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Genetic aspects of dental caries

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Dental caries is a common chronic disease affecting humans in all age groups. Various factors can affect the formation of caries including demineralization and remineralization processes with oral flora; dietary and oral hygiene habits; salivary composition, flow rate, pH and buffering capacity; morphological features of the teeth; fluoride exposure; and environmental and socioeconomic factors. One of the most important factors causing inter-individual variations in caries susceptibility is the host genetics. Several genes affect individual caries susceptibility. Genes play a role in immune response, development of saliva and tooth enamel. The present review aims to overview the literature focusing on the genetic features of dental caries.

KEYWORDS

dental caries, genetic, saliva, gene, pediatric dentistry

Introduction

Dental caries is a common, multifactorial and chronic global health problem that affects all age groups (1–4). Caries formation depends on various factors such as fermentable sugar, cariogenic microbial flora, host factors, time, diet, and other associated environmental factors (5–10).

Environmental factors such as low socioeconomic status, education level, medical health, lifestyle, diet, and access to dental care can also affect the progression of dental caries. In addition, family size may be considered as an influencing factor for dental caries, as individuals having a big family are more likely to present high DMFT values (11, 12).

Dental caries occurs as a result of the association of environmental and genetic factors, including biological, social, behavioral, and psychological components (6, 13). A cariogenic diet, oral hygiene habits, fluoride exposures, and the level of cariogenic bacteria can affect an individual's environmental risk factors. Components such as salivary flow rate, buffering capacity, localization of the tooth in the oral cavity, and surface properties of the teeth are also host factors that can affect caries formation (14). The most associated microorganism with the dental caries process is mutans streptococci (MS). MS adheres to tooth surfaces and can produce acid. MS can also maintain metabolism in low pH conditions. Because of these properties, they contribute to the formation of caries (15). In the process of dental caries, acids from bacterial metabolism diffuse into the enamel, and dentin dissolves the mineral. Thus, the formation of caries begins (16, 17).

Heredity from past to present is associated with dental caries in the literature (8). It has been determined that the caries risk may differ in people exposed to the same environmental factors. Thus, it was thought that genetic factors might also have an effect on the etiology of the caries (5, 6).

The role of genetic factors on caries risk was evaluated by examining the relationship between genetic studies and bacteria, studies in twins, gene polymorphisms related to salivary proteins, taste genes and nutritional preferences, and caries that have a huge effect in the etiology of dental caries (3, 5, 18, 19).

Genetic studies

Genetic studies are carried out by scientists worldwide to search for different kinds of diseases and dental caries (20, 21). It has been shown that there is a genetic effect on caries results with susceptible and resistant strains in experimental studies (22). Research shows that several genes can affect enamel resistance and a different group can affect salivary content and host response to infection. In addition, many linkages and association studies are identified related to the dental caries genomic regions and polymorphisms (5, 6, 8).

The results of a study on children with/without dental caries and mannose-binding lectin (MBL) gene showed an important effect on the immune response in early childhood (23). A significant association was also reported between HladrB1*04 (human leukocyte antigen allele) and early childhood caries (24).

A study on a gene related to specific proline-rich proteins (PRPs), a component of saliva that affects the binding of bacteria, showed a connection between dental caries and the Db allele, and demonstrated the importance of the ethnicity associated with genetic information (25).

Vieira et al. reported positive correlations with 5q13.3, 14q11.2, and Xq27.1, regions and low caries susceptibility, and 13q31.1 and 14q24.3, regions with high caries susceptibility (2). The 5q13.3 gene plays a role in reward, nutrition, and stress. This gene contains the functional properties of an endogenous psychostimulant. A diet that includes less sweet food and fermentable sugar consumption will contribute to a lower incidence of caries. 14q11.2 gene is associated with OR4E2 (olfactory receptor, family 4, subfamily E, member 2). OR4E2 is involved in initiating a neuronal response that triggers an olfactory perception. Genetic variation in the genes that regulate the senses of smell and taste may lead a person to eat more or less certain foods. Thus, the person may become more or less prone to a cariogenic diet (2, 3). 13q31.1 gene is associated with SPRY2 (Sprouty2FGF signaling is premature in controlling the integrity of the oral mucosa. It has mitogenic effects on the salivary glands. SPRY2 acts as an antagonist of FGF signaling (3, 26). 14q24.3 gene is associated with ESRRB (estrogen-related receptor beta). Research has shown that there are gender differences in caries frequency, which may be the result of an estrogen-related function (3, 27, 28).

Twin studies

The genetic link of the disease is defined by familial cluster studies (6). Studies on the same family members show that the caries index correlation is also observed among parents, siblings, and twin siblings (29–32). Studies on monozygotic twins (MZ) and dizygotic twins (DZ) have been conducted to minimize the epidemiological effects (5, 33, 34). A study examining caries incidence included 224 pairs of like-sex children (96 monozygotic; 128 dizygotic), aged 5 to 17 years. It showed that the incidence of dental caries in monozygotic twins was more similar than in dizygotic twins, and unrelated child couples showed less similarity (35). A study of 30 pairs of twins (9 monozygotic; 21 dizygotic) aged 13 to 24 years evaluated the incidence of periodontal disease and dental caries. The researchers concluded that monozygotic twins had higher rates of dental caries and malocclusion than dizygotic twins (36). A high heritability component effect was observed for lesion severity and sucrose sweetness preference (37).

Bacteria and tooth genetics

The majority of studies investigating the correlation between dental caries and genetics have aimed to examine the gene variants of cariogenic bacteria, decode the genetic structures of cariogenic bacteria, and elucidate the metabolism of bacteria that cause dental caries (5, 6). The effect of *S.mutans* and its genotypes on dental caries was investigated and it was found that *S.mutans* is the primary cariogenic pathogen in the oral cavity and is caused by dental caries (38–40).

The genes of amelogenin (*AMELX*), kallikrein 4 (*KLK4*), ameloblastin (*AMBN*), enamelin (*ENAM*), tuftelin (*TUFT1*) and tuftelin interacting protein (*TFIP11*), which are connected to enamel development and mineralization were reported as caries related genes. Among them, the combined effect of the *TUFT1* gene with a high level of *S. mutans* was observed to increase susceptibility to dental caries (14).

Saliva studies

Factors affecting dental caries include salivary factors, the individual's lifestyle, and microbial load (41, 42). Saliva and salivary protein pellets on teeth allow for the colonization of biofilms of Actinomyces and Streptococcus species (such as S. *mutans*) that play a role in caries formation (42–45).

Proteins involved in enamel formation, HLA (human leukocyte antigen), which play a role in the immunity, salivary acidic and basic proline-rich proteins (PRPs), and

agglutinin/DMBT1 (deleted in malignant brain tumors 1) have been associated with caries susceptibility (42, 46, 47).

There are natural or acquired defense factors in saliva that can inhibit mechanisms such as bacterial growth and streptococcal acid production. Some salivary proteins such as lactotransferrin, lysozyme, lactoperoxidase, and agglutinins have antibacterial effects (48). Lactotransferrin (*LTF*) is found in various fluids of organisms such as saliva and is a multifunctional metalloprotein belonging to the transferrin family. Furthermore, it can modulate dental biofilm aggregation and growth by inhibiting *S.mutans* adhesion (49). The *LTF* gene binds to iron and it is located in humans on chromosome 3, position 3p2112. The region responsible for the displacement from an amino acid lys (Lys) to an arginine (Arg) position is a polymorphism (A/G) (rs 1126478) in the second exon of the LTF gene. This variant, which increased antibacterial activity against S.*mutans*, also contained a Lys residue (50).

Taste genes

Nutrition has a role in the pathogenicity of dental caries. Genetically controlled taste preferences also affect what individuals consume in their diet (6, 37).

The heterodimeric G-protein-coupled receptor complex encoded by the TAS1R2 and TAS1R3 genes mediates the human perception of sweet taste, while the TAS2R38 gene largely mediates the perception of the bitter taste. These genes cause sensitivity or insensitivity to cariogenic foods (51, 52). Genetic studies analysis revealed that human taste sensitivity to sucrose was strongly associated with two single-nucleotide polymorphisms of the TAS1R3 coding sequence, rs307355 and rs35744813. People with T alleles are less susceptible to sucrose than those with C alleles (52). An important correlation was reported between TAS2R38 and TAS1R2 and dental caries risk (19).

A genetic study examining caries risk factors and the history of sucrose sweetness involved 115 pairs of twins aged 4–7 years. The result of the study showed the variation in the characteristic of dental caries and sucrose sweetness preference had a significant genetic contribution (37).

The heterodimeric G protein-coupled receptor encoded by the TAS1R2 and TAS1R3 genes directs human taste perception. A study has been conducted examining the functional results of variation in these genes for sweet perception. The single nucleotide polymorphism (SNP) located at positions 21,572 (rs307355) and 21,266 (rs35744813) of the TAS1R3 coding sequence is significantly associated with sucrose sensitivity of human flavors, and these rs307355 and rs35744813 SNPs affect gene transcription by changing the function of regulatory elements. It was suggested that inherited differences in TAS1R3 transcription account for differences in human perception of sweet taste (52).

Conclusion

As with diseases, genetics has an important effect on the etiology of dental caries. This is supported by animal studies, twin studies, and studies on salivary proteins, taste receptors, and bacterial genetics that cause variation in caries susceptibility. Today's caries etiology and treatment process are not designed to take into account the large amount of genetic information that affects oral health. Knowledge of genetic susceptibility and/or familial connection to the host and cariogenic bacteria associated with dental caries may provide preventive dental treatment options for patients and their families. Future studies with a larger number of subjects are needed to identify the effect of genetics on the etiology and treatment process of the dental caries.

Author contributions

Literature research: DC, CS. Writing: DC, CS. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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