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"Gender Basis of Periodontal Diseases."

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Abstract:

Background: Sexual dimorphisms exist in the prevalence and severity of many human conditions and diseases. Risk assessment is a crucial component of personalized medicine in evidence-based clinical practice. Gender is known to for a modifier of the initiation & outcome of many conditions. Establishing whether sex differences exist in the development and progression of periodontitis is the important for both, understanding pathogenesis and developing models of risk assessment for treatment planning taking in consideration effect of various systemic conditions related to gender which can lead to periodontitis.

This paper discusses some risk factors which are to be considered before coming to the conclusion of bias in gender about the treatment planning which if not done, could lead to further complication and progression of the disease

Results: There is evidence to support the higher prevalence of destructive periodontal disease in men than women.The important factor to be considered is that women still have varied periodontal problems due to hormonal fluctuations in various decades of life. Added to it, no study has been done in developing countries which might have different outcomes as compared to other developed countries.

Conclusion: In conclusion we cannot predict the outcome of treatment plans on the basis of gender predilection for periodontal diseases because the pattern of disease progression is different in males and females.

Keywords: Gender, Periodontitis, Hormones, Genetics

Introduction:

Sexual dimorphisms exist in the prevalence and severity of many human conditions and diseases. Risk assessment is a crucial component of personalized medicine in evidence-based clinical practice. Models of risk assessment for periodontitis, which stated that, all individuals were considered susceptible, gingivitis progressed to periodontitis, susceptibility to periodontitis increased with age[1]. However, the models have been inconsistent with respect to the inclusion of sex as a risk factor. Gender is known to be a modifier of the initiation & outcome of many

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conditions.Establishing whether sex differences exist in the development and progression of periodontitis is important for both, understanding pathogenesis and developing models of risk assessment. This paper discusses some risk factors which are to be considered before coming to the conclusion of bias in gender about the treatment planning which if not done, could lead to further complication and progression of the disease

Gender predisposition can be dependent on :

- Hormones
- Genetics
- Behaviour
- Stress

Hormones : The emergence of sex-specific associations between periodontitis and certain systemic disorders has prompted researchers to investigate the possibility of associations between periodontitis and specific women's health issues. Changes in hormone levels, such as those that occur during puberty, pregnancy, menstruation and menopause, as well as those that occur with the use of hormonal supplements, have long been associated with the development of gingivitis.[2]

Kornman and Loesche found that during pregnancy, the ratio of bacterial anaerobes to aerobes and the proportions of *Bacteroides melaninogenicus, Prevotella intermedia* and *Porphyromonas gingivalis* increased.[3]

Bacterial increases are cyclical in nature, they follow the normal physiological changes & generally are of no consequence.[4]

In periodontitis, the inflammatory response results in ulceration of the gingivae and the subsequent entry of bacterial cells, bacterial products, peptidoglycan fragments and hydrolytic enzymes into the systemic circulation. The result is a systemic response of increased cytokines and biological mediators, as well as increased levels of serum antibodies.[5]

Estrogen, Progesterone & Chorionic Gonadotropin (during pregnancy) all affect the microcirculatory system by producing the following changes.[2]

1. Swelling of endothelial cells and periocytes of the venules,

2.Adherence of granulocytes and platelets to vessel walls,

3.Formation of microthrombi,

4. Disruption of the perivascular mast cells

5.Increased vascular permeability and vascular proliferation

Effects on gender[6] : Shape & height of the residual alveolar ridge is lower in women than in men. *(Hirai et al., 1993)*. Might be associated with the ↓ amount of circulating estrogen found in women during menopause. Since this condition is associated with an ↑ frequency of alveolar bone height loss, as well as ↓ crestal and sub crestal bone density *(Payne et al., 1999.)*

EFFECTS OF VARIOUS HORMONES[6]:

ESTROGEN: Influences:

1. Cytodifferentiation of stratified squamous epithelium
2. Synthesis and maintenance of fibrous collagen *(Amar & Chung, 1994).*
3. Amount of circulating estradiol α 1/ prevalence of periodontal disease *(Plancok et al., 1998)*
4. ↑ Amount of plaque with no increase of gingival Inflammation *(Reinhardt et al., 1999)*
5. Inhibit pro-inflammatory cytokines release by human marrow cells *(Gordon et al., 2001).*
6. ↓ T-cell mediated inflammation *(Josefsson et al., 1992)*
7. Suppressed leukocyte production from the bone marrow *(Cheleuitte et al., 1998)*
8. Inhibit PMN chemotaxis *(Ito et al., 1995)*
9. Stimulate PMN phagocytosis *(Hofmann et al., 1986).*

PROGESTERONE:

It plays a role in bone formation and resorption. Acts on bone either by directly engaging the osteoblasts or indirectly by competing with glucocorticoid receptor.

1. ↑ Production of prostaglandins (self limiting process). (*Smith et al 1986)*
2. ↑ PMN & PGE2 in GCF
3. ↓ Glucocorticoid anti-inflammatory effect. (*Chen et al 1977)*
4. Altered collagen and non collagenous protein synthesis. *(Willershausen et al., 1991)*
5. Alter PDL fibroblast metabolism. *(Soory, 1999)*
6. ↑ Vascular permeability. *(Abraham et al., 1996)*

ANDROGEN: *Kasperk et al,1997* stated that both gonodal androgen dihydrotestosterone (DHT) & adrenal androgen dehydro-epiandrosterone (DHEA) have positive impact on bone metabolism by stimulating bone cell proliferation and differentiation. Testosterone has also been associated with bone metabolism, playing a role in the maintenance of bone mass*(Morley 2000).* An effective way to analyze effect of androgens on bone metabolism is the evaluation of the presence of biochemical markers of bone remodeling. Osteoprotegerin (OPG), which is a secreted decoy receptor that inhibits osteoclast formation (Kong et al. 1999)

Androgens may protect the periodontium by positive anabolic effect on periodontal cells, via negative effect on the production & presence of mediators of inflammation and an inhibitory

effect on osteoclastic function.

- Stimulates Matrix synthesis by osteoblasts & fibroblasts *(Kasperk al sorriyamoorthy & Gower, 1989)*
- Stimulates osteoblast proliferation & differentiation. *(Morley, 2000)*
- Inhibit PG secretion. *(Elattar et al., 1982)*
- Enhance OPG Concentration. *(Szulc et al., 2001)*
- IL-6 production during inflammation. *(Gornstein et al., 1982)*

Genetics: Genetic factor is sufficient by itself to cause the disease called as single gene diseases eg Achondroplasia or produce chromosome abnormalities eg: Downs syndrome. In both single-gene diseases and chromosomal abnormalities the disease may be clinically evident in childhood or produces some pathological manifestations in childhood. On the other hand, in muitifactorial diseases the genetics are not, by themselves, sufficient for the disease, and the clinical signs and symptoms are not usually evident until adulthood.[7]

The original 1997 report, found that a specific genotype of the polymorphic IL-1 gene cluster was associated with more severe periodontitis. Boughman et al. reported genetic linkage for localized juvenile periodontitis, only in non smokers segregating as an autosomal dominant trait in Brandywine population from eastern Maryland. *Kornman et al* demonstrated that alterations in specific genes encoding the IL-1α , IL-1β were associated with severe chronic periodontitis in non-smoking subjects. It is well known that MPO activity is increased in inflammatory gingival tissue. The polymorphism of the MPO gene promoter affects the risk of periodontal diseases. **Shows a male predilection.**[8] HLA have been considered as risk factors for periodontitis.[9]

Smoking: Smoker is defined as those who had smoked 100 or more cigarette over their lifetime & still smoking. Most prevalent in **males** especially Hispanic black men & among low income adults.[10] Variation exists. Smoking prevalence among males was highest in East Asia and the Pacific, at 62%, & lowest in sub-Saharan Africa 28%. Among **females** highest in Latin America, at 22%, and lowest in South Asia, at 4% and in the Middle East and North Africa, at 7%. Globally, males account for 81% of all smokers[11]. Multiple cross-sectional & longitudinal studies demonstrated : pocket depth, attachment loss & alveolar bone loss more prevalent in smokers. The effects of smoking on the host are reversible with smoking cessation. Smoking cessation programs should be an integral component of periodontal education & therapy. However, difference in smoking exposure do not appear to account for this.

Alcohol : *Tezal et al*. reported a significant relationship between the frequency of drinking and CAL[12]. **Men** who drank alcohol had an 18-27% higher risk of disease than did non-drinkers[13]. Types of alcoholic beverages had no effect on periodontitis. According to *Gyongyi Szabo*, alcohol impairs the body's primary immunologic defence mechanisms to fight infection. Consequently, bacterial overgrowth and increased penetration into gingival tissues can occur. Alcohol causes dehydration of the mouth, so bacteria are not washed away by saliva, and plaque formation occurs faster.

Oral contraceptives[2:] Responses similar to those seen in pregnancy. Exaggerated response to local irritants. *Kwalkwarf* reported response may be due to altered microvasculature, increased gingival permeability & increased PGE2. *Jenson et al* showed 16 fold increase in Bacteroides species in the OC users. He stated that increased sex hormone substitution for naphthaquinone req of certain bacteroids species were most likely responsible for this increase.

Effects are :

- OC associated inflammation may become chronic cause of prolonged elevation of estrogen & progesterone.
- Decreased concentration of protein, sialic acid, hexosamine fucose, hydrogen ions & electrolytes in saliva
- 2-3 fold increase in incidence of localized osteitis after extraction of mandibular third molars
- Spotty melanotic pigmentation of skin

Stress : Stress, a term continually being redefined in the scientific study of disease and illness. A confirmed and important factor in the etiology and maintenance of many inflammatory diseases, including periodontal disease.[14] Chronic stress is commonly thought to have a net negative effect on the efficacy of the immune response. Leading to an imbalance between host and parasites, and consequently resulting in periodontal break- down.

Selye[15] defined forces that had the potential to challenge the adaptive capacity of the organism as 'stressors' and stated that stressors could be physical or mental (e.g. emotional). He recognized that stressors acting to produce changes in the body could be positive (e.g. exciting, pleasurable), leading to a response state he defined as 'eustress', or stressors could be negative, threatening homeostasis with pain, discomfort and physical pathology. Butterworths,1976 defined the negative response state as **distress**.

STRESS AND PERIODONTAL DISEASE_[2] : Stress diminishes saliva flow which increases dental plaque formation. Also emotional stress modifies the saliva pH and its chemical composition like the IgA secretion. This in turn leads to **Gingivitis.**

Psychosocial factors are predisposing factors for

the development of **Acute necrotizing periodontitis**. The first reports were written about mouth pain among the soldiers of Alexander the Great. The first scientific observations dated from the late 1940s**.**

Page et al. (1983) describes the established the link existing between **Aggressive periodontitis** and psycho-social factors. **Chronic periodontitis** : *Linden et al.* predicted the future attachment loss depending on following criteria: age, socio-economical level, a less satisfactory professional life and a passive and dependent character. Psychosocial stress associated with financial problems and distress are risk indicators to develop a periodontal disease[16].

Epidemiology of periodontal disease:

GINGIVITIS : data shows gingivitis found in early childhood, is more prevalent & severe in adolescence, & tends to level off in older age. Bleeding sites per person was higher in older than in younger **males**, but this was not seen in females as stated in the National Survey of employed adults 1985-1986.

PERIODONTITIS : CAL of all levels of severity is generally more prevalent in males than in females along with pockets & bleeding.[1] **Males** usually exhibit poorer oral hygiene than females, whether measured as calculus or soft plaque deposits.[17]

Conclusion:

There is evidence to support the higher prevalence of destructive periodontal disease in **men** than women. The reasons for these gender differences have not been explored in detail, but are thought to be related more to poorer oral hygiene, less positive attitudes toward oral health, and dental-visit behaviour among males than to any genetic factor. The important factor to be considered is that **women** still have varied periodontal problems due to hormonal fluctuations in various decades of life. Added to it, no study has been done in developing countries which might have different outcomes as compared to other developed countries. Hence, we cannot predict the outcome of treatment plans on the basis of gender predilection for periodontal diseases because the pattern of disease progression is different in males and females.

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