



ASSOCIATION BETWEEN ORAL HEALTH AND NON-COMMUNICABLE DISEASE (NCD); AN OVERALL REVIEW

Dr Deeba farhat	BDS, Dental section of Dept. Of Community Medicine, Sheri-Kashmir Institute of Medical Sciences, Soura.
Dr. Ashraf Ganai	MD, DM Endocrinology, Professor Dept. Of Endocrinology, SKIMS, Soura.
Dr. Shamila Hamid	MD Community Medicine, Assistant Professor Dept. Of Community Medicine, SKIMS, Soura.
Dr. Tanveer Ahmad Rather*	MD, Nuclear Medicine, Additional Professor Dept. Of Nuclear Medicine, SKIMS, Soura.*Corresponding Author

ABSTRACT Association of oral disease with systemic non-communicable diseases has become a great challenge and global priority over the last few decades. Periodontal disease in its two major forms –gingivitis and periodontitis has been found to be associated with increased mortality and increased risk of various non-communicable diseases. A common risk factors approach with integration of oral health and non-communicable disease prevention and control health strategies are being adapted worldwide, to increase the improvement of overall wellbeing and outcome in these patients. The aim of this paper is to review the relationship of periodontitis with various non-communicable diseases in the community and the effect of early management of diseases.

KEYWORDS : Oral health, Non-communicable diseases, Common risk factor, Global health priority, Integrated approach.

INTRODUCTION

Non-communicable diseases (NCD) have become one of the major challenges to human well being over the last few decades and have been recognized as global health priority. A considerable increase in the burden of non-communicable diseases has been observed in the Asia pacific region with Asia being the severely affected area (1,2). Increase in prevalence in diabetes, hypertension, obesity, cancer and hormone related abnormalities have been noted in Asia as per the data of Global Burden of Disease Study 2016 (1, 2). Besides the common non-communicable diseases, Oral diseases like periodontitis have also assumed a prominent significance in contributing to increased morbidity. Oral diseases associated with non-communicable diseases share modifiable risk factors and therefore it is important to adopt a common risk factor approach and fully incorporate oral health into non-communicable disease prevention and control health strategies. The recognition of non-communicable diseases as a global health priority and oral diseases a major health burden , a turning point was observed in recognizing that oral health and non-communicable diseases coexist and can greatly benefit if an integrated and comprehensive approach is undertaken.

Various mechanisms have been postulated to affect the oral health in systemic diseases including non-communicable diseases, which include direct pathological pathways and indirect disease related changes. Periodontitis a chronic inflammatory oral disease with a high prevalence in the community has been found to have prominent relationship with non-communicable diseases. The severity of periodontitis can range from a local infection to a severe systemic infectious /pathological disease involving various systems of the body like cardiovascular system, cerebro-vascular system, endocrine system, peripheral vascular system etc. Recent studies have shown that periodontitis is associated with increased risk of non-communicable diseases such as diabetes mellitus, cardio vascular system and chronic renal failure [3]. Early intervention to manage periodontitis in the high-risk group of developing NCDs and other systemic diseases is needed to improve the treatment outcome and hence reduce the morbidity and mortality.

METHODS

Literature searches were performed in PubMed and google scholar using the following search terms; oral health; non-communicable disease; oral health and non-communicable disease; oral health epidemiology; oral health incidence rate developed countries; oral health incidence rate low and middle income countries, oral health etiology; oral health etiology and oral health treatment. In order to obtain country specific data the search term oral health and the countries or geographical area name were used. Oral health environmental risk factors search term was used to obtain references for the risk factors for the population of these countries. Information on

the different non-communicable disease factors contributing to oral health was obtained by combining the following search terms; oral health and polycystic ovarian syndrome, oral health and Diabetes, oral health and different malignancies, oral health and mental disorders, oral health and diseases. The ethnicity terms used are taken from the data sources that were searched and referenced.

Oral Health and Cardiovascular diseases (CVD)

31% of all deaths worldwide are due to cardio-vascular disease [4] with contributing risks factors being family history, diabetes, hypertension, dyslipidemia, obesity, physical in activity and tobacco use. Periodontal disease has been identified as a new potential risk factor for CVD with growing evidence [5, 6,7]. Both periodontal disease and cardiovascular disease are chronic inflammatory diseases with recent epidemiological studies establishing the effect of periodontitis on cardio vascular disease progression. The inflamed and ulcerated sub gingival epithelium in periodontitis allows the entry of oral bacteria or bacterial component into the blood stream, which leads to increased risk and progression of cardio vascular disease. The acute and chronic inflammatory process initiated by periodontitis both through direct interaction or through indirect stimulation have been shown to have pro atherogenic effects. Leakage of pro inflammatory cytokines from the ulcerated oral tissue causes the production of acute phase proteins like C-reactive protein (CRP), fibrinogen by liver, which in turn stimulates intimal inflammation [8]. As the chronic bacteremia occurs immune response system gets activated and the antibodies that are produced in response to pathogens associated molecular pattern triggers a cross reaction between endothelial cells and modified LDL to enhance lipid movement into the cells of walls of vessel there by propagating atherogenesis. Besides, the antibodies and the inflammatory cytokines act in synergy to promote macrophage formation within the atheroma [9]. A recent Australian study by Joshy G and his colleague involving 172630 individuals with CVD concluded that tooth loss and gum problems were markers for increased ischemic disease[10]. Current evidence emphasizes the importance of including oral health as a part of cardiovascular care to improve the outcome of these patients both in terms of morbidity and mortality. The diagnosis and severity of periodontal disease can be achieved by using a periodontal probe to measure clinical attachment levels and presence of inflammation besides radiographic assessment .Compressive periodontal therapy and life style modification like diet, exercise, and smoking cessation has been found to be beneficial both orally and systemically as both periodontal disease and CVD share similar risk factors.

Periodontitis and Endocarditis

Gingivitis and periodontitis are caused by specific bacterial species like Streptococcus mitis and Streptococcus mutans that are found commonly or exclusively in oral cavity. The surface of inflamed and ulcerated gingival tissue around the teeth is the portal of entry for

streptococci bacteria and causes majority of cases of infection of valves of heart (endocarditis). In a study conducted by Mansaur [11] 56% of recurrent endocarditis were caused by streptococcus species. Endocarditis has been historically associated with periodontitis. The amount and frequency of bacteremia, a precondition for endocarditis, originating from oral cavity depends on degree of invasiveness and degree of inflammation at the interface between hard and soft tissue. Greater the severity and frequency of bacteremia higher are the chances of endocarditis in higher risk groups. Antibiotic prophylaxis has been the main stay of preventing endocarditis in patients who are at high risk of developing bacteremia before any dental, gastrointestinal, genitourinary and other invasive procedures. However, since 2007 American Heart Association guidelines recommended antibiotic prophylaxis only on dental procedures for patients with cardiac conditions who were defined as higher risk patients experiencing morbidity and mortality resulting from infective endocarditis [12].

Oral health and polycystic ovarian syndrome (PCOS)

Polycystic ovarian syndrome is the most common endocrine non-communicable disorder affecting the women [4 to 18%] of reproductive age group [13] and is closely related with periodontal disease in the form of high incidence of gingivitis and periodontitis. Numbers of studies have shown increased risk of periodontitis in patients with PCOS as compared to normal population. In a study conducted by Mohammed Ehsan Rahimenejad in 2015 [13] prevalence of periodontal disease in patients with polycystic ovarian diseases was found to be higher than controls which was attributed to role of chronic systemic inflammation involving both PCOS and periodontal disease. Periodontal parameters including, bleeding on probing, clinical attachment loss were significantly higher in women with polycystic ovarian syndrome as compared to the general population in a study conducted by Tanguturi SC in 2018 [14].

Various studies have suggested that patients with PCOS have altered levels of markers of inflammation both locally in the oral cavity in gingival cervical fluid, saliva as well as systemically. Besides systemic inflammation being the most common mechanism for initiating periodontitis in patients of PCOS, elevated levels of oral pathogens in saliva and their antibody response in serum in PCOS patients have also been implicated for increases incidence of periodontitis as compared to normal subject [15]. Study conducted by Akcali et al in 2014 [15] suggested that patients with polycystic ovarian syndrome had higher levels of salivary porphyromonas gingivalis, Fusobacterium nucleatum, Streptococcus oralis and Tannerella forsythia than matched systemically healthy women. Elevated levels of salivary pathogens and significantly elevated salivary levels of matrix metalloproteinase-8 (MMP-8) and tissue inhibitors of MMP-1 (TIMP-1) in women with PCOS resulted in increased propensity to develop gingivitis [15]. Ozcaka et al [16] suggested altered IL-17 level in non obese females with PCOS for gingival inflammation and a positive correlation between probing depths, bleeding on probing, plaque index with salivary or serum MMP-8 levels or MMP-8/TIMP-1 ratio in patient of PCOS as compared to healthy women. Studies have implicated other factors like alteration of hormone levels in the body, female sex steroid hormones, obesity, vitamin D deficiency as causes of increased incidence of periodontal disease in patients of polycystic ovarian disease [17,18,19].

Oral Health and Diabetes

Diabetes mellitus a public health problem that affects around 8.5 percent adult population worldwide is a heterogeneous group of clinical and genetic metabolic disorders recognized by hyperglycemia. It is broadly classified into two types; type 1 insulin dependent and type 2, the non insulin dependent being the most common. Increasingly, now younger population is coming under the radar of this chronic disease, due to a variety of reasons like sedentary lifestyles, poor eating habits and increased prevalence of obesity. If the graph illustrating the number of adults affected by Diabetes mellitus and its rate of mortality is studied, a sharp rise from 130 million in 1995 to 300 million in 2025 will be observed especially in developing world [20]. Common systemic complications of DM include retinopathy, neuropathy, nephropathy and cardiovascular. Recently periodontitis leading to tooth loss has been added as a systemic complication of DM [21]. Subtle differences in the microbial composition of the subgingival biofilm between individuals with diabetes and those without may be one of the causes for increased risk of periodontitis in diabetes. However, the clinical relevance cannot be substantiated because the differences may arise from the effect of diabetes in altering the local environment in the periodontal pocket itself by favoring the growth of certain bacterial species [22]. Meta-analysis by Papananou P N in

1996 with 3524 subjects greater than 18 years of age, suggested that there was 2-fold increase in periodontal disease in diabetes as compared to controls [23]. Increased inflammatory response both at micro vascular and macro vascular levels to oral bacterial has been postulated as the major cause of periodontitis in uncontrolled diabetes. This hyper inflammatory response coupled with impaired wound healing enhances the periodontal tissue destruction [24]. The effects of untreated periodontitis in diabetic patients was studied by Santos Ret al in which they found chronic periodontitis to be the contributing factor to insulin resistance [25]. A decrease of 10 % in HbA1c from pretreatment values was observed in patients of DM who received oral prophylaxis treatment with systemic doxycycline therapy for periodontitis in a study conducted by Grossi et al [26] in 1997. In 2000 study conducted by Stratton et al [27] showed that there was mean reduction of 0.4% in the HbA1c after 3 to 4 month of non surgical periodontal therapy with or without antibiotics. Apart from periodontitis other major oral manifestation of DM includes caries which involves the demineralization and decalcification of teeth in presence of bacteria and altered pH value of saliva in the oral cavity. Patients suffering from diabetes are more susceptible, to conditions like xerostomia and periodontal disease which increases their vulnerability to recurrent caries. Factors implicated for dental caries in diabetics include decreased salivary secretion, increase of carbohydrate in parotid gland saliva, growth of oral yeasts, increased number of streptococci and lactobacilli etc [28]

Salivary dysfunction due to decreased secretion of saliva by the salivary glands, oral neuropathy in the form of burning mouth syndrome and oral mucosal disease like fissured tongue, lichen planus, recurrent aphthous ulcers, irritation fibroma and oral candidiasis are other oral health disorders occurring in higher frequency in diabetics in comparison to non diabetics.

Many diabetic patients are unaware of association of diabetes and its oral manifestations and only a small percentage visit dentist for routine checkups. To curb this problem, dental professionals must be included in the multidisciplinary team that helps individuals' with diabetes. Regular dental checkups with emphasis on periodontal assessment, and reinforcement of oral health instructions can effectively prevent oral complications of diabetes mellitus 2.

Oral health and cancers

Among the leading causes of global mortality, cancer is the most common cause with oral and pharyngeal cancers being the most common. Besides many other causes of cancer recently a link both in form of specific types as well as overall cancer rate with periodontal disease has been suggested. A number of hypothesis have been put forward in the etiology of relationship between periodontal disease and cancer, the most common being alteration of oral flora and increased systemic circulatory inflammatory markers in periodontitis. A study conducted by Abnet et al [29] revealed that the mechanism of increased cancer risk for Gastro intestinal organs can be the elevated levels of nitrosamine produced by the oral microbes due to poor oral hygiene. It is an established fact that nitrosamines have a link to stomach and esophageal cancers. A two fold increase in salivary acetaldehyde production a known carcinogen by oral microbes in people with poor dental hygiene was observed in a study by Homann et al [30]. Viruses like cytomegalovirus, Epstein Bar virus 1 known to cause cancers like lymphoma and nasopharyngeal carcinomas have been suggested to be associated with increased periodontal disease. Inflammatory markers and mediators present in high levels in patients with periodontal disease have been implicated in causation of various tumors. Elevated levels of myeloperoxidase and superoxide dismutase in periodontitis along with gene polymorphism have been associated with high pancreatic risk. High expression of pro inflammatory receptors for advanced glycation end product [RAGE] have been linked to increase risk of malignancy in patients of oral infection, periodontal disease and malignancies of esophagus, stomach, colon, pancreas, CBD, and prostate. However further studies are needed to establish a definitive link.

The two most common cancers that have been linked to periodontal disease with high evidence in particular are oral cancers and esophageal cancers. Oral cancers especially the gingival squamous cell carcinoma mimics the periodontal disease by showing similar symptoms like swelling, bleeding, tooth mobility, deep periodontal pockets and bone loss. Studies have evaluated a link to tooth loss or periodontal disease with a significant increase of oral cancers in patients with periodontitis even after adjustment of other risk factors

like tobacco and alcohol use [31- 34]. In a study conducted by TAJEL –et al [32] a 5.23 fold increase of tongue cancer was found with each mm of bone loss in periodontal disease in patients with tongue cancer in Buffalo New York. Several studies [35- 38] have a found a link between esophageal cancer and missing teeth but a direct link to periodontal disease is yet to be established. Abnet et al [39] found a direct relationship of esophageal carcinoma with the number of teeth loss in a study conducted in Iran in which he observed that edentulous subjects had two times the risk than the subjects who lost fewer than 13 teeth. Guhae et al (36) found that risk of esophageal cancer was twice in subjects between 16 to 18 teeth loss as compared to subjects with 5 teeth loss in two studies in Europe and Latin America .The same study established no significant association with other indicators of oral health. Studies have shown mixed results in establishing a direct and indirect link specifically to periodontal diseases in cancers like GI, lung, pancreas prostate, breast, hematological etc. However the strongest positive evidence of association to periodontal disease has been found in pancreatic cancer and overall cancer rates, however further multi institutional studies are needed to explore an established definitive links between periodontal disease and specific cancer. A dental care provider needs to be aware of the fact that the periodontal disease can exist as a risk factor for malignancies in particular the oral malignancy and all those known factors that increase the risk and predispose to periodontitis such as life style modifications need to be altered to decrease the risk of malignancies.

Oral health and mental disorders

Approximately 17.6% of the global population is known to suffer from mental illness [40] and had been predicted to become 2nd most common cause of morbidity in 2002[41]. One in four people suffers an episode of mental disorder during their life time amongst the general population. Depression, anxiety, schizophrenia, bi polar disease and dementia are the most common types of mental illness occurring in varying degrees in the population. Stigmatization and discrimination make the accessibility to the health care very difficult in these patients, thus subjecting them to increased susceptibility to oral and periodontal disease as compared to general population. Effects of medication, lack of self-care, lack of access to health services, lack of co-operation to dental care are the most common risk factors for oral and dental disease in patient suffering from mental illness. The mechanism that has been implicated in increased incidence of periodontal disease has been linked to the impact of stress on the immune system and the resultant influence on the acute and chronic inflammatory response [42-45]. Psychological stress can down regulate the cellular response by at least three mechanisms. Firstly, by promoting the release of corticotrophin releasing hormones from the pituitary gland and glucocorticoid hormones from adrenal cortex through hypothalamus-pituitary-adrenal axis [HPA]. Secondly, exposure to stress agents can stimulate sympathetic nervous system to real ease adrenaline and nor adrenaline from the adrenal medulla there by exerting immunosuppressive effect which indirectly provoke periodontal tissue breakdown. Thirdly, stress can induce the release of neuropeptides from sensory fibers which act as neurogenic inflammatory mediators modulating the activity of immune system and release of cytokines [46 47]. Whatever the mechanism cross-sectional studies [44,45, 48] have revealed a clear cut correlation between the progressive course of periodontal disease and psychosocial stress status in patients with mental health disorders. While gingivitis, xerostomia, oral candidiasis, tempromandibular joint lesion are characteristic finding of patients of depression [47], dental cavities, per apical, gingival, periodontal , pulpal lesions and cellulitis or abscess of oral cavity are the manifestation of anxiety [49]. Patients with schizophrenia, bipolar disorder and dementia suffer from varying degree of dental health disease both due to poor oral hygiene as well as antipsychotic medicines [50,51], especially affecting salivation [52,53]. Thus, oral health plays very important part in well being of patients with different forms of mental illness and a multidisciplinary approach involving, dentists, physcists, general practitioner, psychologist and nutritional professional is needed.

Oral health and other diseases.

Disorder like rheumatoid arthritis, hematological disorders, intestinal disorders, juvenile idiopathic arthritis etc have been associated with oral health but the most common association is with diseases of digestive tract both the upper and lower digestive tract. These include disease like GERD, peptic ulcer, inflammatory bowel disease and various gastrointestinal syndromes. Peptic ulcer diseases that are more common gastrointestinal diseases have been found to have close association with oral health. The presence of H-pylori in the oral cavity serves as an extra gastric reservoir for the pathogen for resistant H-

pylori gastric infection. This is because low concentration of antibiotic reaches to the oral fluid, periodontal pocket and dental plaque not enough to eradicate H-pylori present in oral cavity [54]. As H-Pylori has been implicated in diseases like chronic active gastritis, peptic ulcer disease and gastric carcinoma it becomes important for gastroenterologist to consider presence of resistant H-pylori in the oral cavity as a cause of treatment failures and advice patients infected with H-pylori to visit the dentist at least two times a year [54]. Health status of the oral cavity in patients with gastrointestinal disorder should be the first possible line of diagnostic approach for early detection and subsequent multidisciplinary treatment for the successful outcome of gastrointestinal and oral disease.

CONCLUSION

Adequate attention to the oral health in patients of non-communicable disease will result in improvement of quality of life especially in the adult population who is at a higher risk of developing non-communicable disease. Association of common risk factors between oral health disease and various non-communicable diseases in the form of genetic pre disposition, life style modifications, health awareness and preventive behavior necessitates a close coordination between dental health care workers and the physicians for early detection and improvement , prevention and control of these conditions. Combating oral health disease and non-communicable disease like diabetes, hypertension, polycystic ovarian disease and cardiovascular diseases needs to be taken on the same plane by the health policy makers in order to reduce their burden in the society.

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