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Genetic Factors for Periodontal Diseases and Twin Model

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ABSTRACT
It appears that periodontal disease is a collection of illnesses with overlapping symptomatology rather than a single illness with varying clinical signs. Periodontal diseases may have a complex character. Given that many risk factors for periodontal disease tend to cluster in families for genetic or cultural reasons, it will be crucial to take these factors into account when researching familial clustering or potential genetic causes. Finding potential genes that could be the cause of a person's genetic vulnerability to periodontal disease will be crucial. The most obvious candidate genes are those that may influence how the immune system reacts to oral bacteria, but further study of disease-predisposing features, such as those related to tissue response, may reveal new hints regarding potential candidate genes. Clinical professionals may be better equipped to identify high-risk individuals for specialized prevention and treatment if these genes are discovered. The majority of the time, the existence of a number of environmental risk factors combined with a number of susceptibility variables during a specific stage of life is what most often leads to periodontitis developing in a person. The stronger the genetic predisposition and the greater the risk for early periodontitis development, the more susceptibility factors a person has inherited. As our understanding of the genes responsible for both major and modifiable diseases grows, numerous genetic tests may be developed. Medline, the Cochrane Database of Systematic Reviews, and DARE were used to compile the database. The database was compiled over the last 25 years, taking into account all developments and new evidence that occurred during that time. Running a preliminary search and noting the terms used in the titles and abstracts as well as the subject headers helped make the search more sensitive. The key concept was kept in mind, and synonym terms were searched using MeSH headings. By adhering to the inclusion and exclusion criteria for selecting articles, search results were narrowed down to those that supplied information and support for both periodontitis and genetics. The only articles left out were those that covered genetics in general.

Keywords: genetic factor, illness, periodontal, diseases, heritability

I. INTRODUCTION

Due to the complex nature of periodontal diseases, it is typically impossible to identify a single etiologic agent that fully explains the pathologic changes. Risk factors include local and systemic circumstances that alter the beginning and development of periodontal infections. In recent large epidemiologic studies, multivariable statistical methods were used to find systemic components and control for risk factors that might be confusing or related.

Additionally, recent research has identified a number of potentially significant periodontal risk markers. These include osteopenia linked to an estrogen shortage as well as stress and coping mechanisms. Additionally, background variables including gender, age, and hereditary factors are linked to periodontal disease. Family members' shared exposures or experiences with these periodontal disease risk factors have an impact as well.

When thinking about genetic influences on periodontal disease or periodontal measurements, it's vital to think about genetic factors broadly; this allows us to evaluate risk factors accurately and account for those that might have a genetic component or cluster in families for non-genetic reasons.

Johnson et al. [1] acknowledged that poor dental hygiene alone cannot explain severe, destructive periodontal disease and that some people are at relatively high risk of developing the illness, with some of that risk being influenced by genetics. Most research on genetic risk factors for periodontal disease has been done on the early-onset forms of the disease, such as prepubertal, juvenile (localized and generalized), and rapidly developing periodontitis.

After reviewing the periodontal health of various families, Klein [2] came to the conclusion that both vulnerability and immunity to caries and periodontal disease are likely inherited traits. In their study, Gorlin et al. [3] came to the conclusion that the genetic factors involved in periodontal disease are very complicated and hard to separate.

Studying the links between certain medical diseases or syndromes and periodontal disease, as well as the reasons why these links exist, can be helpful.

Find out what traits—possibly genetic ones—affect periodontal risk or severity. There is only weak evidence to establish a genetic component to disease susceptibility from studies evaluating the connection between periodontal disease and known genetic markers.

Periodontal pathology was found in a variety of hereditary diseases. The temporal sequence supports the existence of environmental, behavioral, or biologic risk factors for periodontitis.

The recent release of the architecture of the human genome and what it means for understanding both human biology and disease susceptibility [4] has brought up the question of how this knowledge affects and will eventually change how we treat disease.

Methods for managing periodontal diseases that take advantage of knowledge of relationships between genetic variations and clinical severity were put out even before the publication of the human genome sequence. It is important to look at the current state of the field and try to predict how future knowledge will be used, since clinicians are already being told to use new information about how genetic susceptibility factors affect periodontitis.

According to Delgado and Calderon [5], periodontal damage is linked to actalasia, an enzyme deficiency. while Eastman, Bixler, and Fung [6, 7] came to the conclusion that hypophosphatasia may have essentially no cementum and usually attached periodontal fibers, which would result in poor support and early tooth loss. According to Peterson and Marsh [8], persistent periodontitis has been linked to alpha-1 antitrypsin deficiency and periodontal disease. One's susceptibility to periodontal disease appears to be confirmed by certain leukocyte abnormalities. The genetic risk factors for periodontal disease are analyzed using genetic research such as segregation analysis, linkage studies, genetic heterogeneity, twin studies, and association studies.

In periodontology, research on genetic risk factors is still in its early stages. Finding the genes that cause a specific disease is one of genetic research's ultimate goals. It is necessary to define disease phenotypes more precisely using clinical, immunologic, and bacteriologic standards. Once specific host genetic risk factors have been identified, doctors may then be able to implement more intensive preventative treatments aimed at changing the surroundings of those who are most at risk for developing periodontitis.

II. REVIEW OF THE WORK

2.1 Periodontal Disease's Complex Etiology

Few doctors or researchers would disagree that bacteria are the primary etiological agents of these disorders, not just the different types of periodontitis. Underlying this fundamental etiological concept are additional, poorly known etiological modifiers of disease risk that interact with bacterial infections. For instance, smoking cigarettes is now recognized as a significant moderator of periodontitis risk. It is also believed that other risk factors for periodontitis, such as diabetes and stress, work along with the microbial agents to worsen the condition.

Each of the environmental periodontitis etiological agents defines very intricate pathways by which they can start, spread, or alter the disease. For instance, current dogma states that bacteria can cause host immune responses, gingival inflammation, and periodontitis by generating toxins. In fact, there is enough evidence to think that nonbacterial factors, which may not be etiological agents on their own, can make a big difference in how bad a disease is [4].

2.2 Susceptibility to Periodontitis

The fact remains that not everyone appears to be equally susceptible to periodontal disease, even though environmental circumstances appear to supply sufficient disease-provoking elements. For instance, one may predict that people who were raised in the same home, who shared comparable smoking and dental hygiene practices, and who had similar bacterial loads and compositions would also exhibit the same phenotype for periodontal disease. This is untrue, as we are aware. Even when these well-known etiological factors are taken into consideration, there is still an individual predisposition to periodontitis.

By comparing the symptoms of illness in monozygous (identical, MZ) and dizygous (fraternal, DZ) twins, scientists have systematically looked into the idea that genetic factors are to blame.

According to calculations based on measurements of numerous adult twins, heredity accounts for around 50% of the diversity in attachment loss. The fact that genes play a big role in how periodontal disease symptoms show up adds another layer of complexity to the question of what causes it.

2.2.1 Periodontal Disorders Studied using Genetic Methods

The following methods are employed in the investigation of periodontal diseases:

- Family and population studies: analysis of segregation
- Genetic epidemiology.

- Twin research.
- Linkage Research.
- Periodontitis susceptibility is linked to an inherited disease.
- Association research. Affiliation with well-known genetic markersGene modification: serum IgG
- Using recombinant DNA

2.2.2 Recent Research

A genome-wide association study (GWAS), also known as a whole genome association study (WGA study, or WGAS), or a common-variant association study (CVAS), is a method used in genetic epidemiology to examine a large number of common genetic variants in various individuals to determine whether any variant is linked to a trait. Single nucleotide polymorphisms (SNPs) and features like serious diseases are the main focus of GWASs. These studies often compare the DNA of two participant groups: those who have the disease (cases) and comparable individuals without it (controls). With this method, called "phenotype-first," the participants are first put into groups based on their clinical symptoms.

2.3 Evidence of the Genetic Contribution to Periodontitis

2.3.1 Early-onset Periodontitis, or Aggressive Periodontitis, Heritable

Given that the prevalence of juvenile periodontitis ranges between 0.16 and 2.49% in the United States (Loe & Brown 1991), the high prevalence of JP in these families raises the possibility that the condition has a hereditary basis. The largest JP family study included 227 patients with severe periodontitis [9].

2.3.2 Chronic Periodontitis (Adult Periodontitis) Heritability

In a group of young Indonesians who were denied access to regular dental treatment, Vander Velden et al. (1993) investigated the impact of sibling relationships on periodontal health. There were 23 family units with three or more siblings in the research group. There were 78 individuals in all, all between the ages of 15 and 25. In this population, the mean interproximal loss of attachment was 0.29 mm. The range of the individual mean was 0 to 1.27 mm. A site with a probing depth of 5 mm or greater and an attachment loss of 2 mm was present in 33% of the individuals. Plaque, calculus, loss of attachment, spirochetes on the tongue and in the pocket, P. gingivalis on the gingiva and in the saliva, and P. intermedia in the saliva all had a substantial siblingship effect, according to the analysis's findings. However, there was no significant correlation between attachment loss and the microbiological measures that demonstrated a substantial sibling effect. These results imply that there may be a hereditary component to periodontitis, even in less severe cases [10].

2.4 Twin Model

The largest twin study comprised 4908 twin pairs, of whom 349 (116 MZ and 233 DZ) pairs reported a history of periodontal disease in one or both pair members based on questionnaire data [11]. Michalowicz et al. [12] and colleagues assessed the periodontal health of 110 adult twins with ages ranging from 16 to 70 years old. They looked at factors such as attachment loss, pocket depth, gingival index, and plaque index. Therefore, it can be inferred that genetics appear to be the root cause of the familial aggregation of periodontitis rather than bacterial, environmental, or behavioral factors.

III. PERIODONTITIS AND MAJOR GENETIC DISEASE

So far, genetic research on periodontitis has only found one important disease gene that works according to Mendel's rules. Hart et al. (2000) and colleagues have located a gene on chromosome 11 that is responsible for a severe form of prepubertal periodontitis through an internal marriage event in a family of Jordanian heritage. The R-allele of the cathepsin C (CTS C) gene was first found in four sick children from the fourth generation of two families.

Table 1: Periodontal health-related genes

Polymorphism	Gene
HLA-A28 and HLA-B5	HLA haplotype
FcγRIIIb-NA1	Fc receptor polymorphism

IV. GENE MODIFICATION IN PERIODONTITIS-RELATED DISEASES

Additionally, altering disease genes affects periodontitis susceptibility and severity.

Table 2: Genes linked to an increased incidence of chronic (adult) periodontitis

Polymorphism	Gene
IL-1A (+4845) and IL-1B (+3954)	IL-1 gene
TNF-α-308 allele 1	TNF-α gene
TNF-β NcoI, ET-1 gene, and ACE gene	Lymphotoxin alpha (TNF-β), ET-1 and
insertion/deletion polymorphism FcγRIIIb-NA2 allotype NAT2	ACE genes Fc receptor polymorphism N-acetyltransferase polymorphism

Table 3: Genes that increase the likelihood of developing aggressive (early-onset) periodontitis

Polymorphism	Gene	Disease association
IL-1A (=4845) and IL-1B (-3954)	IL-1 gene	Early onset periodontitis
IL-4 promoter and intron polymorphisms	IL-4 gene	Early onset periodontitis
FcγRIIIb-NA2 allele (and possibly FcγRIIIa-158F)	Fc receptor gene polymorphisms	Early onset periodontitis or generalized early onset periodontitis
Gc locus chrom 4q	Unknown	Early onset periodontitis or localized juvenile periodontitis
fMLP receptor	N-formyl peptide receptor polymorphisms	Early onset periodontitis or localized juvenile periodontitis
VDR gene	Vitamin D receptor polymorphism	Early onset periodontitis or localized juvenile periodontitis

Table 4: Genes linked to systemic diseases

Genetic defect	Disease	Phenotype
Collagen folding defect	Ehlers-Danlos syndrome type 8	Early onset periodontitis or localized juvenile periodontitis
CTSC gene on chromosome 11q14-q21	Papillon-Lefevre syndrome, Haim-monk syndrome	Prepubertal periodontitis
Multiple possible mutations in alkaline phosphatase gene	Hypophosphatasia, alkaline phosphatase deficiency	Prepubertal periodontitis
LAD1 (integrin), LAD2 (selectin) gene defect	Leukocyte adhesion deficiency	Prepubertal periodontitis
OCRL1 gene, x-chromosome	Lowe syndrome	Prepubertal periodontitis (atypical finding)

4.1 Cytokine Gene Variations

The interleukin-1 (IL-1) and tumor necrosis factor-a (TNF-a) genes look like good candidates for genetic research on periodontitis [13] for a number of reasons.

1. There is evidence that IL-1 and TNF-a are key players in the development of periodontitis. IL-1 and TNF-a are powerful immunologic mediators with pro-inflammatory properties. Furthermore, IL-1 and TNF- can stimulate bone resorption and regulate gingival and periodontal ligament fibroblast cell proliferation.

2. When oral leukocytes or peripheral blood mononuclear cells from people with and without periodontitis were compared, it was found that their production of IL-1 and TNF was different based on their genes.These differences in how much IL-1 and TNF are made and released could be risk or severity factors.
3. IL-1 and TNF-allegations have been proposed as disease-related genetic markers. For instance, IL-1 polymorphisms have been linked to psoriasis, Sjogren syndrome, and inflammatory bowel illness. Leishmaniasis, alopecia areata, meningococcal illness, leprosy, and cerebral malaria are only a few of the infectious and inflammatory disease processes that have been linked to TNF-gene polymorphisms.

4.2 1L-1 Gene Polymorphisms

In the IL-1 gene cluster on chromosome 2, the genes that encode IL-1 and IL1 are close together. In Caucasian patients who didn't smoke, the severity of periodontitis was linked to having both the R-allele of the IL-1 gene at nucleotide position +3953 (IL-1 +3953'I) and the R-allele of the IL-1 gene at nucleotide position -889 (IL-1a-889T).

A summary of studies that looked at the link between gum disease and the IL-1 compound genotype It's vital to remember that Caucasians were the subjects of the investigations mentioned above. As a result, the hypothesized severity factor for periodontitis in Caucasians can be the IL-1 composite genotype.

4.3 Polymorphisms in the TNF-A Gene

On chromosome 6, the major histocompatibility complex (MHC) gene cluster contains the TNF-a gene. Numerous studies have looked into potential susceptibility and severity factors for periodontitis related to genetic variants in the TNF-a gene. The majority of the genetic polymorphisms are G-to-A transitions. The TNF-a-308 R-allele was not shown to be connected with aggressive periodontitis, despite research linking TNF-a gene polymorphisms with this condition. Based on the research on TNF-genetics in periodontitis to date, there is no evidence that any of the described gene variants are associated with the susceptibility or severity of periodontitis.

Table 5: Longitudinal research

Study	Patients (n)	Controls (n)	Putative susceptibility	Putative severity
Kornman et al. 1997	99		Not tested	+
Gore et al. 1998	32	32	-	Not tested
Walker et al. 2000	37	37	-	Not tested
Armitage et al. 2000	300		-	-
Mc Devitt et al. 2000	90		Not tested	+
Hodge et al. 2001	56	56	-	Not tested
Papanano et al. 2001	132	73	-	+
Laine et al. 2001	105	53		Not tested

Table 6: Long-term research

Study	Patients (n)	Susceptibility	Severity
McGuire and Nunn 1999	42	Not tested	+
Ehmke et al. 1999	33	Not tested	-
De Santisand Zucchelli 2000	40	Not tested	+
Cattabriga et al. 2001	60	Not tested	-
Cullinan et al. 2001	295	Trend	+

4.4 Gene polymorphisms for IL-1O

IL-lO is found on chromosome 1 in a group of interleukin genes that also includes the genes for IL-19, IL-20, and IL-24. Pro-inflammatory cytokines like IL-1 and TNF-a are controlled in part by IL-lO. Genetic polymorphisms may cause functional changes in IL-IO that are harmful to host tissues and may increase a person's risk of developing periodontal disease. In order to further understand the relationship between IL-lO gene polymorphisms and aggressive periodontitis, 79 Caucasian patients from West Scotland with GJP were recruited and matched with a control sample [14].

V. DISCUSSION

Although aggressive periodontitis and genes may be the nature of periodontal diseases, there has been no conclusive evidence linking multifactorial causes to these conditions. Currently, based on a simulation of them [17]. increased platelet susceptibility to periodontitis, a condition in which the genotype of the patient is paralleled by the reaction to mouth bacteria. Though it also depends on complexes with greater capacity for bacterial presence, lifestyle clearance, and the disease-related increase in platelet-leukocyte (phenotype) formation. Studies have demonstrated that some variables and their interactions may have activated leukocytes and platelets as well as genes. Increased atherothrombotic activity is attributed to a large number of candidates. Most frequently, genes have been investigated [18, 19]. There is mounting evidence that indicates parodontitis. The examined candidate genes' polymorphisms in the innate receptor-related proteins' IL1, IL6, IL10, vitamin D, and CD14 genes may be connected to the system. However, it appears that some members of particular communities have CP. [20] The IL1 and -gencluster contain some candidate gene variants in polymorphisms and bacteria on chronic FcR genes associated with periodontal periodontitis. Thus, sickness is a problem for modern bioinformatics tools [15]. Identification of potential genes that may underlie the complicated character of periodontitis and are useful in modeling the disease is crucial [21]. Periodontal disease vulnerability is due to genetics.

As our understanding of the genes responsible for both major and modifiable diseases grows, numerous genetic tests may be developed. When periodontitis has not yet manifested, such as in children of periodontitis patients, these tests may be performed to determine the degree of a hereditary risk. The results of recent studies, including a genome-wide association study of cerebral palsy (CP) conducted in a cohort of 4504 European Americans (EA) taking part in the Atherosclerosis Risk in Communities (ARIC) Study, showed no significant association signals for CP across the entire genome. However, suggestive evidence of association (P <5 3 1026) was found for six loci, including NIN, NPY, and WNT5A for severe CP and NCR2, EMR1, Analysis revealed a considerable enrichment of cytokine, immunological response, and neurological system signaling pathways. Health ABC did not find evidence of a significant interaction between smoking and NUAK1 (rs11112872, interaction P 5 2.9 3 1029) in ARIC, but estimates of the heritable variance in severe CP explained by all single nucleotide polymorphisms increased from 18 to 52% with the inclusion of a genome-wide interaction term with smoking. These genome-wide association findings offer details on numerous potential areas and pathways that might be investigated in the next genetic investigations of CP [16].

VI. CONCLUSION

The challenge of defining precise disease categories makes genetic investigations in period ontology more challenging. Nevertheless, molecular genetics has advanced. The discovery of highly polymeric markers and polymerases chain reaction technologies has improved the ability to conduct more thorough linkage analyses. Lastly, it's likely that there isn't a unique periodontal disease vulnerability that comes from the genes that control one or more parts of the host's response, at least until more new information comes out.

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