

Periodontal Disease and Its Genetic Link

Dr. Aditi Bhalla¹, Dr. Shailendra Singh Chauhan²

¹Sr. lecturer, Department of periodontology, K.D Dental College Mathura),

²Head of the Department, Department of Periodontology) K.D Dental college, Mathura.

ABSTRACT:

This era of modern technology has opened up various routes for improvement and detection of the root cause of diseases. Many studies regarding periodontal disease and their relation with genetics have been conducted which clearly show that large number of genes play a predisposing and progressing factors in periodontal disease. Thus, this review article aims to enlighten the genetic risk factors and their influence on periodontal disease.

KEYWORDS: Genetics, Genetic test, Genetic studies, Periodontal disease

INTRODUCTION

Periodontal diseases are a heterogeneous group of pathologies that share common clinical signs and symptoms, chiefly inflammation and destruction of the periodontium.^[1] Role of oral hygiene and bacteria is the primary factor in the progression of periodontal diseases but there are some other risk factors as well which play a vital role in the progression of the periodontal disease out of which one of the crucial factors is 'genetics'. In general, Genetics is termed as the branch of biology concerned with the study of genes, genetic variations and heredity in organisms.^[2] Periodontitis is a chronic multifactorial inflammatory disease associated with dysbiotic plaque formation and characterized by the progressive destruction of tooth supporting structure. Basically, there are two common forms of periodontitis which are aggressive periodontitis and chronic periodontitis. These are further classified into localized and generalized types depending on the percentage of attachment of bone and attachment loss according to the site assessed in mouth. Periodontitis less than 30% of bone loss and attachment loss is considered as localized while more than 30% comes under the category of chronic periodontitis.^[3] Genetic make-over plays a crucial role in initiation and progression of periodontal diseases. So, it is important to understand that the interactions of genetic mutations and polymorphisms of genes in periodontal disease. Hence the aim of this review article is to understand the crucial and direct linkage of genetics in periodontal diseases.^[4]

PERIODONTAL LINKED GENETIC STUDIES

Although a lot of studies have been done on genetic linkage we can categorize them into 5 those are as follows:-

1. Twin studies
2. Population studies
3. Family studies
4. The study of inherited disease and genetic syndrome
5. Single nucleotide polymorphisms

TWIN STUDIES

There are mainly two types of twins monozygous and dizygous. Monozygous twins develop from one fertilized egg while dizygous twins arise from two different eggs and sperms. Monozygous twins have similar genetic identity whereas dizygous only have similarity as those of siblings. A study conducted by Corey et al in 1993 on 4908 twins shows that 116 identical and 233 non-identical twins have shown the history of periodontitis. Thus, this study has proven as one of the most innovative studies of periodontal disease and genetics relationship.^[5] Another study conducted by Michalowozic et al in 2000 suggested that monozygous twins show more similarity in parameters used in the diagnosis of periodontitis. Thus, these studies have given many evidences in linkage between genetics and periodontal diseases.^[6]

POPULATION STUDIES

According to these studies various population of Europe and China was performed on that an interleukin 1 (IL-1) gene cluster which is linked with periodontitis was found in around 30% of European population whereas 2.3% was found in Chinese population which was significantly low as compared to European. Hence these studies prove that different population shows significant variation in the genetic which affects the prevalence and onset of periodontal diseases in particular population^[7]

FAMILY STUDIES

As per Mendel's law any disease which has a genetic base can be transferred from parents to child in a predictable mannerism. Melnick et al (1976) have proposed X-linked inheritance of aggressive periodontitis in which he has shown that female ratio was 2:1 as that of men in prevalence of aggressive periodontitis⁽⁸⁾. Another study conducted by Schenkein in 1998 shows that Aggressive Periodontal disease and IgG2 response to bacterial lipopolysaccharide (LPS) segregate independently as dominant and codominant trait. Study shows that person with one copy of IgG2 allele have more prevalence of developing periodontal disease as compared to the person with two copies of IgG2 allele⁽⁹⁾

STUDY OF INHERITED DISEASES AND GENETIC SYNDROMES

Chediak-Higiashi syndrome is a rare disease which is transmitted as an autosomal recessive trait. Its linkage with periodontal disease is based on abnormal polymorphonuclear leukocytes function. On the periodontal point of view rapidly progressive periodontitis is seen including premature tooth and bone loss⁽¹⁰⁾. Ehler-Danlos syndrome shows association of periodontal disease to its syndromes type I, VII, III, or IV. The type I shows a predisposition to periodontal disease while type VIII shows an early onset of periodontitis, Early loss of permanent teeth, fragile alveolar mucosa and gingival bleeding. Defect in type III collagen, present in 16% of the total collagen of the periodontal ligament, affecting the integrity of the periodontal junction. Also *Fusobacterium nucleatum*, is also found in the active lesion sites which is one of the aggregating bacteria of periodontal diseases⁽¹¹⁾.

Genetic linkage analysis and mutational analysis done on chromosome 11q14 shows some mutation on cathepsin C gene in patients with Papillon-Defeverre syndrome⁽¹²⁾. It shows clinical features such as palmar-plantar hyperkeratosis and severe periodontitis, premature loss of teeth in both deciduous and permanent dentitions⁽¹³⁾. Another syndrome named Hyper-IgE (Job's Syndrome) is included in the list, studies have shown increased level of IgE are present, chromosome mainly affected is

7q21. This syndrome causes chronic dermatitis with severe recurrent infections mainly caused by staphylococcus aureus and candida albicans, recurrent pulmonary infection are also seen in this condition. Oral ulceration and severe periodontitis is also associated with the syndrome⁽¹⁴⁾ Another syndrome known Weary-kindler also shows an early signs of periodontitis. This syndrome shows epidermal keratinocytes abnormalities, its basement membrane fails to express the type VII collagen.⁽¹⁵⁾⁽¹⁶⁾ Thus, these studies have given a sufficient relation between the periodontal disease and genetics.

SINGLE NUCLEOTIDE POLYMORPHISMS IN PERIODONTAL DISEASE

Korman et al mentioned in his study which was conducted in 1997 that there is a relationship between polymorphism in genes encoding for interleukin - 1α and interleukin- 1β also known as composite genotype and an increased in the severity of periodontitis.⁽¹⁷⁾ IL-10 gene which is located on chromosome 1, in a cluster with closely related interleukin genes, including IL-19, IL-20 and IL-24. It helps in the regulation of the proinflammatory cytokines such as IL-1 and TNF- α . Functional abnormalities in IL-10 affects the host response of the tissue which can be associated with the high prevalence of periodontal diseases.⁽¹⁸⁾ Fc γ R Gene is the polymorphism receptor of the Fc fragment of immunoglobulin IgG. Fc γ R receptors are found on Leukocytes from both the myeloid and lymphoid lineages. It links the humoral part of the host defense with the cellular part in that of immune system. Wilson and Kalmer in 1996 speculated that the Fc γ RIIa-R-allele might be associated with aggressive periodontitis due to reduced capacity to phagocytose IgG2 opsonized Actinobacillus actinomycetemcomitans. A study conducted on a group of dutch patient found that Fc γ RIIIa N-allele may be play a crucial risk factor for periodontitis.⁽¹⁹⁾ Thus all these studies have given decent proof of genetic linkage of periodontal disease.

GENETIC TEST FOR PERIODONTAL DISEASE

BTD (Biotechnica Diagnostics, Inc and Omnigene (Omnigene Inc) Diagnostics, Inc) are DNA probe systems use to detect the various periodontopathogens subgingival bacterias. Sample of subgingival plaque is taken in paper point and transferred into a container provided and then send to the respective companies for assay. Probes are available for P.Gingivalis, P.intermedia, A.actinomycetemcomitans, F.nucleatum, C.recta, T.denticola and T.pectinovorum respectively.⁽²⁰⁾

IAI PADO TEST 4.5 With the PADO RNA probe test kit are use for the detection of mainly four periodontal pathogens named as A. actinomycetemcomitans, P. gingivalis, T. forsythia and T. denticola. This test uses oligonucleotide probes complementary to conserved fragments of the 16S rRNA gene that encodes the rRNA, which forms a subunit of the bacterial ribosome. It has a detection threshold of 103 for A. actinomycetemcomitans and 104 for P. gingivalis, T. forsythia and T. denticola. The detection frequencies found indicated a low sensitivity of the PadoTest 4.5 method compared to the checkerboard method. The PadoTest 4.5 have high number of false negatives result which reduces its accuracy.⁽²¹⁾

Oral Fluid Nano Sensor Test (OFNASET) is a micro electromechanical system based on detection of electrochemical platform that is capable of quick, ultrasensitive, ultraspecific multiplex detection of RNA biomarkers and salivary proteins. It is used for detection of multiplex salivary biomarkers for oral cancer. It analyzes saliva for the presence of four salivary mRNA biomarkers (SAT, ODZ, IL-8, and IL- 1β) and two salivary proteomic biomarkers which are thioredoxin and IL-8. Benefits of its is detection of multiple salivary proteins and nucleic acids.⁽²²⁾

The periodontitis susceptibility trait test (PST) is the genetic susceptibility test for diagnosis of periodontitis, PST is commercially available test thus making it easily assessable. It evaluates the occurrence of allele 2 at the IL-1A +4845 and 1B +3954 loci simultaneously.⁽²³⁾ It is mostly used in early diagnosis of periodontal disease as it can differentiate between IL-1 genotypes, which said to have an association with multiple inflammatory responses.⁽²⁴⁾

CONCLUSION

As an emerging branch, genetics can prove to be vital in early diagnosis and assessing the prognosis of the periodontal disease. Various studies have given us multiple clues regarding the relation between genetics and periodontal disease. Many genetic tests are giving us a new ray of hope in diagnosing the periodontal disease. Thus, we can conclude that more studies and tests are required for world wide acceptance of genetic linkage in periodontal diseases assessments.

REFERENCES

1. Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999;4:1-6.
2. Peterson PE. The World Health Report 2003: continuous improvement of oral health in the 21st century – the approach of the WHO global oral health programme. *Community Dent Oral Epidemiol.* 2003;31(1):3-23. PMID:15015736.
3. Michalowicz BS, Aeppli D, Viraj JG, Klump DG, Hinrichs E, Segal NL, et al. Periodontal findings in adult twins. *J Periodontal* 1991;62(5):293-9.
4. Rik Derynck. *Nature genetics*, Vol.23, Dec.1999; 379.
5. Corey LA, Nance WE, Hofstede P, Schenkein HA. Self-reported periodontal disease in a Virginia twin population. *J periodontal* 1993;64(12):1205-8.
6. Michalowicz BS, Diehl SR, Gunsolley JC, Sparks BS, Brooks CN, Koertge TE, et al. Evidence of substantial genetic basis for risk of adult periodontitis. *J Periodontal* 2000;71(11):1699-707.
7. Armitage GC, Wu Y, Wang HY, Sorrell di, Giovine FS, Duff GW. Low prevalence of a periodontitis associated interleukin-1-composite genotype in individual of chinese heritage. *J. Periodontal* 2000;71(2):164-71.
8. Melnick M, Shields ED, Bixler D. Periodontosis: a phenotypic and genetic analysis. *Oral Surg Oral Med Oral Pathol* 1976;42:32-41.
9. Schenkein HA. Inheritance as a determinant of susceptibility for periodontitis. *J Dent* 1998;62:840-851.
10. Delcourt-Debruyne EMC, Boutigny HRA, Hildebrand HF. Features of severe periodontal disease in a teenager with Chediak-Higashi Syndrome. *J Periodontol* 2000;71:816-24.
11. Perez LA, Al-Shammari KF, Giannobile WV, Wang H. Treatment of periodontal disease in a patient with Ehlers-Danlos Syndrome. A Case Report and literature review. *J Periodontol* 2002;73:564-70.
12. Hart TC, Hart PS, Bowden DW, Michalec MD, Clilison SA, Walker SJ, et al. Mutation of Cthepsin gene are responsible for Papillon-Leferve syndrome. *J Med Genet* 1999;36(12):881-7.
13. Hart TC, Shapira L. Papillon-Lefevre syndrome. *Periodontal* 2000 1994;6(1):88-100.
14. He YY, Liu B, Xiao XP, [Hyper-IgE syndrome] LinChaung Er. *Bi Yan Hou Tou Jing Wai Ke Za Zhi.* 2017 Jun 05;31(11):892-896.

15. Wiebe CB, Silver JG, Larjava HS. Early onset periodontitis associated with weary-kindler syndrome: A Case Report. *J Periodontol* 1996;67(10):1004-10.
16. Wiebe CB, Larjava HS. Abnormal deposition of type VII collagen in Kindler Syndrome. *Arch Dermatol Res* 1999;291(1):6-13.
17. Denis F, Kinane, Hideki Shiba. *Periodontology* 2000, Vol. 39, 2005, 91–117.
18. Eskade J, Gallagher G. A polymorphic dinucleotide repeat in the human IL-10 promoter. *Immunogenetics* 1995;42(5):444-5.
19. Loss BG, Van de Winkel JG, Van der Velden U. Fc γ receptor polymorphism in relation to periodontitis. *J Clin Periodontol* 2003;30(7):595-602.
20. van Steenberghe TJM, Timmerman MF, Mikx FHM, de Quincey G, van der Weijden GA, van der Velden U, de Graaff J. Discrepancy between culture and DNA probe analysis for the detection of periodontal bacteria. *J Clin Periodontol* 1996; 23:955-959.
21. Leonhardt A, Carlen A, Dahlen G. Detection of Periodontal Markers in Chronic Periodontitis. *Open Dent J* 2011; 5: 110-115
22. Priyanka N et al. Recent approaches in saliva as a credible periodontal diagnostic and prognostic marker. *Arch Oral Sci Res* 2012; 2(1):40-46.
23. Greenstein G, Hart T. A critical assessment of IL-1 genotyping when used in a genetic susceptibility test for severe chronic periodontitis. *J Periodontol* 2002; 73(2):231- 247.
24. Ravishankar P L, Mithra D, Chakraborty P, Kumar A. Chairside diagnostics in periodontics. *SRM J Res Dent Sci* 2017;8:78-81