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Research Paper

Vitamin D Receptor Gene Polymorphism as a Risk Factor for Chronic Periodontitis: Indian Scenario -A Short Review

Dr Anika Daing
Assistant professor, Dept. of Periodontology, Faculty of Dentistry, Jamia Millia Islamia, New Delhi
**Corresponding author: Dr Anika Daing*

ABSTRACT: *Chronic Periodontitis is an inflammatory disease affecting the tooth supporting tissues, and is highly prevalent in India. It is multifactorial in nature which is initiated by bacteria but many risk factors including gene polymorphism play an important role in its pathogenesis. Studies on association of gene polymorphism of Vitamin D receptor with chronic periodontitis have been reported in various ethnicities worldwide; however there are very few studies reported in Indian population. This short review attempts to give an overview on the importance and the status of studies on Vitamin D receptor gene polymorphism in India.*
KEY WORDS : *Vitamin D receptor, chronic periodontitis, single nucleotide polymorphism, Indian*

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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. Periodontitis has been associated with increased prevalence of systemic diseases such as, cardiovascular diseases, diabetes mellitus, rheumatoid arthritis, preterm birth[1-4]. Severe chronic periodontitis is sixth most prevalent disease wordwide [5,6]. Advanced periodontal disease leading to tooth loss affects 40-45% of total Indian population with a high prevalence ranging from 46-85% in North India[7,8]. Thus a need for a better understanding of patho-physiology of this widespread disease is highly warranted. Though initiated by microorganisms, both environmental and genetic factors are largely contributory in pathogenesis and progression of periodontitis. 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. Mediators of bone metabolism also play a role in the pathophysiology of periodontitis. 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 nuclear Receptor (VDR) in the pathogenesis of the disease.

II. ROLE OF VDR IN PATHOGENESIS OF PERIODONTITIS

VDR is a ligand-dependent transcription factor which, in concert with its endogenous ligand, 1,25 hydroxivitamin D ($1,25(OH)_2D3$), is involved in the expression of many genes[11]. Researches have revealed that most immune cells express VDR which synchronizes the interaction between the innate and adaptive immune systems by tightly regulating their activities [12-15].

VDR inhibits the differentiation, maturation and immune stimulating ability of dendritic cells by downregulating the expression of Major Histocompatability Complex class II molecules. VDR suppresses interleukin (IL)-12 production and enhances IL-10 production in dendritic cells.VDR also regulates the production of T-cell helper 1 and 2 cytokines and IL-17, by which it influences adaptive immunity and inflammation. Further, specific T-cell cytokines are able to influence the TLR-induced VDR dependent antimicrobial pathway in human monocytes[16,17].

It has been demonstrated that VDR also plays an important role in both the innate and the adaptive immune response to P.gingivalis. VDR has also been shown to inhibit IL-8 expression induced by P.gingivalis in periodontal ligament cells and thus shows an anti-inflammatory effect in periodontal disease[18-20].

III. VDR GENE POLYMORPHISM AND CHRONIC PERIODONTITIS

The gene encoding the VDR is located on chromosome 12q13.11, harbours eight exons that are translated, and six that are alternatively spliced[21]. The VDR gene exhibits several SNPs, located in both the coding and the non-coding portions of the gene. Both rs7975232 (ApaI) and rs1544410 (BsmI) SNPs are found in the region of the gene from intron 8 to the 3' untranslated region, a silent mutation within codon 352 of the exon 9 creates the rs731236 (TaqI) polymorphic site [22]. In addition, the genetic variation rs2228570 (FokI), located in the exon 2 at the 5' portion , has been regarded as a start codon polymorphism [23].

Many previous studies have examined the association between VDR polymorphisms and combinations of these variants and periodontal disease at TaqI, ApaI, BsmI and FokI restriction sites [24–31]. Several studies have found a significant association between TaqI polymorphism and periodontal disease [24–28], though other studies have failed to find a significant associations of this type [29–31]. Studies on the association between VDR polymorphisms of ApaI, BsmI and FokI, and the risk of periodontal disease are limited and have reported conflicting results [26,28-33].

A meta-analysis including 18 studies indicated that the TaqI and FokI polymorphisms were associated with chronic periodontitis in Asians, but not in whites, while there were no associations between polymorphisms of ApaI or BsmI and periodontitis [34]. Another meta-analysis inclusing 15 studies concluded that polymorphisms of TaqI, ApaI and BsmI, but not FokI, were associated with chronic periodontitis in Asians [35]. It is necessary to accumulate further evidence in order to clarify whether VDR polymorphisms affect periodontal disease in different ethnic groups.

IV. VDR GENE POLYMORPHISM AND CHRONIC PERIODONTITIS IN INDIAN POPULATION

Only two studies have been reported for Indian population, one each in North Indian and South Indian ethnicities. Kaarthikeyen et al 2013 analyzed the association of VDR TaqI (T>t)gene polymorphism with the chronic periodontitis in Dravidian ethnicity [36]. A total of 120 subjects were recruited for this study, which included 60 CP and 60 healthy controls. TaqI VDR gene polymorphism was analyzed using specific primers and amplified by polymerase chain reaction (PCR) and visualized under 2% agarose gel. Study results showed that Tt and tt genotype had a higher frequency of occurrence in Chronic Periodontitis compared with controls. Study concluded that TaqI VDR gene polymorphism is associated with CP in South Indian Dravidian ethnicity. Daing et al in their pilot study in a small sample of North Indian population concluded that genotype CC and allele C of VDR TaqI(T>C) were significantly associated with a higher risk for chronic periodontitis as compared to subjects with TT genotype and allele T [37] .They concluded that mutant genotype CC and allele C of VDR TaqI were associated with risk of chronic periodontitis; however they suggested that results should be extrapolated in a larger sample size.

V. FUTURE DIRECTIONS

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 the genetic makeup of the poor responders is identified, the clinician can right away think of specific treatment options for that group and would encourage patient compliance with periodic periodontal maintenance, smoking cessation and monitoring the other risk factors.

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 [38]. 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.

VI. CONCLUSION

Further studies with more comprehensive methodologies; including more gene polymorphisms of VDR, with a larger sample sizes in various ethnic groups in Indian are needed to provide with a stronger evidence about possible role of VDR gene in prevalence of chronic periodontitis in Indian population.

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**Corresponding Author: Dr Anika Daing*
Dept. Of Periodontology, Faculty Of Dentistry, Jamia Millia Islamia, New Delhi

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