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Association Of Vitamin D Receptor (VDR) Gene Polymorphism With Chronic Periodontitis / A Preliminary Study Among Egyptian Population.

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Abstract

Background: Chronic periodontitis is caused by a microbial infection and usually leads to progressive resorption of alveolar bone. Both genetic and environmental factors play a role in progress of this disease. Vitamin D performs its action through interaction with vitamin D receptor (VDR). Several polymorphisms have been recognized in the VDR gene.

Objective: The aim of the present study was to to evaluate the association of the polymorphisms (TaqI , BsmI and FokI) of the VDR gene with chronic periodontitis among a sample of Egyptian population as a preliminary study.

Subjects and methods: This is a case-control study which included twenty patients diagnosed with chronic periodontitis. Twenty Egyptian subjects with healthy periodontium served as a control group. All cases were subjected to estimation of polymorphisms of the VDR gene (Fok I, Taq I & BSM I).

Results: A statistically significant difference was observed between patients & control groups as regards Fok I and BSM I polymorphism of VDR genes. While No statistically significant difference was observed between patients & control groups as regards Taq I of VDR genes.

Conclusion: The present study support an association of polymorphisms (BsmI and FokI) of the VDR gene with chronic periodontitis among studied population.

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Introduction:

Chronic periodontitis (CP) is considered one of the most prevalent diseases globally, and it is the major cause of losing teeth in old age **(1)**.

Periodontal disease usually leads to progressive resorption of alveolar bone. Both genetic and environmental factors play a role in progress of this inflammatory disease which is affected by interaction of pathogenic organism and responses of host **(2).**

Several studies have been performed trying to find a relation between identified genetic factors and increased susceptibility to chronic periodontitis **(3).**

Vitamin D (1.25-dihydroxyvitamin D3) is a fat-soluble vitamin that perform its action through interaction with its receptor, vitamin D receptor (VDR). The biological action include bone metabolism and modulation of immune response. Moreover, VDR is responsible for regulation of genetic expression which is critical for the action of vitamin D **(4).**

The VDR gene is present on the long arm of chromosome 12 (12q12-14) and consist of 10 exons, the first one is not transcribed**.** Several polymorphisms have been recognized in the VDR gene, and majority are identified by biallelic variation in restriction enzyme sites. TaqI , BsmI, and FokI are examples of nucleotide polymorphisms in the VDR gene **(5).**

The results of various studies investigating the relation of TaqI, BsmI, and FokI VDR gene polymorphisms with CP in different ethnic populations are inconsistent. Factors including wide separated areas and genetic effect may be different in various ethnic groups. Therefore, we aimed in this study to evaluate the association of the polymorphisms (TaqI , BsmI and FokI) of the VDR gene with chronic periodontitis among a sample of Egyptian population as a preliminary study.

Subjects and Methods:

The present study included twenty patients diagnosed with chronic periodontitis recruited from the outpatient clinic at the Faculty of Dentistry, Ain Shams University in the period from January to November 2018.

The diagnosis of periodontal diseases was made on the basis of evaluation of clinical signs in peridontial tissues through full mouth examination at six sites per tooth (mesiobuccal, buccal, distobuccal, mesiolingual, lingual and distolingual).

The study was designed as a case control study; 20 Egyptian periodontitis patients (Cases) and 20 Egyptian cases with healthy periodontium (Control).

Twenty age matched healthy controls recruited during routine checkup, who were proven to be free of any periodontal disease, were also included in this study. Healthy periodontium was recognized by being stippled, pale pink and continuous with lining mucosa.

The proposal was reviewed and approved by the Faculty of Dentistry Ain Shams University Research Ethics Committee (FDASU-REC) on December 2016.

Both cases and controls signed an informed consent after understanding the purpose of the research and received standard periodontal treatment after sample withdrawal. Genetic samples were not used for any other purposes and individual patients' results were kept confidential. All cases were subjected to estimation of polymorphisms of the VDR gene (Fok I, Taq I & BSM I).

Results:

In our results, as regards Taq I gene polymorphism, no statistically significant difference was observed between patients & control groups ($\chi 2$ = 5.523, p = 0.063) as regards Taq I genotypes. In addition, no statistically significant difference as regards Taq I allele frequencies among studied groups (p = 0.508).

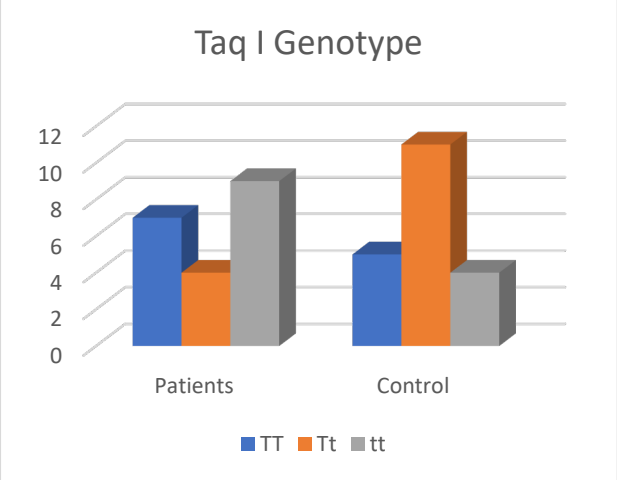

Figure (1): Taq I Genotype among studied groups.

Concerning Fok I gene polymorphism in our study, a statistically significant difference was observed between patients & control groups ($\chi 2$ = 8.79, p = 0.012) as regards Fok I genotypes. The results also showed showing a statistically significant difference as regards Fok I allele frequencies among studied groups (p = 0.0075).

Table 1 : Comparison of Genotype frequency of Fok I polymorphism in patients and control groups :

As regards the third gene in our study (BSM I) gene polymorphism, a statistically significant difference was observed between patients & control groups ($\chi 2$ = 7.86, p = 0.019) as regards BSM I genotypes. Also, a statistically significant difference as regards BSM I allele frequencies among studied groups (p = 0.04).

Fok I	Genotype				χ2	P-value
	FF	Ff	ff	Total		
Patients % within group	4 (20%)	4 (20%)	12 (60%)	20 (100%)	8.79	0.012*
Control % within group	7 (35%)	10 (50%)	3 (15%)	20 (100%)		
Total % within group	11 (27.5 %)	14 (35 %)	15 (37.5 %)	40 (100 %)		

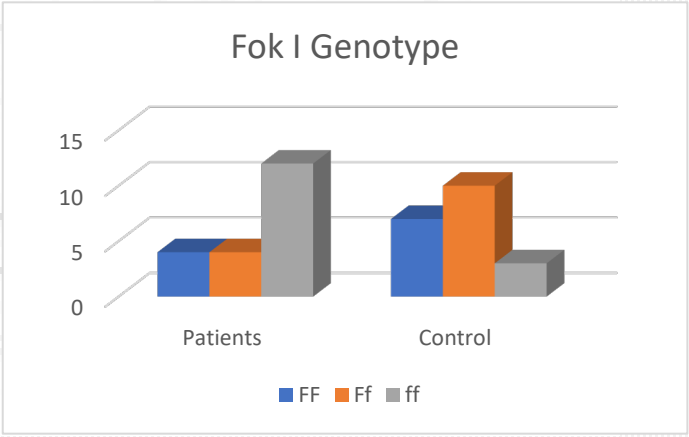

Figure (2): Fok I Genotype among studied groups.

Discussion:

Genetics is considered a factor in susceptibility to periodontitis. The role of genetic polymorphism in modeling host response in periodontal disease has been demonstrated in numerous studies.

Genetic polymorphism may determine the modification of the amino acid sequence or the expression of encoded protein and may result in alterations of natural and adaptive immunity. Polymorphism can therefore determine the disease outcome; however, genetic polymorphism can also provide protection against disease **(6).**

In the current study, no statistically significant difference was observed between patients & control groups as regards Taq I of VDR genes. This came in agreement with a study carried on western Romanian population, which reported no statistically significant differences in Taq I polymorphism (p = 0.169) **(6).** Also, a Taiwanese study, which included cases with chronic and aggressive periodontitis in addition to healthy controls, showed that that Taq I gene polymorphism was not related to the susceptibility to periodontitis **(7).**

In another study carried among Turkish population, no statistically significant differences were observed between patients with CP and control groups as regards Taq I VDR genotypes and as regards the frequency of the Taq I allele frequencies **(8).**

This in contrast to a Japanese study carried in 2003 that reported a strong relation between the VDR gene Taq I polymorphism and development of CP (X2 = 4.48, P = 0.034) **(9).** This contrast can be explained by criteria used for selection of participants in this study, which included smokers and cases with diabetes mellitus. CP development is affected by many risk factor. One of them is smoking, which is identified as a main risk factor. In the mentioned study, although, a significant association was observed between CP and gene polymorphism, the subjects contained a number of smokers.

Concerning Fok I gene polymorphism in our study, a statistically significant difference was observed between patients & control groups as regards Fok I genotypes and Fok I allele frequencies.

This is in accordance with ***Marian et al,*** who pointed to a statistically significant correlation between Fok I polymorphism in VDR gene and the incidence of CP in the studied group (p= 0.049) **(6)**.

Another study, carried among Brazilian population, suggested an association between Fok I polymorphism and extent of periodontitis **(10)**.

This is in contrast to a study carried among Syrian population, and concluded that FokI VDR polymorphism was not associated with chronic periodontitis in the studied Syrian population. The age group of subjects in this study was much higher than in the majority of studies investigating chronic periodontitis **(11)**.
The other study was performed in Libya, and had found no association between chronic periodontitis and Fok I gene polymorphism. Unlike most studies, extraction of genomic DNA was performed from buccal swabs instead of extraction from whole blood sample **(12).**

Our results showed a statistically significant difference between patients & control groups as regards BSM I genotypes. Also, a statistically

significant difference as regards BSM I allele frequencies.

These results came in agreement with results of a study carried in Jordan, this study reported an association between BSM I polymorphism of VDR gene and development of chronic periodontitis in Jordanian population **(13).**

In another study investigating BSM I gene polymorphism carried in 2019, a positive relationship was observed between VDR gene polymorphism (Fok I) and chronic periodontitis ($p = 0.041$) **(6).**

A similar result was also obtained by ***De Brito et al*** in their investigations in a Brazilian population; where they concluded that BSM I VDR gene polymorphism might be a risk indicator for susceptibility to chronic periodontitis but only in association with Taq I polymorphism **(14).**

On the other hand, a study performed in Turkey showed no statistically significant difference as regards BsmI polymorphism of VDR gene when comparing severe generalized CP patients and healthy controls. This study had some limitations in sample selection where the patients group consisted only of cases with severe generalized chronic periodontitis **(8).**

In general, the discrepancy between our findings and other studies might be related to ethnicity as the BsmI, FokI, and TaqI alleles frequencies alter among different populations.

In genetic studies investigating association between gene polymorphism and certain disease, performed among different ethnic groups , the results are usually inconsistent. This may be explained by the difference in genetic alleles frequencies in addition to gene-gene interactions. Thus, although the results of association studies may be valid in a given ethnic group, it may be irrelevant in another ethnic group **(15).**

In conclusion, the present study , despite within the limitations in selection of cases and number, showed that the TaqI polymorphisms of the VDR gene was not associated with chronic periodontitis. While on the other hand, an association between Fok I and BSM I genes polymorphism and development of chronic periodontitis.

Clearly, Further studies with larger sample size, and in variable geographic areas in the country and among different ethnic populations will be valuable for objective evaluation of VDR gene polymorphism as a risk factor for development of chronic periodontitis.

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