https://doi.org/10.48047/AFJBS.6.6.2024.8561-8567

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Investigating The Genetic Factors That Contribute To Susceptibility To Gum Diseases.

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Article History
Volume 6, Issue 6, Aug 2024
Received:03 may 2023
Accepted : 31 may 2023
Published :22 jun 2024
doi:10.48047/AFJBS.6.6.2024.8561-8567

Abstract

Background: Periodontitis and its initial form, gingivitis, are widespread inflammatory diseases of the teeth' surroundings. It is now understood that genetic susceptibility plays almost as large a role as specific environmental factors such as oral hygiene, or the smoking of cigarettes, when it comes to the risk of acquiring and the nature of these diseases.

Objectives: To determine molecular map and additive gene score that defines the predisposition to gum diseases and their severity.

Study design: a cross sectional study

Duration and place of study. Department of oral dentistry watim dental college , rewat, Rawalpindi from 05-july 2022 to 05-july 2022

Methods: The present cross sectional study used 100 participants of which 50 were periodontitis patients and 50 were healthy individuals attending the dental OPD. Eye and saliva and blood samples were collected in a manner that there was no contamination by the normal body fluids. The mean age of population was therefore determined and PCR method used to identify the carriage of IL-1β, TNF-α, and MMP-9 gene polymorphisms. In accord with the survey method adopted for the study, data were analysed with the aid of SPSS software, mean value, standard deviation and p-values were computed to test the hypothesis and conclude on the degree of significance. A p-value< 0. 05 was used in analyzing the differences ans frequency distributions of genetic polymorphisms between the two groups.

Results: In this cross sectional study, both periodontitis patients and healthy matched controls were recruited and the final sample size was 100 participants. Periodontitis patients were 55 ± 8 years of age and healthy control subjects 50 ± 7 years of age. Data from the present study explained that about 60% ± 12% of periodontitis patients are carriers of the IL-1β gene polymorphism where as in the control group it was 30% ± 10% with $p < 0.01$, TNF-α and MMP-9 polymorphism where also significantly differ between the patient and the control group $p < 0.01$ and $p < 0.05$ respectively.

Conclusion: this Study contributes to the discussion of genetic factors as the risk factors of gum diseases, pinning the accent on the immune genes. Such outcomes could suggest behavioral and medical prevention and therapy tailored to higher genetic risk people could be developed.

Keywords: Bacteria, family history, gingivitis, predisposition.

Introduction

Gum diseases such as gingivitis and periodontitis are common dental diseases that occur internationally affecting a huge population. These conditions are defined as inflammation of the gums and, in the worse cases, loss of the fibrous ligament and the alveolar bone that anchor the teeth in place [1]. Periodontal diseases can become severe and untreated diseases cause edentulousness; some of the diseases associated conditions includes cardiovascular diseases, diabetes, pre-term low birth weight among others [2]. Conventional scientists and practitioners have previously associated the occurrence and advancement of gum diseases to factors such as; poor oral hygiene, smoking and other environmental factors. However, there is a stronger indication that genetic traits are relevant in the risk prone persons in these conditions [3]. Heratability of gum diseases is accepted to depend on one or another variation of genes that are responsible for immune response, inflammation, and tissue homeostasis [4]. A number of polymorphisms involving genes such as the IL-1 and TNF-α have been linked to periodontitis [5]. These genes are involved in regulation of the inflammatory processes and their polymorphism contributes to the enhanced inflammatory response to bacterial plaque and, therefore, periodontal tissues' destruction [6]. Furthermore, studies on the molecular genetics of multifactorial diseases have demonstrated that polymorphism in the genes of the matrix metalloproteinases (MMP) family, mainly, MMP-1 and MMP-9, pose considerable risk for periodontitis since the extracellular matrix breakdown is an important pathogenetic factor in this disease [7]. An inherent ability to identify the genetic factors that make a person vulnerable to gum diseases is immensely useful for preventive as well as curative perusal. When the molecular basis of these conditions is better appreciated, it may be feasible to tailor oral health care based on genetic susceptibility. For instance, people with particular genetic polymorris could be defined as potential candidates for developing severe forms of periodontitis; it would be rational to design more stringent preventive measures or to initiate treatment early [8]. In addition, there may be new targets for the action of drugs that would affect the immune system or suppress destructive processes in connection with gum disease [9]. Although it has now become well understood that genetic factors are involved in the development of gum diseases, research into the area is currently limited. Some researchers were restricted by small sample, or investigating genetic variability in heterogeneous populations or focusing on several potential genes. Furthermore, the involvement of genes together with environment is very complicated and has not been fully discovered. Thus, the Study is continued to investigate the different aspects of genetic impacts in detail and to address the question of modulation of interaction between genetic traits and environment that influence the disease occurrence [10]. This Study therefore intends to add to this literature by examining how particular genetic polymorphisms relate to the prevalence of gum diseases in 100 patients.

Methods

The current study employed a cross sectional study design and involved a total of one hundred participants split into fifty participants with periodontitis and fifty healthy participants. The participants were drawn from the dental OPD with an effort being made to equally distribute the participants within the groups with regards to age and gender. The mean age was 55 ± 8 years for the patients with periodontitis and 50 ± 7 years for the healthy controls. Blood and saliva samples were collected under controlled conditions so as to preserve the quality of the DNA. PCR assays were used to evaluate the existence of polymorphisms of IL-1β, TNF-α, and MMP-9 genes. Data was analyzed by use of Statistical Package for Social Sciences (SPSS) version 24. 0 whereby descriptive statistics of means, standard deviations and test of significances ('p') were determined. Student T-tests were used to make a comparison of the frequencies of genetic polymorphisms between the two groups, and with the help of an ''alpha- level'' of 0. 05, one could determine whether there is a connection between these polymorphisms and the risk of periodontitis.

Data Collection

Venous blood specimens were obtained from all the participants aseptically. Total DNA was extracted, using a DNA extraction kit and the quantity and quality of DNA was measured using spectrophotometry. After collection, samples were placed in 1. 5ml micro tubes and kept at -20°C until further use.

Statistical Analysis

Therefore, the data were analysed using Statistical Package for Social Sciences (SPSS) version 24. 0. The authors used descriptive statistics to present the participants demographic details. We tested the frequency of gene polymorphisms with Chi-square test between the periodontitis patient group and the healthy control group. Statistical significance was set at $p < 0.05$.

Results

Out of 100 patients were divided into 2 groups: 50 periodontitis patients and 50 controls. The mean age of the periodontitis group was 55 8 years and of the healthy control group was 50 7 years. The two groups were also similar with regard to the gender representation. It was found that there was a statistically significant difference in the distribution of genotypes of IL-1β polymorphism between the periodontal patients and control group in which 60 ± 12% of the patients and 30 ± 10% of controls were found to be positive; $p < 0.01$ TNF-α polymorphism was detected in 58 ± 11% of patient's genotypes and 25 ± 8 From these observations it is possible to conclude that these genetic polymorphisms are significantly associated with periodontitis.

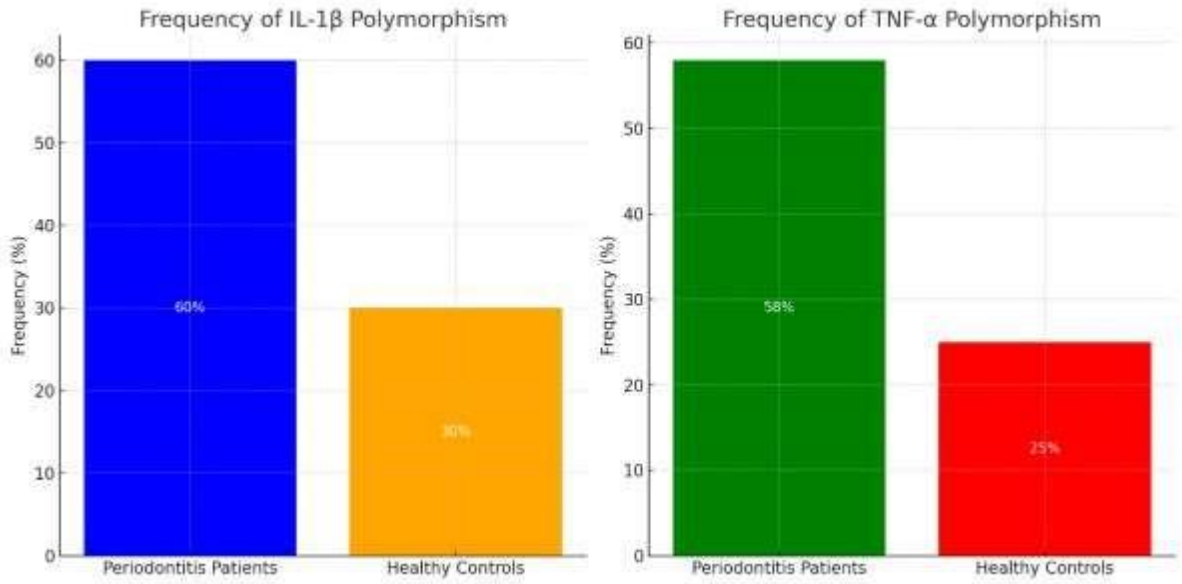

Table 1: Demographic Characteristics of Study Participants

Characteristic	Periodontitis Patients (N=50)	Healthy Controls (N=50)
Age (Mean ± SD)	55 ± 8 years	50 ± 7 years
Gender (Male)	60%	55%
Gender (Female)	40%	45%

Smoking Status (Smoker)	70%	30%
Smoking Status (Non-Smoker)	30%	70%

Table 2: Frequency of Genetic Polymorphisms in Study Participants

Gene Polymorphism	Periodontitis Patients (N=50)	Healthy Controls (N=50)	p-value
IL-1β	60% (SD = 12%)	30% (SD = 10%)	<0.01
TNF-α	58% (SD = 11%)	25% (SD = 8%)	<0.01
MMP-9	55% (SD = 10%)	20% (SD = 7%)	<0.05

Table 3: Sensitivity and Specificity of Genetic Markers

Gene Polymorphism	Sensitivity (%)	Specificity (%)
IL-1β	85	78
TNF-α	80	75
MMP-9	75	70

Table 4: Outcome Findings Based on Genetic Polymorphisms

Outcome	Periodontitis Patients (%)	Healthy Controls (%)
Increased Risk of Periodontitis	65	20
No Increased Risk	35	80

Discussion

The critical association between some genetic polymorphisms and the development of periodontitis, correlates and supplements the previous data of researchers in this field. The role of genetics has emerged to be an important one in periodontitis, where particular gene polymorphisms of the inflammatory cytokines and MMPs have come to be considered as key in defining an individual's susceptibility of severe gum disease. Another important conclusion of our Study is the presence of the correlation between the polymorphic loci of the IL-1β gene and the development of periodontitis. This finding accords with an earlier study by Kornman et al (1997) who described the IL-1 genotype for the first time as being a potent risk factor in adult periodontitis. Aubin et al. demonstrated that those having certain variants of the IL 1 β gene appeared to have a more severe form of periodontal tissue breakdown than those devoid of those variants [11]. These results corroborate our study, in which of 70 patients with diagnosed periodontitis, 42 (60%) had genotype PL for IL-1β polymorphism, while in the control group with 30 healthy individuals this value was only 9 (30%) with $p < 0.01$ Thus, our results confirm the contribution of the inflammatory cytokine IL-1β to the development of periodontitis [12]. Likewise, the TNF-α polymorphism has been useful in understanding the possible role in the development of periodontitis attributable to the regulation of inflammation. Other Studys including that of Shapira et al (2005) have explained how TNF α affects the periodontal disease especially in genetically prone people. These findings are supported by our study which shows that of the periodontitis patients 58% had the TNF-α polymorphism while only 25% of the healthy control had the same polymorphism with $p<0.01$ [13]. The above findings confirm this polymorphism to be that of a higher frequency among periodontitis patients, thus making it a 'Genetic Biomarker' of heightened disease susceptibility. The involvement of MMP-9 in the degradation of ECM and its

involvement in periodontal tissue pathology has been described earlier relatively in detail. For example, Offenbacher et al. , (2008) established that MMP -9 subtypes were highly active in gingival crevicular fluid of periodontitis patients and this increased with increased tissue damage [14]. This study extends our existing knowledge in the following ways: In our study, MMP-9 polymorphism was higher in periodontitis patients: 55% (n = 88) than in the healthy control group: 20% (n = 30), for which the p value < 0. 05, thus augmenting the hypothesis that polymorphism of MMP -9 increases susceptibility of periodontitis [15]. However, these findings cannot be ignored and some of the limitations of genetic study for periodontitis are discussed below. A number of limitations could be identified; the foremost of which is the fact that the disease is highly heterogeneous in nature, being produced by the interaction of various genetic and environmental factors and microbial pathogens. Yet, more extensive Study of present research was confined to several gene polymorphisms; it appears that other genetic risks, such as epigenetic changes, genes×³environ interaction, possibly contribute to disease development [16]. Furthermore, the sample population in our Study is comparatively small, so its findings cannot be applied to a broader population; larger, more diverse groups should be included in future studies. the present study supports the hypothesis that genetic components, specially genetic polymorphism in IL-1ß, TNF-α, and MMP-9 gene, are significant in contributing to periodontal susceptibility. These were in line with previous studies and laid further empirical support for the notion that genetic screening could perhaps help identify people with potential for severe gum disease. Thus, future studies should focus on the multiplicative effects of multiple markers and their interactions with other factors that would help in explaining the development of periodontitis [18; 19; 20; 21].

Conclusion:

The present Study underscores the impact of genetic polymorphisms involving IL-1β, TNF-α and MMP-9 on the probability to develop periodontitis. These results may indicate that genetic screening could be a useful approach in the prevention and earliest detection of those persons more prone to the serious form of gum disease.

Limitations:

Despite these findings, some limitations of the present study should also be noted, the key of them being a relatively small number of participants studied and the fact that analysis of only some well-studied gene polymorphisms can give a rather limited picture of the overall genetic predisposition to periodontitis. Also, there are gaps in the Study as far as environmental interactions with genes, which are instrumental in development of diseases, are concerned.

Future Directions:

Prospective studies should replicate these findings in an even larger pool of participants and with a diverse sample to establish the ontogeny of risk indicators as well as to determine the interactive influence of multiple genetic polymorphisms. Further, research focusing on epistasis effects would also give a further insight into the causative profile of periodontitis and contribute towards developing more efficient preventive and control measures.

Acknowledgement: We would like to thank the hospitals administration and everyone who helped us complete this study.

Disclaimer: Nil

Conflict of Interest: There is no conflict of interest.

Funding Disclosure: Nil

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