies, segregation analysis, linkage analysis, association studies and Genome Wide Association Studies (GWAS), for no/weak/moderate/strong associations between numerous genes and Periodontitis.

Some of the genes that are frequently associated include: Interleukin-1 gene, Interleukin-6 gene, TNF-α gene, Fc receptor gene, N-formyl peptide receptor gene, Vitamin D receptor gene, Human Leukocyte Antigen gene, N-acetyl transferase gene and Matrix Metallo Proteinase (MMP) gene. (Wankhede AN *et al*, 2017)

The presence or absence of such genes can be detected by subjecting the patient to genetic testing, which may be categorized to laboratory tests and chairside tests.



The Human Genome Project opened the new potential territories to be explored in identification of the diseased-gene / disease causing gene. One of the doctrines used for the same purpose include, the candidate gene approach.(Mario Taba Jr *et al*,2012)

Candidate Gene Approach: It is a method of genetic testing, where the presence or absence of a pre-determined gene of interest is detected in a patient.

This can be done via Laboratory tests namely

1. Polymerase Chain Reaction
2. DNA sequencing
3. Fluorescence in situ hybridization (FISH)

Polymerase Chain Reaction

This technique of DNA amplification was developed by the American biochemist, Kary Mullis in 1980s. In the beginning, a DNA template, complementary to the target sequence is fed to the reactor. The test is further based on the ability of the DNA Polymerase enzyme to multiply the small DNA fragment into a billion copies that can be detected. PCR can be used to analyze the samples both quantitative and qualitatively.

DNA sequencing

It is the process of determining the nucleotide sequence that code for a particular gene / DNA. The common methods employed for this purpose are the Sanger sequencing, developed by the British biochemist, Fred Sanger and colleagues in 1977 and the Next-generation sequencing that are a set of newer DNA sequencing technologies.

Fluorescence in situ hybridization (FISH)

It is a gene mapping technique that utilizes fluorescent probes to detect a desired gene. It can be used to detect both deoxy- and ribo- nucleic acid sequences. The fluorescence can be detected using the fluorescent microscopy.

However, these techniques have the limitations such as the requirement of equipments and infrastructure. These tests are also expensive and may cause patient incompliance. In such situations, chairside diagnostics are of great help.

Genetic chairside tests

In 1997, Kornman *et al* found an association between the polymorphism in the genes encoding for Interleukin-1α and Interleukin-1β and increased severity of periodontitis. Chairside tests have been introduced to predict this behavior in individuals who carry gene polymorphism in their genome.

PST® genetic susceptibility test

It is a simple saliva test processed by a commercial laboratory in Flagstaff, Arizona where the genetic makeup of the Interleukin-1 gene site is determined.

PST® (Periodontitis Susceptibility Testing) is the first and only genetic test that analyzes two sites of IL-1 i.e., position -889 and + 3953 for gene variations.

MyPerioID

MyPerioID test detects genetic variation/polymorphism within the IL-1 gene in patient's saliva samples. The patient is asked to swish saline solution in his/her mouth for 30 seconds and then expectorate into a funneled collection tube with a screw cap. This saliva samples are then FedEx-ed to the OralDNa laboratory for results.

Detection of the Subclinical Phase

Periodontitis is a chronic disease, which signifies/implies that disease progression and establishment does not occur quicklyand gradually ensues over a period of time. However, the changes in both, the microbial profile and host response can be detected way ahead in time before the subjective/objective symptoms appear.

Various sources for intraoral sample collection can be used for the same, such as

1. Supra/subgingival plaque sample
2. Saliva
3. Gingival Crevicular Fluid (GCF)

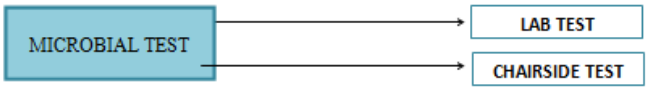
These oral samples are analyzed and detected for the presence of any "markers" of the disease process, which are also known as the biomarkers. The biomarkers may be a bacteria /bacterial products, host cells or host derived proteins (e.g., immunoglobulins) and volatile compounds that can be indicative of the disease.

Based on the biomarker being analyzed the tests can be broadly classified as

1. Microbial Test
2. Biochemical Test

Microbial Test

In 1998, Socransky & Haffajee claimed that presence of mixed infection of the "red complex pathogens" in the periodontal sites was strongly correlated with increased severity of periodontitis, as they found that these bacteria were the most crucial for the progression of periodontal disease. Similarly, Darveau *et al*., 1997 found that presence of *Aggregatibacter actinomycetemcomitans* to be the most probable causal factor for aggressive periodontitis (terminology now obsolete) in adolescents.



Thus, microbiological tests can be used to analyze the composition of oral microbial flora, in order to provide a microbiological diagnosis and also evaluate/estimate its effect on periodontal destruction, so as to initiate an early intervention with periodontal therapy.[3]

Microbiological tests can be carried out using numerous techniques or methods. Therefore it is of prime importance that the clinician is crystal clear about the purpose of the microbial test (Qualitative or quantitative analysis; Detection of antibiotic resistance) being carried out and in doing so, appropriately chooses the right test. (Grover V, 2014.Listgarten MA, 1992)

Technique/ method	Type of test	Principle	Advantage	Disadvantage
Routine culture	Laboratory	Multiplication of microorganisms using a suitable medium under controlled conditions.	Viable and pure colony obtained. Antibiotic sensitivity tests can be performed	Time consuming Requires skilled personnel and infrastructure/equipment.
Conventional PCR	Laboratory	Detection of bacteria by DNA amplification	High sensitivity.	Cannot discriminate between living and dead cells. Quantitative detection is not available.
Real-time PCR	Laboratory	Detection of bacteria by DNA amplification	High sensitivity Quantification	Cannot discriminate between living and dead cells
Immunological	Laboratory	Detection of specific bacteria using antibodies	Available for specific bacteria.	Cannot discriminate between living and dead cells.
Evalusite (Kodak, Eastman company, Switzerland)	Chairside	Immunological detection of antigens of *Aggregatibacter actinomycetemcomitans, P. intermedia,* and *P. gingivalis* using antibodies	Can identify dead target cells, thus not requiring stringent sampling and transport methodology	Cannot be used to determine antibiotic susceptibility. Poorer detection limits than nucleic acid probes of PCR assays.
Omnigene	Chairside	Genetic engineered species-specific DNA probe tests for 8 periodontal pathogens i.e., *Porphyromonas gingivalis, Prevotella intermedia, Actinobacillus actinomycetemcomitans, Fusobacterium nucleatum, Eikenella corrodens, Campylobacter pylori, Tanerella forsythia, Treponema denticola.*	Detection of all major periodontopathic organisms. Specificity of the reaction	Requires expensive & sophisticated technology
Perioscan	Chairside	Exploits an unusual enzyme found in *Porphyromonas gingivalis, Treponema denticola and Bacteroides forsythus* that are capable of hydrolyzing the synthetic peptide Benzoyl-DL-Arginine-NapthylAmide (BANA).	Fast and inexpensive test. Detects the red complex organisms that frequently associated with periodontitis.	Limited number of organisms detectable

Biochemical Test

The 1990s saw the value in utilization of analyzing the biomarkers of periodontal disease activity, with voluminous data and literature to support it. The GCF served as the preferred sample of choice and the biomarkers were categorized as below (Mani A *et al*, 2016.Srivastava N *et al*, 2017)

1. Markers of gingival and periodontal inflammation,
2. Markers of the host's inflammatory-immune response
3. Markers of host tissue destruction

There are numerous biochemical tests available in the market today, that analyze a range of biomarkers. They can be broadly classified as follows:

	Commercial kit	Mechanism	Source
Earlier diagnostic kits	Periocheck	Detects presence of neutral proteinases, that is, collagenase	GCF
	Prognostik	Aids in detection of serine proteinases and elastases	GCF
	Biolise	Aids in detection of elastase	GCF
	Periogard	Detects the presence of aspartate aminotransferase.	GCF
	Pocket watch	Detects aspartate aminotransferase through colorimetric detection	GCF
	TOPAS	Detects toxins derived from anaerobic metabolism and measures GCF protein level	GCF

	Commercial kit	Mechanism	Source
Recent diagnostic kits	MMP dipstick method	Helps in detection of MMPs	GCF
	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 , IL-8)	Saliva
	Electronic Taste Chips	Detects multiple biomarkers for early diagnosis of periodontal disease	Saliva
	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
	Salivary diagnostic and research assay kits (Salimetrics)	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

However, one can obtain accurate diagnostic information only if a combination of appropriate biomarkers with the necessary sensitivity and specificity is identified. For this purpose, several combinations of biomarkers are analyzed to determine their validity in predicting periodontal disease status. One among them is a study done by Hanioki T *et al*, 2005 on the relationship between periodontal disease status and combination of biochemical assays claimed that the combination of IgA and neutrophil elastase in GCF may be crucial for prediction of periodontal disease status. (Hanioka T *et al*, 2005)

Furthermore, they suggested that this biochemical assay may have a potential to serve as a satisfactory screening test for periodontal disease. Similarly, a critical analysis by Loos and Tjoa, 2005 on biomarkers in gingival crevicular fluid found that only 8 of 94 molecules fulfilled the criterion for periodontal biomarker status. These eight biomarkers were alkaline phosphatase, β-glucuronidase, cathepsin B, MMP-8 and MMP-9, dipeptidyl peptidases II and IV, and neutrophil elastase. Therefore, selection of the right biomarker of disease activity becomes utmost important.

CONCLUSION

The success of any treatment is dependent primarily on the accuracy of the diagnosis. At present, the majority of chronic periodontitis cases can be adequately managed using existing diagnostic methodology, although it is clearly more desirable to be able to diagnose "active disease" as it occurs, rather than months later.

Validation of novel periodontal diagnostics need to be benchmarked with existing gold standards of disease, such as alveolar bone level, clinical attachment levels in large populations. However, the clinician must ensure that the use of such tests will benefit the patient both in terms of diagnostic data obtained and cost in time and money.

References

Bolerázska B *et al*. Trends in laboratory diagnostic methods in periodontology. ACTA MEDICA (Hradec Králové) 2016; 59(1):3–9

Grover V. Clinical Relevance of the Advanced Microbiologic and Biochemical Investigations in Periodontal Diagnosis: A Critical Analysis. *Journal of Oral Diseases Volume* 2014, Article ID 785615, 11 pages.

Hanioka T. Relationship between periodontal disease status and combination of biochemical assays of gingival crevicular fluid. *J Periodont Res* 2005; 40; 331–338.

Listgarten MA. Microbiological Testing in the Diagnosis of Periodontal Disease. *J Periodontol* 1992; 63:332-337

Mani A, Anarthe R, Marawar PP, Mustilwar RG, Bhosale A. Diagnostic kits: An aid to periodontal diagnosis. J Dent Res Rev 2016;3:107-13.

Mario Taba Jr *et al*. Periodontal disease: a genetic perspective. Braz Oral Res., (São Paulo) 2012;26(Spec Iss 1): 32-8.

Pajnigara NG *et al*. Chair side diagnostic kits in Periodontics. *Int Dent J Stud Res*; April 2016;Vol 4:1.

Srivastava N *et al*., Point of Care- A Novel Approach to Periodontal Diagnosis. *J Clin Diag Res*.2017 Aug, Vol-11(8): ZE01-ZE06.

Wankhede AN, Wankhede SA, Wasu SP. Role of genetic in periodontal disease. *J Int Clin Dent Res Organ* 2017; 9:53-8.

Yoshida A. Microbiological Diagnosis for Periodontal Diseases. Periodontal Disease- A Clinician's Guide, Jane Manakil, IntechOpen, DOI: 10.5772/26482.

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