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Influence of genetic on periodontal disease

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Abstract

Periodontitis is inflammatory condition of periodontium, caused by interplay of infectious bacteria and host susceptibility. And modified by environmental, host's risk factors and genetic susceptibility. The role of genetics (host's susceptibility) is evident as many microbial studies suggested that, the presence of microbial factor that is responsible for periodontitis alone doesn't indicate the presence or the severity of the disease. Therefore, in high risk patients host susceptibility might play important role in the etiology and progression of disease.

***Keywords**: Aggressive, chronic, genetic, periodontitis, Heredity disease.*

1. Introduction

Periodontitis is a dental disorder involving inflammation and infection of the ligaments and bones that support the teeth and results from progressive and uncontrolled gingivitis. Classification of periodontitis is based on the rate of disease progression. Periodontitis can be divided into two major types (Aguirre et al, 2014)

1. Aggressive (Localized aggressive and generalized aggressive periodontitis); - It is less common disease affects younger patients, there is rapid bone &attachment loss, Periodontal abscess formation, sensitive root surface and bleeding with or without stimulation.
2. Chronic periodontitis: - chronic inflammation of the periodontal tissue that it is caused by accumulation of profuse amount of dental plaque, redness or bleeding of gums while brushing teeth, using dental floss or biting into hard food, halitosis and gingival recession.

Periodontal disease was thought to be determined by environmental factors like poor oral hygiene, smoking, low socioeconomic condition, bacterial infections of oral cavity. It is a common observation that given the same status of poor oral hygiene and sharing the same environmental factors ,some people show severs periodontal disease while some of the same people suffer from mild or no disease ;this indicates the existence of individual difference in susceptibility to the disease and perhaps towards a genetic basis for the susceptibility. It is well known that the periodontal disease is multifactorial(complex) and its susceptibility is influenced both by genetic and environmental factors. Genes responsible for multifactorial disease are also known as susceptible genes. These gene alone do not produce the disease unless they are exposed to the necessary environmental factors; Periodontitis is also associated with different with many types of syndromes and genetic disorders. Periodontitis present itself as one of the clinical manifestations of the syndrome. This establishes the genetic basis of periodontitis as these syndrome results due to mutation in a single gene, genes (Hart & Kornman, 2010).

Genetic of periodontitis

Many studies have indicated familial aggregation for both aggressive and chronic periodontitis (Marazita et al 2011 ; Hassel and Harries, 2013 and Hart and Korman 2011).

However ,the families aggregation of the disease may also reflect on the common environmental factors prevalent in the family i.e., levels of oral hygiene ,shared of genetics basis but does not prove a definite genetic etiology , they were believed that various forms of aggressive periodontitis are due to single gene defects that are inherited as autosomal-dominant disorder with incomplete penetrance or as an autosomal recessive or as X-linked inheritance , these studies unable to point towards a single type of mode of inheritance, because of the multifactorial or polygenic nature of the disease or probably due to the fact that the origin of periodontitis is heterogeneous in nature (Kinane et al , 2005).

Studies in Genetic of periodontitis

1. Michalowics et al 1991: - investigated alveolar bone height and probing depth in twins from the Minnesota study and showed significant variation in them, according to differences in their genotype. The twin groups had similar smoking histories and oral hygiene practices. It was concluded that the genetics play role in modeling the susceptibility to periodontal disease.
2. Moore et al, (1993): - Is a twin study was also used to know about the effect of host genes on the composition of micro bacteria in the oral cavity may be due to genetic constitution of the host.
3. Hart et al, (1993): study on a different population of USA failed to locate the gene aggressive periodontitis on chromosome number 4. This finding indicated that the aggressive periodontitis was heterogeneous in nature i.e. different gene may be responsible for different forms of aggressive form of periodontitis.
4. Michalowicz et al, (1999): -Study in adult twins indicated that neither the host nor the environment play a significant influence on the presence of bacteria in the sub gingival plaque.
5. Michalowicz et al, (2000): - Study in large human twins indicated that hereditary factors

accounted for approximately 50% of adult periodontitis, and the heritable component for periodontitis was not associated or influenced by behaviors such as smoking, utilization of dental care, and oral hygiene habits. This indicated that the development of periodontitis was influenced by genes that mediated biological mechanism.

6. Li et al. (2004): - Mapped the gene responsible for localized aggressive periodontitis on the long arm of chromosome number 1.

2. Discussion

2.1 Association of HLA (human leukocyte antigens) with periodontitis

The human leukocyte antigens (HLA) complex play important role in immune response. At present time more than 150 HLA are known. The HLA molecules are involved in antigen recognition of periodontal pathogens interaction between T and B –lymphocyte and in production of IgG. Appositive association was reported between aggressive periodontitis and HLA-A9 and B12 antigen. Person having these two genes are at 3.5 times higher risk of developing the disease as compared to those who are negative for these antigens. Thus HLA 9 and B15 seem to represent susceptible factors for aggressive periodontitis (Sofaer, 2010 and Rotter et al ,2013).

2.2 Association between periodontitis and interleukin -1 (IL-10) gene polymorphism

IL-1 gene plays an important role in the initiation and progression of periodontal disease. It is found in two different forms (il-1a and IL-1b0. Genes for IL-1are present on chromosomes number 2, mainly produced by activated monocytes .There is an increased level of IL-1 in periodontal tissue which(stimulate bone Resorption , inhibits collagen synthesis ,up regulates matrix metalloproteinase activity and synthesis of prostaglandin),appositive association between polymorphism in the genes for IL-1a and IL-1b and increased severity of periodontitis . This association in nonsmokers.IL-1 genotype increased the risk of tooth loss by 2.7 times and heavy smoking increased it by 2.9 times, genetic polymorphism of IL-1 and smoking seems to have synergistic risk factors. Nonsmokers are at low risk of tooth loss (Korhman et al 2015: McGuire and Nunn, 1999 and Axelsson,2001).

2.3 Tumor necrosis factor TNF-a and periodontitis

It is the (proinflammatory cytokines) which is involved in pathogenesis of periodontitis. It is located on number 6. Two different polymorphisms have been reported in the gene, this result in increased production of TNF-a. The level of TNF-a is high at the site of active tissue destruction and low at healthy sites. Individuals expressing the TNF-a polymorphism manifest greater susceptibility to certain infections, although till date TNF-a polymorphism has not directly been linked to susceptibly to periodontitis, there is a strong possibility that such link exists (Fassmann et al, 2003 and Craandijk et al, 2004).

2.4 Association between IgG2production and periodontitis

Immunoglobulin G2(IgG2) is produce in response to periodontal infections .The production of IgG2under control of specific genes .Levels of production of it vary from person to person .The reduction in the production of it during course of periodontal infection may lead to an increased susceptiplity to disease .On the other hand an increase in the production of IgG2 provides sufficient protection against the disease. Patients with periodontitis and normal subjects vary greatly in their capacity to produce IgG2. Patients with periodontitis and normal subjects vary greatly in their capacity to produce IgG2. Patient with high titers of IgG2antibodies have significantly less attachment loss than do patients with low titers. It is observed that patient with localized aggressive periodontitis have high titers of IgG2 compared to patients with generalized periodontitis. This indicates that IgG2 provide sufficient protection against spread of disease and tries to limit the same (Kobayashi et al, 2001).

2.5 Heredity disease \ Syndromes associated with periodontitis

There is a clear association between some type of genetically determined syndromes and periodontitis. These syndromes increase the susceptibly of the individual to periodontitis by interfering with structural integrity of periodontal tissue or periodontitis may be a concomitant feature of the syndrome. These syndromes are due to mutation in a single gene of the syndrome. These syndromes are due to mutation in a single gene (monogenic or Mendelian syndromes) (Lowe et al, 2010).

1. Leukocyte Adhesion Deficiency syndromes (LAD Syndromes): - Polymorphonuclear leukocytes play important role in restriction of infection. There are several adhesion

receptors on the surface of Polymorphonuclear leukocytes adhesion receptor are necessary for proper function of leukocytes (phagocytosis and chemotaxis). If the circulating leukocyte have defective or reduced adhesion surface receptor will not adhere to vascular endothelium. A result leukocyte will not accumulate at the site of inflammation where they needed to combat the infection. This will lead to susceptibility to infectious disease. Recurrent bacterial infections impaired pus formation and impaired wound healing. A number of these infections are associated with increased susceptibility to periodontitis. It is occurred due to mutation in the integrin chain gene (ITGB2) which is located at chromosome number 22. This mutation leads to defect in cell adhesion and chemotaxis result in increased susceptiplity to per pubertal aggressive periodontitis (Lowe et al ,2010)

2. Chediak –Higashi Syndrome:- It is characterized by decreased pigmentation of eyes and hairs, photophobia ,nystagmus and susceptible to infection. It is occured due to mutation in lysosome trafficking regulator gene (LYST); which is located on chromosome number 1. This lead to an abnormal transport of vesicle to and from neutrophil lysosomes or to defect in the ability of cells to produce lysosomes. This syndrome associated with sever periodontitis unresponsive to conventional periodontal treatment. Periodontitis is only seen in sever form of the syndrome (Pal and Mahato, 2009).
3. Neutropenias:- It is define as an abnormally low number of circulating neutrophils this condition is associated with increased susceptible to infection such as aggressive periodontitis (Ishikawa et al ,2005).
4. Papillion-Lefever syndrome (PLS): - It is due to mutation in the cathepsin C gene which is located on chromosome 11. Cathepsin C is a cysteine protease that play role in degrading proteins and activation of proenzymes in immune and inflammatory cells. This syndrome is characterized by sever early onset periodontitis, which affect both primary band permanent dentitions and hyper keratosis of palmer and planter surfaces, it was observed in some of the PLS patient's aggressive periodontitis were associated with a kind of virulent microorganism. Elimination of this microorganism prevent the periodontal destruction, this suggest that the periodontitis was not a direct of the gene but the gene mutation increased the susceptibly of person to infection (Jobard et al

,2003)

5. Ehlers-Danlos syndrome (EDS):- It is associated with connective tissue disorders ;it is characterized by defective formation of collagen fibers .The abnormal collagen leads to fragility ,and hyperextensibility of the skin, hypermobility of the joints ,easy bruising and also with early onset of periodontitis .It is due to mutation in type 111collagen gene (COL3AL) which is located on chromosome number 2.(Charette et al ,2007).
6. Hypophosphatasia:- This patient has decreased levels of alkaline phosphates in the serum .It is associated with abnormal bone mineralization ,skeletal abnormalities ,and cementum hypoplasia .These patient present a sever loss of alveolar bone and premature loss of primary teeth ,pulp chamber are also get enlarged .Lack of connective tissue attachment to bone is responsible for early exfoliation of the primary teeth. Hypophosphatemia may be considering as an etiology of aggressive periodontitis. It is due to mutation in (alkaline phosphates, liver, kidney and bone) gene, which is localized on chromosome number 1 (Lowe et al, 2010).

3. Conclusion

Periodontitis is a multifactorial dental disorder involving inflammation and infection of the periodontium, which is composed of the gingiva, alveolar mucosa, cementum, periodontal ligament, and alveolar bone. Each part of periodontium interacts differently with environmental factors which needed to be examined simultaneously with the genetics factors who in turn interact with oral bacteria that contribute to the disease, making this interaction difficult to understand and how it’s alters the disease risk factors.

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