

Genetic association of Chronic Periodontitis in North Indian population: The trends so far-A short review

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I. INTRODUCTION

Chronic periodontitis is a multifactorial inflammatory disease which affects the tooth supporting tissues and is one of the major cause of tooth loss in adult population. Considerable evidence also suggests periodontitis has been associated with increased prevalence of systemic diseases such as Diabetes mellitus^[1], cardiovascular diseases^[2], rheumatoid arthritis^[3], preterm birth^[4]. Severe chronic periodontitis is sixth most prevalent disease worldwide^[5,6]. Surveys in Indian population also reflect that advanced periodontal disease leading to tooth loss may affect 40-45% of total population^[7]. Surveys in North Indian states of Delhi and Uttar Pradesh have shown a high prevalence of periodontitis ranging from 46-85%^[8]. Thus a need for a better understanding of pathophysiology of this widespread disease is highly warranted. Though initiated by microorganisms, both environmental and genetic factors are largely instrumental in pathogenesis and progression of periodontitis. Studies suggest that approximately half of the clinical variability in Chronic periodontitis may be attributed to the host genetic factors^[9,10]. There has been a constant search for genetic markers associated with the severity and the susceptibility of periodontal disease.

Recent genetic researches have focussed on association of Chronic Periodontitis with Single nucleotide polymorphisms (SNPs) of genes encoding cytokines, enzymes, cell surface receptors in various ethnic groups worldwide. However, in India there have been very few studies and that too largely in ethnicities of South Indian regions^[11-15]. On the basis of ethnic origin, Indian population can be sub-structured as four morphological types- Caucasoid, Mongoloid, Australoid, and Negrito; and on the basis of language families as: Indo European, Dravidian, TibetoBurman, and Austro Asiatic^[16]. Caucasoid morphological subtype and Indo linguistic group predominates in North Indian region. Owing to genetic differences in ethnic group, findings of genetic study for any one ethnic group in India cannot be used for another.

II. GENETIC ASSOCIATION OF CHRONIC PERIODONTITIS IN NORTH INDIAN POPULATION

There have been very few studies on selected SNP's evaluating the genetic association of Chronic periodontitis in North Indian population.

2.1 Interleukin- 1 α & Interleukin- 1 β

Interleukin (IL)-1 is a key proinflammatory cytokine and is known to be one of the most active stimulator of osteoclastic activity. IL-1 enables ingress of inflammatory cells into the sites of infection, causes eicosanoid release by monocytes and fibroblasts, stimulates matrix metalloproteinases, and contributes to the inflammatory cascades of microbial immune response^[17,18]. It has been proposed that a particular genotype of IL-1 could predispose individuals to periodontal disease by enhancing the inflammatory process. Kornman et al was the first one to report a significant association between severe adult periodontitis and composite genotype (IL-1A +4845 and IL-1B +3954) located on chromosome 2q13^[19]. Genotype positive non-smokers were found to be 6-8 times more likely to have chronic periodontitis than individuals who were genotype negative.

In North Indian population, Daing et al reported that genotypes and alleles of SNP IL-1 β + 3954 did not show a significant association with chronic periodontitis^[20]. Puri et al concluded that allele 2 of Interleukin-1 α (-889) gene polymorphism were significantly associated with risk of aggressive periodontitis but not with chronic periodontitis^[21]. A very small sample size was limitation of both these studies.

2.2 OTHER CYTOKINES

Prakash et al 2014 analyzed the role of gene polymorphism of pro-inflammatory cytokines TNF- α , IL-6 and anti-inflammatory cytokine IL-4 with the susceptibility to chronic periodontitis in North Indian population. A total of clinically diagnosed 200 chronic periodontitis cases and 200 age and gender matched

controls were genotyped using PCR-RFLP methods. Analysis showed association of TNF- α 308GA (rs1800629) with risk of CP whereas IL-6-174GC (rs1800795) and IL-4-590CT (rs224325) polymorphisms did not show any significant differences^[22].

2.3 CYCLOOXYGENASE (COX)

COX2 is the crucial enzyme involved in conversion of arachidonic acid to Prostaglandins (PGE2). COX2 dependent PGE2 plays an important role in tissue destruction and bone resorption in Periodontitis. Polymorphisms within the COX2 gene therefore influence the inflammatory disease processes and are potentially important genetic markers for periodontitis.

Daing et al in their pilot study in North Indians observed that mutant genotypes (GA and AA) of COX2 -1195(rs 689466) showed more than a twofold risk and TC and CC genotypes of COX2 8473 (rs 5275) showed a reduced risk for the disease, but the findings were not statistically significant. Thus they concluded that genotypes of both the SNPs were not independently associated with risk of chronic periodontitis in North Indians while haplotype AT was found to be associated^[23].

In another study Prakash et al investigated the association of COX-2 polymorphisms (rs20417, rs689466, and rs5275) in susceptibility to chronic periodontitis (CP) for Northern Indian population. Genotyping of COX-2 polymorphism was carried out through PCR-RFLP in 200 CP cases and 200 controls. Authors concluded that no association was observed in any of the studied COX-2 polymorphisms with Chronic Periodontitis in North India^[24]. However, both the above mentioned authors suggested that the study should be replicated in larger sample size to arrive at a definitive conclusion.

2.4 VITAMIN D RECEPTOR (VDR)

As alveolar bone loss is a key feature of chronic periodontitis, particular attention has been paid to the role of mediators of bone like vitamin D receptor (VDR) in the pathogenesis of the disease. Investigators presume that VDR is involved in variety of biologic process including bone metabolism and the modulation of the immune response, a role in which it functions as a vitamin D3-dependent transcription factor^[25]. There have been only two studies in Indian population, one in North Indian^[20] and one in South Indian population^[26]; who have investigated the potential association of VDR *TaqI* with Chronic Periodontitis

Daing et al in their study concluded that mutant Genotype CC and allele C of VDR *TaqI* were significantly associated with a higher risk for chronic periodontitis as compared to subjects with wild genotype TT and allele T in a sample of North Indian population^[20]. However, sample size was very small to make significant conclusions.

III. DISCUSSION

The Human Genome Project started two decades back which increased the acceptance and awareness about genetic predisposition of the disease. Since then there has been a constant quest to search and identify novel genetic markers which can be potential risk factors for a population group. Till date there have been number of reports on genetic association of Chronic periodontitis in ethnicities like South Indian^[11-15] but very few in North Indian^[20-24].

Genetic assessment can provide a valuable tool for clinician for evaluating an individuals risk for Periodontitis. It can help meet the need for improved surveillance and risk stratification of high risk patients, enabling personalization of treatment plans and improved outcomes. Once we have identified the genetic makeup of the poor responders to standard treatment protocol, the clinician will right away think of specific treatment options for that group and would encourage patient compliance with regular periodontal maintenance and smoking cessation.

Studies to find high risk gene polymorphisms in a population group will ultimately lead the pathway to formulation of genetic periodontal susceptibility tests for that ethnicity. One such test is already popular in western population by name of Perio-Predict, which is an easy to use genetic test that identifies individuals with high risk of periodontitis by analyzing gene polymorphism of IL-1 from a buccal swab^[27,28]. Formulating a genetic risk assessment tool for a highly prevalent disease like periodontitis for Indian population as a whole and for individual ethnicities in India is highly warranted.

IV. CONCLUSION

Further studies with more comprehensive methodologies; including more gene polymorphisms, larger sample sizes, with simultaneous analysis of gene expression in gingival tissue are needed to provide with a stronger evidence about possible role of genes in prevalence of periodontitis in North Indian population.

REFERENCES

- [1]. Preshaw PM., Alba AL., Herrera D, Jepsen S, Konstantinidis A, Makrilakis K. & Taylor R. Periodontitis and diabetes: a two- way relationship *Diabetologia* 2012;55: 21–31.
- [2]. Karnoutsos K, Papastergiou P, Stefanidis S et al. Periodontitis as a risk factor for cardiovascular disease: the role of anti-phosphorylcholine and anti-cardiolipin antibodies. *Hippokratia* 2008; 12:144–149.
- [3]. Kaur S, S White & M. Bartold. Periodontal disease as a risk factor for rheumatoid arthritis: a systematic review. *JBILibr. Syst. Rev* 2012 ; 10: 1–12.
- [4]. Marakoglu I, Gursay UK, Marakoglu K, Cakmak H, Ataoglu T. Periodontitis as a risk factor for preterm low birth weight. *Yonsei Med J* 2008; 49: 200–203.
- [5]. Tonetti MS, Jepsen S, Jin L, Otomo-Corgel J. Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action 2017; 44(5):456-462
- [6]. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*, 388, 1545–1602
- [7]. Shah N. National Commission on Macroeconomics and Health, Ministry of Health and Family Welfare. New Delhi: Government of India; 2005. Sep, Oral and dental diseases: Causes, prevention and treatment strategies In NCMH Background Papers—Burden of Disease in India (New Delhi, India) pp. 275–98.
- [8]. Shah N, Pandey RM, Duggal R, Mathur VP, Rajan K. Oral Health in India: A report of the multi centric study, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India and World Health Organisation Collaborative Program. 2007 Dec
- [9]. Michalowicz BS, Diehl SR, Gunsolley JC, et al. Evidence of a substantial genetic basis for risk of adult periodontitis. *J Periodontol* 2000; 71:1699-1707
- [10]. Michalowicz BS, Aeppli D, Virag JG, et al. Periodontal findings in adult twins. *J Periodontol* 1991; 62:293-299.
- [11]. Prakash PS, Victor DJ. Interleukin-1b gene polymorphism and its association with chronic periodontitis in South Indian population. *Int J Gen Mol Bio.* 2010; 2(8):179-83.
- [12]. Shete AR, Joseph R, Vijayan NN, Srinivas L, Banerjee M. Association of single nucleotide gene polymorphism at interleukin-1β+ 3954,– 511, and– 31 in chronic periodontitis and aggressive periodontitis in Dravidian ethnicity. *J Periodontol.* 2010; 81(1):62-9.
- [13]. Kaarthikeyan G, Jayakumar ND, Padmalatha O, Sheeja V, Sankari M, Anandan B. Analysis of the association between interleukin1β (+ 3954) gene polymorphism and chronic periodontitis in a sample of the south Indian population *Ind J Dent Res.* 2009; 20(1):37.
- [14]. Jain N, Joseph R, Balan S, Arun R, Banerjee M. Association of interleukin-4 and interleukin-17F polymorphisms in periodontitis in Dravidian ethnicity. *Ind J Human Genetics.* 2013;19(1):58.
- [15]. Chaudhari HL, Warad S, Ashok N, Baroudi K, Tarakji B. Association of Interleukin-17 polymorphism (-197G/A) in chronic and localized aggressive periodontitis. *Braz Oral Res.* 2016;30(1)
- [16]. Gadgil M, Joshi NV, Manoharan S, Patil S, Prasad UVS. Peopling of India. In: Balasubramanian D, Appaji Rao N. editors. *The Indian Human Heritage*. Hyderabad: Universities Press 1998;100-129
- [17]. Kornman KS, di Giovine FS. Genetic variations in cytokine expression: A risk factor for severity of adult periodontitis. *Ann Periodontol* 1998;3: 327-38.
- [18]. Taylor JJ, Preshaw PM, Donaldson PT. Cytokine gene polymorphism and immunoregulation in periodontal disease. *Periodontol* 2000 2004; 35:158-82.
- [19]. Kornman KS, Crane A, Wang HY, di Giovine FS, Newman MG, Pirk FW, et al. The interleukin-1 genotype as a severity factor in adult periodontal disease. *J Clin Periodontol* 1997; 24:72-77.
- [20]. Daing A, Singh SV, Saimbi CS, Khan MA, Rath SK. Single nucleotide polymorphisms at interleukin(IL)-1β+ 3954 and vitamin D (VDR) TaqI in chronic periodontitis patients:A pilot study in North Indian population. *J Int Clin Dent Res Organ* 2015;7:18-23
- [21]. Puri K, Chhokra M, Dodwad V, Puri N. Association of interleukin-1 α (–889) gene polymorphism in patients with generalized aggressive and chronic periodontitis. *Dent Res J* 2015;12(1):76.
- [22]. Prakash G, Ajay S, Gupta KK, and Mittal B. Role of TNF-A, IL-6 and IL-4 with the susceptibility to chronic periodontitis in North Indian population: a multi-analytic approach *Molecular Cytogenetics* 2014; 7(1):72
- [23]. Daing A, Singh SV, Saimbi CS, Khan MA, Rath SK. Cyclooxygenase 2 gene polymorphisms and chronic periodontitis in a North Indian population: a pilot study. *J Periodontal & Implant Sci.* 2012; 42(5):151-7.

- [24]. Prakash G, Umar M, Bansal SA, Bali D, Upadhyaya R, Gupta K, Dixit J et al. COX-2 gene polymorphisms and risk of chronic periodontitis: A case-control study and meta-analysis. *Oral Diseases* 2013; 21(1):38-45
- [25]. Uitterlinden AG, Fang Y, Bergink AP, van Meurs JB, van Leeuwen HP, Pols HA. The role of vitamin D receptor gene polymorphisms in bone biology. *Mol Cell Endocrinol* 2002; 197: 15-21.
- [26]. Kaarthikeyan G, Jayakumar ND, Padmalatha O, Varghese S, Anand B: Analysis of association of TaqI VDR gene polymorphism with the chronic periodontitis in Dravidian ethnicity. *Indian J Hum Genet* 2013; 19:465-468.
- [27]. Higashi MK, Veenstra DL, Agnila MD, Hijoel P. The cost effectiveness of Interleikin-1 genetic testing for periodontal disease. *J Periodontol* 2002 1474-1483
- [28]. Interleukin genetics. <http://ilgenetics.com/interleukins-periopredict>

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