

# Prevalence of periodontal disease, its association with systemic diseases and prevention

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## ABSTRACT

Periodontal diseases are prevalent both in developed and developing countries and affect about 20-50% of global population. High prevalence of periodontal disease in adolescents, adults, and older individuals makes it a public health concern. Several risk factors such as smoking, poor oral hygiene, diabetes, medication, age, hereditary, and stress are related to periodontal diseases. Robust evidence shows the association of periodontal diseases with systemic diseases such as cardiovascular disease, diabetes, and adverse pregnancy outcomes. Periodontal disease is likely to cause 19% increase in the risk of cardiovascular disease, and this increase in relative risk reaches to 44% among individuals aged 65 years and over. Type 2 diabetic individuals with severe form of periodontal disease have 3.2 times greater mortality risk compared with individuals with no or mild periodontitis. Periodontal therapy has been shown to improve glycemic control in type 2 diabetic subjects. Periodontitis is related to maternal infection, preterm birth, low birth weight, and preeclampsia. Oral disease prevention strategies should be incorporated in chronic systemic disease preventive initiatives to curtail the burden of disease in populations. The reduction in the incidence and prevalence of periodontal disease can reduce its associated systemic diseases and can also minimize their financial impact on the health-care systems. It is hoped that medical, dental practitioners, and other health-care professionals will get familiar with perio-systemic link and risk factors, and need to refer to the specialized dental or periodontal care.

**Keywords:** Periodontal disease, epidemiology, risk factors, systemic disease, preventive strategy

## Introduction

Periodontal disease is a chronic inflammatory disease of periodontium and its advanced form is characterized by periodontal ligament loss and destruction of surrounding alveolar bone.<sup>1</sup> It is the main cause of tooth loss and is considered one of the two biggest threats to the oral health.<sup>1,2</sup> There are approximately 800 species of bacteria identified in the oral cavity<sup>3</sup> and it is hypothesized that complex interaction of bacterial infection and host response, modified by behavioral factors such as smoking, can result in periodontal disease.<sup>4</sup>

The aim of the review is two-fold: (1) To evaluate the prevalence of periodontal disease in different populations, risk factors, and its association with systemic diseases and (2) to discuss the strategies and measures to prevent and control periodontal disease.

## Prevalence of Periodontal Disease

Periodontal disease is the most common oral condition of human population.<sup>5</sup> The prevalence and incidence

statistics of periodontal diseases vary because of bias, case misclassification, and the number of teeth and the sites examined.<sup>6</sup> According to the Canadian Health Measures Survey 2007-2009, the measurement of loss of periodontal ligament attachment is considered the gold standard in reporting the prevalence of periodontal disease.<sup>7</sup> National Health and Nutrition Examination Survey (NHANES) determined the attachment loss (AL) and probing depth (PD) at six sites of all teeth (excluding third molars) for the estimation of periodontal disease in the U.S.<sup>8</sup>

The world Health Organization (WHO) has maintained global oral health data bank using community periodontal index (CPI).<sup>9</sup> This global oral health data from large epidemiological studies from different countries were gathered to show the distribution of periodontal disease in adolescents, adults and elderly populations (Figures 1-3).<sup>9</sup> CPI index score ranges from 0 to 4 and describes the periodontal condition of individuals at population level. CPI score 0 represents no periodontal disease; score 1 means gingival bleeding on probing; score 2 shows the presence of calculus and bleeding; score 3 indicates shallow periodontal pockets of

4-5 mm; score 4 represents deep periodontal pockets of 6 mm or above.<sup>9</sup>

Compared with developed countries, developing nations have higher prevalence of calculus and bleeding on probing among adolescents (Figure 1). The proportion of adolescents with calculus deposits ranged from 35% to 70% in developing countries while it ranged from 4% to 34% in developed nations (Figure 1).

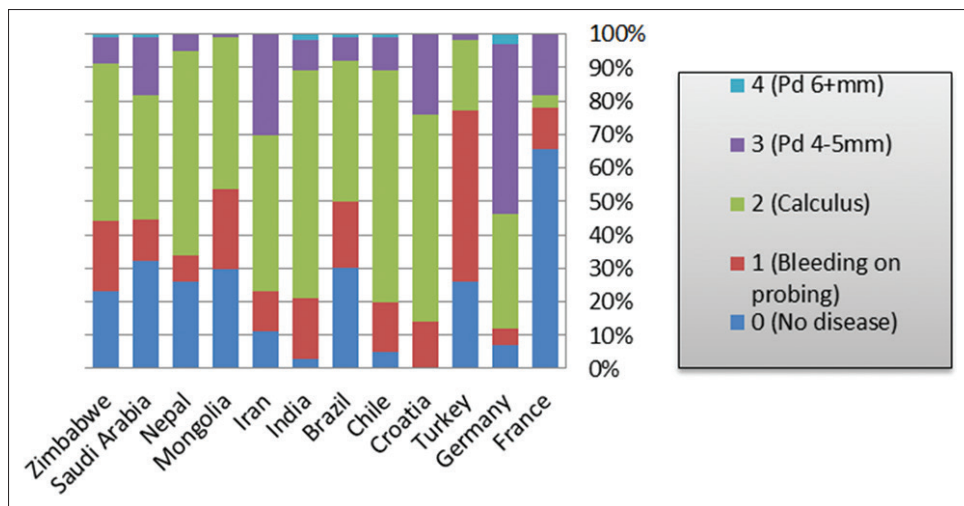
Similarly, 14-47% of adult populations in developed countries had calculus deposits compared with 36-63% of adults in developing nations. However, developed countries have higher percentage of individuals with periodontal pockets of 4-5 mm (Figure 2).

Greater proportions of older individuals (65-74 years) exhibit periodontal pockets of 6 mm or above compared with adult populations in both developed and developing countries (Figures 2 and 3).

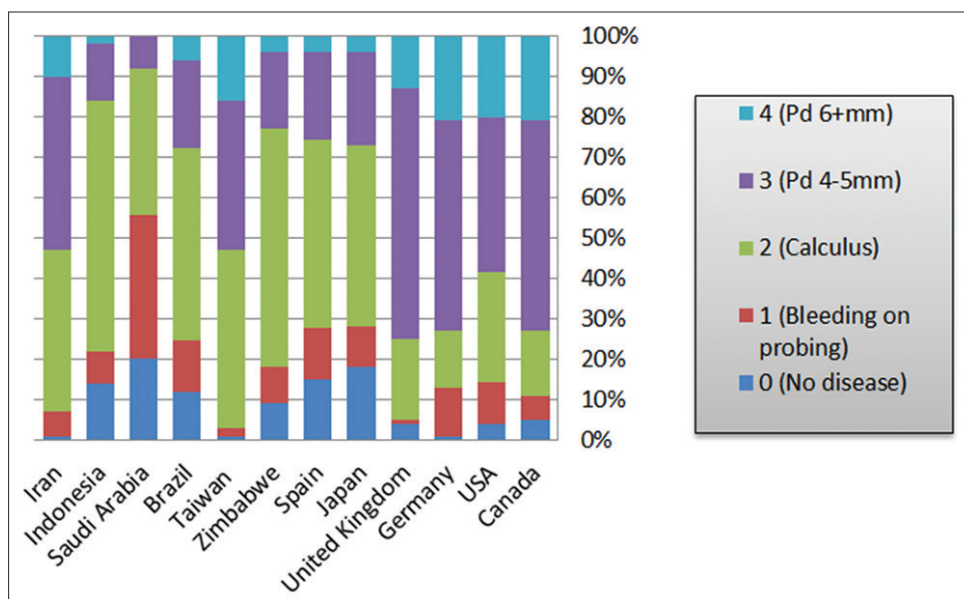
Overall, periodontal disease affects about 20-50% of the population around the globe.<sup>10</sup>

### Risk Factors for Periodontal Disease

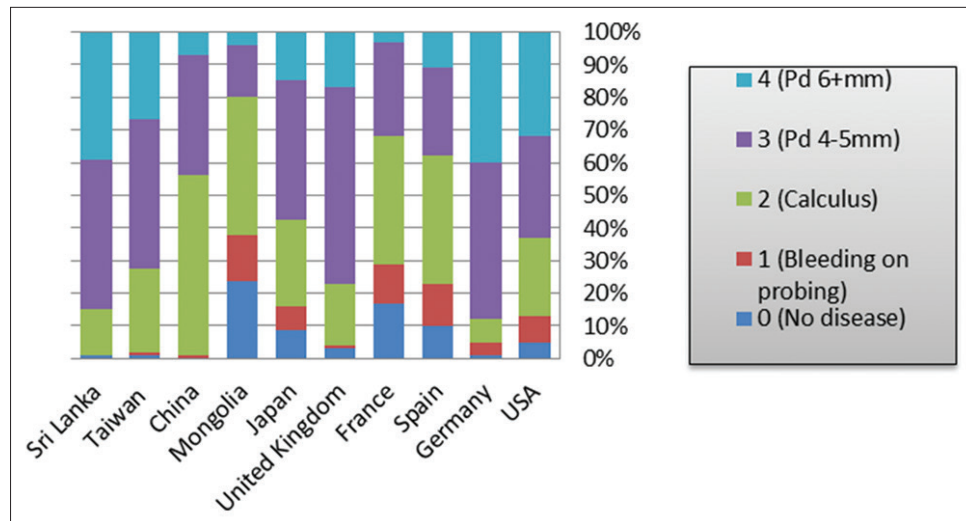
Several factors increase the risk of periodontal diseases. These risk factors, modifiable and non-modifiable, contribute toward the clinical significance of periodontal diseases.



**Figure 1:** Proportions of adolescents (15-19 years) with and without periodontal conditions using community periodontal index in different countries<sup>9</sup> Pd: Pocket depth



**Figure 2:** Proportions of adults (35-44 years) with and without periodontal conditions using community periodontal index in different countries<sup>9</sup> Pd: Pocket depth



**Figure 3:** Proportions of older adults (65-74 years) with and without periodontal conditions using community periodontal index in different countries<sup>9</sup> Pd: Pocket depth

## Modifiable Risk Factors

### Smoking

Smoking is one of the most important risk factors for periodontitis, and the reduction in periodontal disease prevalence is related to the drop in smoking rates.<sup>11</sup> Negative effects of smoking cigarette, cigar, cannabis, and pipe on periodontal tissues are similar.<sup>12</sup> The smokers are 3 times more likely to have a severe form of periodontal disease than non-smokers.<sup>13</sup> The smokers also present significantly increased the loss of alveolar bone and higher prevalence of tooth loss compared with non-smokers, and they have poor outcomes of all forms of periodontal treatments.<sup>10,12,14,15</sup> Evidence suggests that smoking changes oral microbial flora increases the level of certain periodontal microorganisms or affects host response.<sup>11</sup> The nicotine has been shown to cause periodontal tissue breakdown, directly or indirectly through interaction with other factors.<sup>16</sup>

### Poor oral hygiene

Poor oral hygiene is linked with periodontal disease, and lack of proper tooth brushing and other measures of oral hygiene can encourage bacterial deposition and build-up of dental plaque on teeth and gums which can set a stage for inflammatory changes in periodontal tissues.<sup>17</sup> There is pronounced relationship between poor oral hygiene and increased accumulation of dental plaque, high prevalence and increased severity of periodontal disease.<sup>18</sup> Axelsson *et al.* conducted a prospective study of 15 years duration and found no further deterioration of periodontal structure among the subjects who maintained proper oral hygiene and took routine professional dental care.<sup>19</sup>

### Hormonal changes in females

Hormonal changes in women increase the likelihood of periodontal disease.<sup>20</sup> Females may experience gingival

inflammation before menstruation and during ovulation due to a high level of progesterone which blocks the repair of collagen fibers and causes the dilatation of blood vessels.<sup>21</sup> Similarly, pregnant women most frequently exhibit gingival changes, gingivitis, and sometimes localized growth of gingival tissues. Fortunately, these inflammatory changes disappear within few months after delivery without causing persistent damage to periodontal tissues.<sup>22</sup> Estrogen deficiency reduces bone density after menopause which can culminate in alveolar bone loss and eventually falling of teeth. A longitudinal study of 42,171 women at their postmenopausal stages showed that the treatment of osteoporosis with estrogen hormonal therapy resulted in reduced tooth loss.<sup>23</sup>

### Diabetes mellitus

Literature consistently shows that diabetes mellitus is one of the systemic risk factors for periodontal diseases which can play a major role in initiation and progression of the disease.<sup>24-26</sup> Diabetes mellitus is associated with periodontal ligament destruction which subsequently can lead to tooth loss.<sup>27,28</sup> Gingival crevicular fluids and saliva have higher concentrations of inflammatory mediators including different types of cytokines among diabetic patients with periodontitis as compared to non-diabetic individuals with periodontal disease.<sup>29</sup> A report of a joint workshop of European Federation of Periodontology and American Academy of Periodontology identified dose-response relationship between the severity of periodontal disease and adverse consequences of diabetes, and periodontal treatment has been found as beneficial as giving an antidiabetic medication to the diabetic patients.<sup>29</sup>

### Medications

Vulnerability to infections and periodontal diseases intensifies when there is diminished salivary flow due to certain medications.<sup>20</sup> The most common medications which can

minimize the flow of saliva and produce dryness of mouth include tricyclic antidepressants, atropine, antihistamine, and beta blockers.<sup>30</sup> Some drugs (phenytoin, cyclosporine, and nifedipine) can induce the abnormal growth of gingival tissues which frequently complicates the appropriate removal of dental plaque underneath the enlarged gingival mass, and thus, can further aggravate the existing periodontal disease.<sup>20</sup>

## Stress

It is clear from evidence that stress reduces the flow of salivary secretions which in turn can enhance dental plaque formation.<sup>15</sup> Rai *et al.* observed a positive association between stress scores and salivary stress markers (cortisol, salivary CgA, b-endorphin, and a-amylase), tooth loss, clinical AL (5-8 mm), and PD of 5-8 mm.<sup>31</sup> A meta-analysis of about 300 empirical articles has indicated that stress is related to immune system and different immunological changes occur in response to different stressful events.<sup>32</sup> The depressed individuals have been shown to possess a higher concentration of cortisol in gingival crevicular fluid, and they respond poorly to periodontal treatment. Academic stress also results in poor oral hygiene and inflammation of gingiva with increased concentration of interleukin-1 $\beta$ .<sup>15</sup>

## Non-modifiable Risk Factors

### Age

The risk of periodontal disease increases with the advancing age that is why the high prevalence of periodontal disease is seen among elderly population.<sup>23</sup> Research identified that age is associated with periodontal disease, and clinical AL was significantly higher among individuals aged 60-69 years compared with group of adults 40-50 years.<sup>33</sup>

### Hereditary

Hereditary is one of the factors associated with periodontitis which makes some people more susceptible to the disease than the others.<sup>24</sup> The complex interplay of genetic factors with environmental and demographic factors has been hypothesized to demonstrate wide variations among different racial and ethnic populations.<sup>34</sup>

## Association of Periodontal Disease with other Medical Conditions

### Cardiovascular disease

Consistent body of evidence explains the relationship between cardiovascular diseases and periodontal diseases. A systematic review identified that periodontitis is a risk factor for coronary heart disease, and the association is independent of other risk factors such as diabetes, smoking, and socioeconomic status.<sup>35</sup> In a meta-analysis of eight prospective and one retrospective studies, it has been found that periodontal disease is likely to

cause a 19% increase in the risk of cardiovascular disease and this increase in relative risk reaches to 44% among individuals aged 65 years and over.<sup>36</sup> Another systematic review and meta-analysis of 11 studies (five cohort and six cross-sectional studies) found that periodontal disease with increased levels of systemic bacterial markers was associated with coronary heart disease.<sup>37</sup> Similarly, a meta-analysis of 29 studies (22 case-control and cross-sectional studies, and seven cohort studies) reported pooled odds ratio of 2.35 and pooled relative risk of 1.34 which suggest that individuals with periodontal disease had greater risk and higher odds of developing heart disease than those without periodontal disease.<sup>38</sup> Periodontal disease association with stroke and peripheral artery disease is even stronger than coronary heart disease (Figure 4).<sup>10</sup>

### Metabolic disease

There are bi-directional relationship and synergism between diabetes and periodontal disease.<sup>39</sup> A prospective cohort study of 628 subjects (35 years and older) with a follow-up of 11 years identified that type 2 diabetic individuals with severe periodontal disease had 3.2 times the risk of mortality due to ischemic heart disease compared to the individuals with no or mild periodontal disease (Figure 4).<sup>40</sup> Likewise, a meta-analysis concluded that periodontal therapy improves glycemic control for at least 3 months in type 2 diabetic subjects.<sup>41</sup> A systematic review provided the evidence to support the role of periodontal disease in the development of type 2 diabetes and its complications.<sup>42</sup>

Scientific literature consistently supports a relationship between periodontitis and insulin resistance. It has been argued that periodontal disease exacerbates insulin resistance, a chronic condition implicated in the pathogenesis of metabolic disease and type 2 diabetes mellitus.<sup>43</sup> Lim *et al.* evaluated data of 16,720 subjects from a national survey and identified an association between insulin resistance and periodontitis in postmenopausal Korean women.<sup>44</sup> It has also been suggested that periodontal intervention can reduce insulin resistance in diabetic patients.<sup>45</sup>

Several systematic reviews have proposed an association between obesity and periodontal disease and it has been identified as a risk factor for the development of periodontitis.<sup>46-48</sup> Recently, obesity has been shown to increase oxidative stress in periodontal tissues and cause their destruction.<sup>49,50</sup> The prevalence of obesity is increasing dramatically around the globe<sup>51</sup> and its association with periodontitis calls for the attention of health-care providers to prevent these public health issues.

### Adverse pregnancy outcomes

Periodontitis is related to adverse pregnancy outcomes which include maternal infection, preterm birth, low birth weight, preeclampsia, and microbiological and immunological factors are implicated in the underlying mechanisms.<sup>52-55</sup> Low socioeconomic status, smoking, and urinary tract



infection are already known to be associated with premature birth; however, more recently it was found that periodontal disease is also strongly linked with premature birth incidents (Figure 4).<sup>56</sup>

### Rheumatoid arthritis (RA)

Periodontal disease is prevalent among RA patients, and the disease is thought to initiate autoimmune response in RA (Figure 4).<sup>57</sup> It is suggested that both periodontal disease and RA have similar underlying pathogenic mechanisms.<sup>57</sup> The individuals with RA have high prevalence of alveolar bone destruction and tooth loss which are also sequelae of periodontal disease.<sup>58</sup>

### Respiratory diseases

The importance of maintaining optimum oral care among patients with chronic obstructive pulmonary disease (COPD) has been emphasized due to its association with periodontitis. Chung *et al.* used data of 5,878 adults from a Korean national survey and found significantly higher prevalence of periodontitis among COPD patients compared with healthy individuals.<sup>59</sup> In a large cohort study, about 22,332 patients with COPD were compared with individuals without COPD and it was suggested that subjects with COPD were at increased risk of developing periodontal disease.<sup>60</sup> Similarly, a meta-analysis of 14 epidemiological studies revealed a significant association between periodontal disease and COPD and periodontal disease was recognized as an independent risk factor for COPD (Figure 4).<sup>61</sup> It has also been suggested that oral and periodontal microorganisms are implicated in bacterial pneumonia.<sup>62</sup>

### Chronic kidney disease (CKD)

There is a bidirectional relationship between periodontal disease and CKD. Fisher and Taylor identified periodontitis as a risk factor for CKD in an epidemiological study of 11,955 adults in the U.S.<sup>63</sup> A systematic review of four observational and three interventional studies found that patients with periodontitis are at increased risk of CKD and periodontal treatment results in positive outcomes in persons with CKD.<sup>64</sup> Ioannidou and Swede observed a dose-response relationship between periodontal disease and different stages of CKD, and they found that individuals with CKD were 30-60% more likely to develop moderate periodontitis.<sup>65</sup> Later, in another study by Ioannidou *et al.*, it was shown that Mexican Americans with low kidney functions were twice more likely to have periodontal disease compared with subjects with normal kidney functions.<sup>66</sup> Similarly, Iwasaki *et al.* demonstrated a link between periodontitis and reduced kidney functions in Japanese older individuals.<sup>67</sup> In a recent prospective cohort study with 14 years of follow-up, Ricardo *et al.* found that CKD individuals with periodontitis had 35% greater risk of mortality compared with CKD patients without periodontal disease (Figure 4).<sup>68</sup>

### Cancers

Increased cancer risk because of periodontal disease has been demonstrated by Michaud and colleagues.<sup>69</sup> The risk of tongue cancer increases 5.23 times with each millimeter loss of alveolar bone.<sup>70</sup> Fitzpatrick and Katz observed that the relationship between periodontitis and oral, esophageal, gastric, and pancreatic cancers have been reported more consistently in literature than with lung and prostate cancers (Figure 4).<sup>71</sup>

### Impairment of cognitive function

Older adults face decline in their cognitive abilities, which affect their behaviors including oral hygiene habits.<sup>72</sup> There is modest evidence about an association between periodontal disease and poor cognitive functions as periodontal inflammation has been shown to affect cognition in elderly populations.<sup>73,74</sup> The analysis of data from Third NHANES-III identified high levels of serum maker of periodontitis (*P. gingivalis* IgG) in individuals with impaired cognitive performance.<sup>75</sup> Further, a recent study by Kamer and associates found that clinical AL can promote amyloid  $\beta$  accumulation in the brain which can cause cognitive dysfunction.<sup>76</sup>

### Prevention of Periodontal Disease

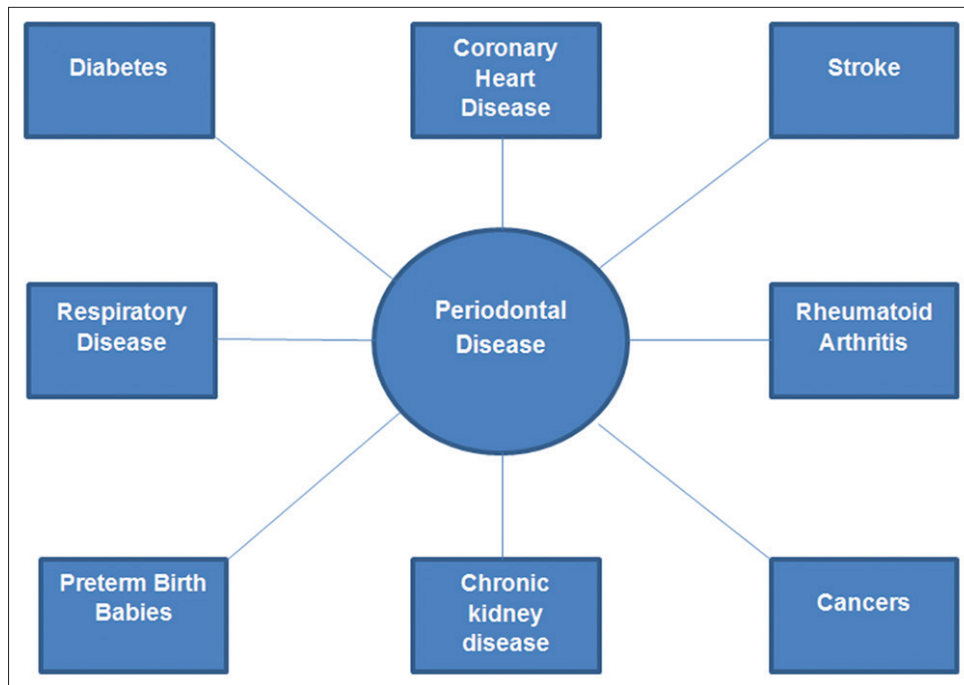
WHO recommends employing integrated public health preventive strategies which should be based on common risk factor approach. Risk factors such as smoking, stress, and low socioeconomic status are associated with periodontal disease as well as other systemic chronic diseases; therefore, inclusion of oral disease prevention strategies in chronic systemic disease preventive initiatives can curtail the burden of disease at the level of population.<sup>77</sup>

### Oral hygiene practices

Proper mouth cleaning, regular tooth brushing, and dental flossing are most effective in preventing oral disease and periodontitis. Despite utmost significance of tooth brushing, about half of the population brush twice a day.<sup>78</sup> There are various sizes, shapes, and types of toothbrushes; however, two more common types include powered toothbrushes and manual toothbrushes. Powered toothbrushes offer more advantage over the manual toothbrushes in reducing dental plaque.<sup>79</sup>

### Diet

Although the role of diet in the prevention of dental caries is more significant compared with preventing periodontal disease; nonetheless, poor diet can negatively affect periodontal tissues causing rapid progression of disease.<sup>80</sup> The vitamin C deficiency as a risk factor for periodontal disease has been discussed in the literature. Nishida *et al.* used a sample of 12,419 adults and showed that there was increased risk of periodontal disease due to the poor dietary intake of vitamin C, and also observed a dose-response relationship between vitamin C and the severity



**Figure 4:** Association between periodontal disease and various systemic conditions

of periodontal disease.<sup>81</sup> A diet high in fruits, vegetables and low in fat and sugars is required for the healthy periodontal tissues. Vitamins C and E have antioxidant properties which help to reduce the production of reactive oxygen radicals formed during the inflammatory process.<sup>80</sup> Low-calorie intake has been shown to reduce inflammatory changes and diminish the tissue damage in periodontal disease.<sup>82</sup>

### Use of fluoride

Stannous fluoride has antiplaque and antigingivitis effects and it reduces the proportion of bacteria and spirochetes in subgingival areas, thus can help to promote gingival health.<sup>83,84</sup> He *et al.* conducted a randomized double-blinded trial to investigate the antimicrobial role of stannous fluoride dentifrice in periodontal disease and found a significant reduction in gingival bleeding over a period of 2-month.<sup>85</sup>

### Use of antimicrobial agents

Chlorhexidine, triclosan, essential oils and zinc in toothpastes, mouthwashes and gels are used to control specific periodontal bacteria as well as plaque.<sup>86,87</sup> Chlorhexidine reduces dental plaque (55% reduction in dental plaque) and gingival inflammation (30-45% decrease in gingivitis) by lowering inflammatory mediators.<sup>88</sup> Gunsolley compared the effectiveness of antiplaque and antigingivitis mouthrinses with oral hygiene instructions and adult prophylaxis and found great improvement in oral hygiene due to antiplaque and antigingivitis mouth rinses.<sup>89</sup> Moreover, research data from several clinical trials support that antimicrobial mouth rinses have equal or greater efficacy

in controlling gingival disease than the use of interproximal dental floss.<sup>90-92</sup>

### Smoking cessation

Since smoking is a major risk factor for periodontal disease, therefore smoking cessation can prevent a considerable proportion of periodontitis cases.<sup>93</sup> Smoking cessation not only inhibits further progression of periodontal disease but can also reduce the periodontal tissue destruction.<sup>94</sup>

### Community and high risk approaches

Breast cancer and cervical cancer screening are considered successful examples of screening for the prevention of diseases, but the decision of oral screening should be based on careful evaluation of financial burden, ethical aspects, and efficacy and adverse effects of the intervention.<sup>95</sup> In addition, implementation of oral health promotion policies at local, national and international levels can help bring sustainable reduction in periodontal disease burden and improve the quality of life of people. Scaling is considered the most common professional preventive measure for periodontal disease. Because of the association between periodontal disease and cardiovascular disease, scaling has recently been shown to reduce the incidence of acute myocardial infarction and stroke.<sup>96</sup>

### Conclusion and Recommendations

- Although periodontal disease is the most prevalent infectious oral condition but is treatable and preventable.
- The reduction in the incidence and prevalence of

periodontal disease can result in lowering its associated systemic diseases and complications.

- Decreased periodontal disease burden can minimize treatment needs and can reduce financial impact on health-care systems.
- High prevalence of periodontal disease also necessitates the establishment of surveillance system for oral diseases in the community.
- Preventive programs for periodontal disease should utilize common risk approaches to reduce the magnitude of other chronic diseases.
- Cost-effective strategies would also enhance interdisciplinary collaborations among health-care providers.
- Health-care providers should be familiar with periodontal-systemic link and should be able to diagnose and refer the patients to specialized dental or periodontal care to improve the quality of life of their patients.

Further research is needed to explore the underlying mechanisms and risk factors of periodontal disease and develop innovative preventive strategies.

## References

- de Pablo P, Chapple IL, Buckley CD, Dietrich T. Periodontitis in systemic rheumatic diseases. *Nat Rev Rheumatol* 2009;5:218-24.
- Benjamin RM. Oral health: The silent epidemic. *Public Health Rep* 2010;125:158-9.
- Ashby MT, Kreth J, Soundarajan M, Sivuilu LS. Influence of a model human defensive peroxidase system on oral streptococcal antagonism. *Microbiology* 2009;155:3691-700.
- Fenesy KE. Periodontal disease: An overview for physicians. *Mt Sinai J Med* 1998;65:362-9.
- Raitapuro-Murray T, Molleson TI, Hughes FJ. The prevalence of periodontal disease in a Romano-British population c 200-400 AD. *Br Dent J* 2014;217:459-66.
- Locker D, Slade GD, Murray H. Epidemiology of periodontal disease among older adults: A review. *Periodontol* 2000 1998;16:16-33.
- Health Canada. Report on the Findings of the Oral Health Component of the Canadian Health Measures Survey; 2007-2009. Available from: <http://www.fptdwc.ca/assets/PDF/CHMS/CHMS-E-summ.pdf>. [Last accessed on 2014 Nov 07].
- Eke PI, Dye BA, Wei L, Thornton-Evans GO, Genco RJ; CDC Periodontal Disease Surveillance workgroup; James Beck (University of North Carolina, Chapel Hill, USA), *et al*. Prevalence of periodontitis in adults in the United States: 2009 and 2010. *J Dent Res* 2012;91:914-20.
- World Health Organization. WHO Global Oral Health Data; 2005. Available from: [http://www.who.int/oral\\_health/databases/niigata/en](http://www.who.int/oral_health/databases/niigata/en). [Last accessed on 2014 Nov 07].
- Sanz M, D' Aiuto F, Deanfield J, Fernandez-Avilés F. European workshop in periodontal health and cardiovascular disease-scientific evidence on the association between periodontal and cardiovascular diseases: A review of the literature. *Eur Heart J Suppl* 2010;12 Suppl B:B3-12.
- Bergstrom J. Smoking rate and periodontal disease prevalence: 40-year trends in Sweden 1970-2010. *J Clin Periodontol* 2014;41:952-7.
- Underner M, Maes I, Urban T, Meurice JC. Effects of smoking on periodontal disease. *Rev Mal Respir* 2009;26:1057-73.
- Johnson GK, Hill M. Cigarette smoking and the periodontal patient. *J Periodontol* 2004;75:196-209.
- Albandar JM, Streckfus CF, Adesanya MR, Winn DM. Cigar, pipe, and cigarette smoking as risk factors for periodontal disease and tooth loss. *J Periodontol* 2000;71:1874-81.
- Reners M, Brex M. Stress and periodontal disease. *Int J Dent Hyg* 2007;5:199-204.
- Nociti FH Jr, Nogueira-Filho GR, Tramontina VA, Machado MA, Barros SP, Sallum EA, *et al*. Histometric evaluation of the effect of nicotine administration on periodontal breakdown: An *in vivo* study. *J Periodontol Res* 2001;36:361-6.
- de Oliveira C, Watt R, Hamer M. Toothbrushing, inflammation, and risk of cardiovascular disease: Results from Scottish Health Survey. *BMJ* 2010;340:c2451.
- Albandar JM. Global risk factors and risk indicators for periodontal diseases. *Periodontol* 2000 2002;29:177-206.
- Axelsson P, Lindhe J, Nyström B. On the prevention of caries and periodontal disease. Results of a 15-year longitudinal study in adults. *J Clin Periodontol* 1991;18:182-9.
- Güncü GN, Tözüm TF, Caglayan F. Effects of endogenous sex hormones on the periodontium - Review of literature. *Aust Dent J* 2005;50:138-45.
- Markou E, Boura E, Tsalikis L, Deligianidis A, Konstantinidis A. The influence of sex hormones on proinflammatory cytokines in gingiva of periodontally healthy premenopausal women. *J Periodontol Res* 2011;46:528-32.
- Laine MA. Effect of pregnancy on periodontal and dental health. *Acta Odontol Scand* 2002;60:257-64.
- Grodstein F, Colditz GA, Stampfer MJ. Post-menopausal hormone use and tooth loss: A prospective study. *J Am Dent Assoc* 1996;127:370-7.
- Casanova L, Hughes FJ, Preshaw PM. Diabetes and periodontal disease: A two-way relationship. *Br Dent J* 2014;217:433-7.
- Chávarry NG, Vettore MV, Sansone C, Sheiham A. The relationship between diabetes mellitus and destructive periodontal disease: A meta-analysis. *Oral Health Prev Dent* 2009;7:107-27.
- Preshaw PM, Bissett SM. Periodontitis: Oral complication of diabetes. *Endocrinol Metab Clin North Am* 2013;42:849-67.
- Grossi SG, Zambon JJ, Ho AW, Koch G, Dunford RG, Machtei EE, *et al*. Assessment of risk for periodontal disease. I. Risk indicators for attachment loss. *J Periodontol* 1994;65:260-7.
- Patel MH, Kumar JV, Moss ME. Diabetes and tooth loss: An analysis of data from the national health and nutrition examination survey, 2003-2004. *J Am Dent Assoc* 2013;144:478-85.
- Chapple IL, Genco R; Working group 2 of the joint EFP/AAP workshop. Diabetes and periodontal diseases: Consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *J Periodontol* 2013;84 4 Suppl:S106-12.
- Scully C. Drug effects on salivary glands: Dry mouth. *Oral Dis* 2003;9:165-76.
- Rai B, Kaur J, Anand SC, Jacobs R. Salivary stress markers, stress, and periodontitis: A pilot study. *J Periodontol* 2011;82:287-92.
- Segerstrom SC, Miller GE. Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. *Psychol Bull* 2004;130:601-30.
- Rheu GB, Ji S, Ryu JJ, Lee JB, Shin C, Lee JY, *et al*. Risk assessment for clinical attachment loss of periodontal tissue in Korean adults. *J Adv Prosthodont* 2011;3:25-32.
- Albandar JM, Rams TE. Global epidemiology of periodontal diseases: An overview. *Periodontol* 2000 2002;29:7-10.

35. Humphrey LL, Fu R, Buckley DI, Freeman M, Helfand M. Periodontal disease and coronary heart disease incidence: A systematic review and meta-analysis. *J Gen Intern Med* 2008;23:2079-86.
36. Janket SJ, Baird AE, Chuang SK, Jones JA. Meta-analysis of periodontal disease and risk of coronary heart disease and stroke. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;95:559-69.
37. Mustapha IZ, Debrey S, Oladubu M, Ugarte R. Markers of systemic bacterial exposure in periodontal disease and cardiovascular disease risk: A systematic review and meta-analysis. *J Periodontol* 2007;78:2289-302.
38. Blaizot A, Vergnes JN, Nuwwareh S, Amar J, Sixou M. Periodontal diseases and cardiovascular events: Meta-analysis of observational studies. *Int Dent J* 2009;59:197-209.
39. Kinane DF, Marshall GJ. Periodontal manifestations of systemic disease. *Aust Dent J* 2001;46:2-12.
40. Saremi A, Nelson RG, Tulloch-Reid M, Hanson RL, Sievers ML, Taylor GW, *et al.* Periodontal disease and mortality in Type 2 diabetes. *Diabetes Care* 2005;28:27-32.
41. Teeuw WJ, Gerdes VE, Loos BG. Effect of periodontal treatment on glycemic control of diabetic patients: A systematic review and meta-analysis. *Diabetes Care* 2010;33:421-7.
42. Borgnakke WS, Ylöstalo PV, Taylor GW, Genco RJ. Effect of periodontal disease on diabetes: Systematic review of epidemiologic observational evidence. *J Periodontol* 2013;84 Suppl 4:S135-52.
43. Gurav AN. Periodontitis and insulin resistance: Casual or causal relationship? *Diabetes Metab J* 2012;36:404-11.
44. Lim SG, Han K, Kim HA, Pyo SW, Cho YS, Kim KS, *et al.* Association between insulin resistance and periodontitis in Korean adults. *J Clin Periodontol* 2014;41:121-30.
45. Sun WL, Chen LL, Zhang SZ, Wu YM, Ren YZ, Qin GM. Inflammatory cytokines, adiponectin, insulin resistance and metabolic control after periodontal intervention in patients with Type 2 diabetes and chronic periodontitis. *Intern Med* 2011;50:1569-74.
46. Chaffee BW, Weston SJ. Association between chronic periodontal disease and obesity: A systematic review and meta-analysis. *J Periodontol* 2010;81:1708-24.
47. Nascimento GG, Leite FR, Do LG, Peres KG, Correa MB, Demarco FF, *et al.* Is weight gain associated with the incidence of periodontitis? A systematic review and meta-analysis. *J Clin Periodontol* 2015;42:495-505.
48. Keller A, Rohde JF, Raymond K, Heitmann BL. Association between periodontal disease and overweight and obesity: A systematic review. *J Periodontol* 2015;86:766-76.
49. Atabay VE, Lutfioglu M, Avci B, Sakallioğlu EE, Aydogdu A. Obesity and oxidative stress in patients with different periodontal status: A case-control study. *J Periodontol Res* 2017;52:51-60.
50. Dursun E, Akalin FA, Genc T, Cinar N, Erel O, Yildiz BO. Oxidative stress and periodontal disease in obesity. *Medicine (Baltimore)* 2016;95:e3136.
51. WHO. Global Health Observatory (GHO) Data. Obesity. Available from: [http://www.who.int/gho/ncd/risk\\_factors/obesity\\_text/en](http://www.who.int/gho/ncd/risk_factors/obesity_text/en). [Last accessed on 2015 Jan 21].
52. Ide M, Papapanou PN. Epidemiology of association between maternal periodontal disease and adverse pregnancy outcomes-systematic review. *J Clin Periodontol* 2013;40 Suppl 14:S181-94.
53. Bobetsis YA, Barros SP, Offenbacher S. Exploring the relationship between periodontal disease and pregnancy complications. *J Am Dent Assoc* 2006;137 Suppl:7S-13.
54. Polyzos NP, Polyzos IP, Mauri D, Tzioras S, Tsappi M, Cortinovis I, *et al.* Effect of periodontal disease treatment during pregnancy on preterm birth incidence: A metaanalysis of randomized trials. *Am J Obstet Gynecol* 2009;200:225-32.
55. Azarpazhooh A, Tenenbaum HC. Separating fact from fiction: Use of high-level evidence from research syntheses to identify diseases and disorders associated with periodontal disease. *J Can Dent Assoc* 2012;78:c25.
56. Piscoya MD, Ximenes RA, Silva GM, Jamelli SR, Coutinho SB. Maternal periodontitis as a risk factor for prematurity. *Pediatr Int* 2012;54:68-75.
57. Mercado FB, Marshall RI, Bartold PM. Inter-relationships between rheumatoid arthritis and periodontal disease. A review. *J Clin Periodontol* 2003;30:761-72.
58. Detert J, Pischon N, Burmester GR, Buttgereit F. The association between rheumatoid arthritis and periodontal disease. *Arthritis Res Ther* 2010;12:218.
59. Chung JH, Hwang HJ, Kim SH, Kim TH. Associations between periodontitis and chronic obstructive pulmonary disease: The 2010-2012 Korean National Health and Nutrition Examination Survey. *J Periodontol* 2016;25:1-11.
60. Shen TC, Chang PY, Lin CL, Chen CH, Tu CY, Hsia TC, *et al.* Risk of periodontal diseases in patients with chronic obstructive pulmonary disease: A nationwide population-based cohort study. *Medicine (Baltimore)* 2015;94:e2047.
61. Zeng XT, Tu ML, Liu DY, Zheng D, Zhang J, Leng W. Periodontal disease and risk of chronic obstructive pulmonary disease: A meta-analysis of observational studies. *PLoS One* 2012;7:e46508.
62. Paju S, Scannapieco FA. Oral biofilms, periodontitis, and pulmonary infections. *Oral Dis* 2007;13:508-12.
63. Fisher MA, Taylor GW. A prediction model for chronic kidney disease includes periodontal disease. *J Periodontol* 2009;80:16-23.
64. Chambrone L, Foz AM, Guglielmetti MR, Pannuti CM, Artese HP, Feres M, *et al.* Periodontitis and chronic kidney disease: A systematic review of the association of diseases and the effect of periodontal treatment on estimated glomerular filtration rate. *J Clin Periodontol* 2013;40:443-56.
65. Ioannidou E, Swede H. Disparities in periodontitis prevalence among chronic kidney disease patients. *J Dent Res* 2011;90:730-4.
66. Ioannidou E, Hall Y, Swede H, Himmelfarb J. Periodontitis associated with chronic kidney disease among Mexican Americans. *J Public Health Dent* 2013;73:112-9.
67. Iwasaki M, Taylor GW, Nesse W, Vissink A, Yoshihara A, Miyazaki H. Periodontal disease and decreased kidney function in Japanese elderly. *Am J Kidney Dis* 2012;59:202-9.
68. Ricardo AC, Athavale A, Chen J, Hampole H, Garside D, Marucha P, *et al.* Periodontal disease, chronic kidney disease and mortality: Results from the third national health and nutrition examination survey. *BMC Nephrol* 2015;16:97.
69. Michaud DS, Liu Y, Meyer M, Giovannucci E, Joshipura K. Periodontal disease, tooth loss, and cancer risk in male health professionals: A prospective cohort study. *Lancet Oncol* 2008;9:550-8.
70. Tezal M, Sullivan MA, Reid ME, Marshall JR, Hyland A, Loree T, *et al.* Chronic periodontitis and the risk of tongue cancer. *Arch Otolaryngol Head Neck Surg* 2007;133:450-4.
71. Fitzpatrick SG, Katz J. The association between periodontal disease and cancer: A review of the literature. *J Dent* 2010;38:83-95.
72. Brennan LJ, Strauss J. Cognitive impairment in older adults and oral health considerations: Treatment and management. *Dent Clin North Am* 2014;58:815-28.
73. Kamer AR, Morse DE, Holm-Pedersen P, Mortensen EL, Avlund K. Periodontal inflammation in relation to cognitive function in an older adult Danish population. *J Alzheimers Dis* 2012;28:613-24.
74. Kaye EK, Valencia A, Baba N, Spiro A 3<sup>rd</sup>, Dietrich T, Garcia RI. Tooth



- loss and periodontal disease predict poor cognitive function in older men. *J Am Geriatr Soc* 2010;58:713-8.
75. Noble JM, Borrell LN, Papanou PN, Elkind MS, Scarmeas N, Wright CB. Periodontitis is associated with cognitive impairment among older adults: Analysis of NHANES-III. *J Neurol Neurosurg Psychiatry* 2009;80:1206-11.
  76. Kamer AR, Pirraglia E, Tsui W, Rusinek H, Vallabhajosula S, Mosconi L, *et al.* Periodontal disease associates with higher brain amyloid load in normal elderly. *Neurobiol Aging* 2015;36:627-33.
  77. Petersen PE, Ogawa H. Strengthening the prevention of periodontal disease: The WHO approach. *J Periodontol* 2005;76:2187-93.
  78. Bhardwaj VK. Tooth brushing behaviours and dental abrasion among the population in Shimla, Himachal Pradesh in India: A cross-sectional study. *J Cranio Maxillary Dis* 2014;3:89-94.
  79. Niederman R. Moderate quality evidence finds statistical benefit in oral health for powered over manual toothbrushes. *Evid Based Dent* 2014;15:77-8.
  80. Moynihan PJ. The role of diet and nutrition in the etiology and prevention of oral diseases. *Bull World Health Organ* 2005;83:694-9.
  81. Nishida M, Grossi SG, Dunford RG, Ho AW, Trevisan M, Genco RJ. Dietary vitamin C and the risk for periodontal disease. *J Periodontol* 2000;71:1215-23.
  82. Branch-Mays GL, Dawson DR, Gunsolley JC, Reynolds MA, Ebersole JL, Novak KF, *et al.* The effects of a calorie-reduced diet on periodontal inflammation and disease in a non-human primate model. *J Periodontol* 2008;79:1184-91.
  83. Gunsolley JC. A meta-analysis of six-month studies of antiplaque and antigingivitis agents. *J Am Dent Assoc* 2006;137:1649-57.
  84. Mazza JE, Newman MG, Sims TN. Clinical and antimicrobial effect of stannous fluoride on periodontitis. *J Clin Periodontol* 1981;8:203-12.
  85. He T, Barker ML, Goyal CR, Biesbrock AR. Anti-gingivitis effects of a novel 0.454% stabilized stannous fluoride dentifrice relative to a positive control. *Am J Dent* 2012;25:136-40.
  86. Axelsson P. Current role of pharmaceuticals in prevention of caries and periodontal disease. *Int Dent J* 1993;43:473-82.
  87. García-Caballero L, Quintas V, Prada-López I, Seoane J, Donos N, Tomás I. Chlorhexidine substantivity on salivary flora and plaque-like biofilm: An *in situ* model. *PLoS One* 2013;8:e83522.
  88. Puig Silla M, Montiel Company JM, Almerich Silla JM. Use of chlorhexidine varnishes in preventing and treating periodontal disease. A review of the literature. *Med Oral Patol Oral Cir Bucal* 2008;13:E257-60.
  89. Gunsolley JC. Clinical efficacy of antimicrobial mouthrinses. *J Dent* 2010;38 Suppl 1:S6-10.
  90. Sharma N, Charles CH, Lynch MC, Qaqish J, McGuire JA, Galustians JG, *et al.* Adjunctive benefit of an essential oil-containing mouthrinse in reducing plaque and gingivitis in patients who brush and floss regularly: A six-month study. *J Am Dent Assoc* 2004;135:496-504.
  91. Mythri H, Ananda SR, Prashant GM, Subba Reddy VV, Chandu GN. The efficacy of antiseptic mouth rinses in comparison with dental floss in controlling interproximal gingivitis. *J Int Soc Prev Community Dent* 2011;1:31-5.
  92. Bauroth K, Charles CH, Mankodi SM, Simmons K, Zhao Q, Kumar LD. The efficacy of an essential oil antiseptic mouthrinse vs. Dental floss in controlling interproximal gingivitis: A comparative study. *J Am Dent Assoc* 2003;134:359-65.
  93. Tomar SL, Asma S. Smoking-attributable periodontitis in the United States: Findings from NHANES III. National health and nutrition examination survey. *J Periodontol* 2000;71:743-51.
  94. Hodge P, Binne V. Smoking cessation and periodontal health - A missed opportunity? *Evid Based Dent* 2009;10:18-9.
  95. Deep P. Screening for common oral diseases. *J Can Dent Assoc* 2000;66:298-9.
  96. Chen ZY, Chiang CH, Huang CC, Chung CM, Chan WL, Huang PH, *et al.* The association of tooth scaling and decreased cardiovascular disease: A nationwide population-based study. *Am J Med* 2012;125:568-75.