Review Article

Association of periodontal and cardiovascular diseases: South-Asian studies 2001–2012

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Abstract:

Large proportion of Asian populations have moderate to severe periodontal disease and a substantial number are anticipated to be at high risk of cardiovascular diseases (CVD). This study reviews epidemiology and association of periodontal and CVDs from the South-Asian region. Observational studies and clinical trials published during January 2001–December 2012 focusing association between periodontitis and CVDs in South-Asian countries were retrieved from various databases and studied. Current evidence suggests that both periodontal and CVDs are globally prevalent and show an increasing trend in developing countries. Global data on epidemiology and association of periodontal and CVDs are predominantly from the developed world; whereas Asia with 60% of the world's population lacks substantial scientific data on the link between periodontal and CVDs. During the search period, 14 studies (5 clinical trials, 9 case–controls) were reported in literature from South-Asia; 100% of clinical trials and 77% case–control studies have reported a significant association between the oral/periodontal parameters and CVD. Epidemiological and clinical studies from South-Asia validate the global evidence on association of periodontal disease with CVDs. However, there is a need for meticulous research for public health and scientific perspective of the Periodontal and CVDs from South-Asia.

Key words:

Cardiovascular diseases, periodontal diseases, South-Asian countries

INTRODUCTION

Periodontal and cardiovascular diseases (CVD) are prevalent globally. In Asia, the periodontal disease remains at higher levels[1] and CVDs are predicted to rise to epidemic levels.[2] In developed and developing countries, CVDs are one of the leading causes of death and the main underlying pathological process is atherosclerosis. No single factor can account for all the causes of CVD, and a considerable section of CVD patients do not carry any of the traditional risk factors like hypertension, smoking, obesity, hypercholesterolemia or genetic predisposition.[3,4]

Scientific evidence regarding the link between CVDs and emerging risk factors that also include infectious and/or inflammatory diseases is growing. Epidemiological, pathological, microbiological and immunological studies show that infectious agents, such as periodontopathic pathogens and inflammatory markers in the blood have been correlated with increased risk of CVD.[5] Inflammatory biomarkers including high-sensitive C-reactive protein (CRP), fibrinogen, serum amyloid A, tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and cellular adhesion molecules are known CVD risk markers.[6] Scientists have explored the potential mechanisms of association between periodontal disease and CVDs. As a result, different theories have emerged that include: The theory of bacterial invasion, the cytokine theory, the autoimmunization theory.[7]

Global data on epidemiology and association between periodontal and CVDs is predominantly from the developed world; the corresponding situation in Asian countries which are going to face an increasing burden of noncommunicable diseases including CVDs, are not well studied.[8] In this review paper, we have explored and analyzed relevant scientific literature to account for the level of evidence available on the status and association of periodontal and CVDs from South-Asian region including Pakistan, India, Bangladesh, Sri Lanka, and Nepal.

METHODOLOGY

Databases (January 2001 to December 2012), including MedLine, EMBASE, Google scholar, Scopus and Web of Science were searched by the PubMed interface on December 2012, using the following MeSH headings: "Periodontal disease, periodontitis, or periodontal therapy," and "CVD, coronary heart disease (CHD), coronary artery disease, stroke, cerebrovascular disease, peripheral arterial disease," and global, Asian countries, developed/developing countries."

All articles on observational (cohort, case–control, cross-sectional) and intervention studies (comparison studies, randomized controlled trials,) and systematic reviews/meta-analysis investigating epidemiology and/or association between periodontal disease and CVDs were screened. Articles, not available in full text, printed in a language other than English, reporting association of periodontal disease with systemic condition (s) other than CVDs, and review papers were excluded. The electronic search yielded 1524 references and the inclusion criteria were relatively broadly specified to include articles, which have analyzed the epidemiology and association of periodontal conditions and CVDs with respect to the South-Asian perspective. Fourteen (14) most relevant articles were retrieved and analyzed for this paper. Articles were screened and retrieved by author (SAHB) and analyzed independently by authors (SAHB and GW) for inclusion in review. Authors (AAK and KWL) contributed in manuscript preparation.

RESULTS

Scientific literature on the association of oral/periodontal and CVDs available from South-Asia includes five clinical/intervention trials,[9-13] nine case–control studies[14-22] [Table 1].

All studies reported on the topic were either from India or Pakistan. Five randomized and nonrandomized trials were conducted in India and Pakistan. Indian researchers have contributed six case–control studies while three case–control studies have been reported from Pakistan. Five studies from Pakistan observed 2263 individuals and 9 Indian studies were conducted on 1248 individuals.

Oral parameters of bleeding on probing; probing depth; clinical attachment loss (AL)/level; plaque index; gingival index; papillary bleeding index; alveolar bone level; community periodontal index (CPI); oral hygiene index-simplified; loss of attachment; decayed, missing and filled teeth; periodontal disease index; AL; missing teeth and dental prosthesis were used in studies to measure status of oral/periodontal diseases. Systemic parameters of hsCRP, fibrinogen, white blood cells, TNF-α, IgG, IgM, high density lipoprotein (HDL), triglycerides, total cholesterol, IL-6, serum leptin, CHD, stroke, hypertension, acute myocardial infarction, and cardiac disease were noted as outcome measures.

Four hundred and eighty-five subjects were observed in 5 clinical trials for the effect of nonsurgical periodontal therapy on serum levels of hsCRP, fibrinogen, WBC, TNF-α, IgG, IgM, HDL and triglycerides. A significant reduction of ≥14% in all systemic parameters except TNF-α was observed in all trials.

Seven out of nine case–control studies showed a significant association of oral parameters and CHD/CVA/hypertension/total cholesterol, low density lipoprotein, HDL and triglycerides on 2846 individuals; however two studies conducted on 180 individuals reported no association between periodontal and systemic outcome parameters.

In summary, of the 14 studies, 12 studies (5 RCTs and 7 case–controls) suggested an association of oral/periodontal disease parameters with increased risk of cardiovascular outcome measures. Randomized trials showed that periodontal health may significantly reduce CVD associated risk markers.

DISCUSSION

The majority of the studies analyzed in this systematic review were from India and then from Pakistan, no study has been reported from Bangladesh, Nepal, and Sri Lanka. All studies have observed an association of oral/periodontal clinical parameters with various systemic biomarkers and systemic conditions of CHD, Stroke, and hypertension.

Tonetti and Claffey[23] noted variations in the epidemiology of periodontal disease (PD) because of the lack of uniformity in case definition of PD used in studies of different populations. Globally in all WHO regions, the most severe form of periodontal disease (CPI score 4) varies from 10% to 15% and the most prevalent form is gingival bleeding and calculus (CPI score 2) that reflects poor oral hygiene and lack of appropriate dental care.[24] Corbet *et al*.[1] reported periodontal status of low- and -middle income countries, and observed a very low percentage with healthy periodontal status (0–7%) and a high percentage of gingival bleeding and calculus (55–99%) in the younger age groups (15 years old) and shallow PD is not a common condition (0–20%), a higher prevalence, as high as 44%, of shallow pocket was observed in slightly older age groups. In Eastern Mediterranean Region (EMRO) periodontal diseases affect 95% of populations and 5–15% people are presented with bleeding gums, 40% with calculus, 20–25% with shallow pockets and 15% with deep pockets when measured through CPI.[25]

Cardiovascular diseases, the most prevalent category of systemic diseases in developed as well in developing countries,[26] are the prevailing noncommunicable ailment in the Indian subcontinent, and will become the major cause of mortality among inhabitants of South Asia in the next 20 years.[27] South Asian countries, namely Bangladesh, India, Nepal, Pakistan and Sri Lanka, not only represent a quarter of the world's population but also contribute to the highest proportion of CVD burden when compared with any other region globally.[28] Lifestyle changes resulting from urbanization, industrialization; economic transition and globalization are promoting increased prevalence of CVDs.[25,29] Risk factors of tobacco consumption, physical inactivity, unhealthy diet, including foliate deficiency and emerging risk factors such as chronic infections are common in the underprivileged populations of the low- and middle-income countries.[29] South Asian ethnicity *per se* is a risk factor for CVD that appeared to be independent of traditional risk factors.[26] CHD occurs at least 10 years earlier in South Asians as compared to other ethnic groups, and the average age of stroke is much lower than in the western countries.[30]

Asian Indians are at 3–4 times higher risk of coronary artery disease (CAD) than white Americans, 6 times higher than Chinese, and 20 times higher than Japanese.[31] Median age for first presentation of acute MI in the five South Asian populations is 53 years, whereas the corresponding age in Western Europe, China, and Hong Kong is 63 years, with more men than women affected.[32] The incidence of CHD has increased in Pakistan over the past three decades.[33] Two

Table 1: South-Asian studies on "Perio-CVD" association: 2001-2012

Author/year	Country	Journal	Study sample/age	Exposure/study parameter/s	Intervention	Outcome variables	Results S (significant) NS (non-significant)
Randomized/non-randomized clinical trials							
Bokhari *et al.*[9]	Pakistan	J Clin Periodontol	317 CHD patients	Chronic Periodontitis (BOP, PD, CAL)	Non-surgical Periodontal therapy	hsCRP, Fibrinogen and WBC	hsCRP ↓ by 30% S FIB ↓ by18% S WBC ↓ by 11% S
Rastogi *et al.*[10]	India	J Cardiovasc Dis Res	20 CAD patients	Periodontitis (BOP, PD)	Non-surgical Periodontal therapy	hsCRP, WBCs, TNF-α	hsCRP ↓ by 28% S WBC ↓ by 14% S TNF-α ↓ by 2% NS
Gunupati *et al.*[11]	India	J Periodontol	72 individuals	PI, GI, PD, CAL	Phase 1 Periodontal therapy	IgG, IgM anti-cardio-lipin antibodies	IgG and IgM significantly reduced postoperatively
Acharya *et al.*[12]	India	Metab Syndr Relat Disord	31 individuals	generalized chronic periodontitis	Non-surgical Periodontal therapy	CRP, Leukocyte counts, HDL and triglycerides	hsCRP ↓ by 21% S Leukocytes ↓ by 24% S Triglycerides ↓ by18% S HDL ↑ by 8% S
Hussain Bokhari *et al.*[13]	Pakistan	J Periodontol	27 CHD and 18 non-CHD individuals	BOP and PD	Non-surgical Periodontal therapy	CRP, Fibrinogen and WBC	hsCRP, FIB & WBC levels ↓ by ≥21% S in both groups
Case-control studies							
Ashraf *et al.*[14]	Pakistan	J Periodontol	145 CAD cases and 145 healthy controls	PI, CPI, missing teeth	x	Coronary heart disease	CHD cases at higher odds (OR 1.20, CI=0.93-15.68) for poor oral health after adjusting age, gender and education
Bokhari *et al.*[15]	Pakistan	J Epidemiol Glob Health	936 CHD and 595 non-CHD individuals 40-70 years	Tooth loss	x	Coronary heart disease	Tooth loss associated with CHD independent of age, gender, smoking, and diabetes (OR 2.82, CI=2.287-3.663)
Gita *et al.*[16]	India	J Ind Soc Periodontol	60 individuals 30-50 years	OHI-S PD, CAL Furcation & Tooth mobility	x	Total cholesterol, LDL, HDL and Triglycerides	No association between periodontal parameters and outcome variables
Bokhari *et al.*[17]	Pakistan	J Indian Soc Periodontol	45 CHD and 35 Non-CHD individuals	BOP, PD, Tooth loss	x	Coronary heart disease	BOP (OR 1.02, CI=1.006-1.049) and tooth loss (OR 1.22, CI=1.047-1.422) significantly associated with CHD, PD association was non-significant
Sikka *et al.*[18]	India	N Z Med J	100 cases, 100 controls	CPI, LOA, DMFT	x	Coronary heart disease	CPI and LOA significantly higher in CHD cases but DMFT showed insignificant association
Thakere *et al.*[19]	India	Indian J Dent Res	45 individuals 35-55 years	PI, PBI, PD, CAL, ABL	x	CRP levels	CRP levels significantly associated with clinical oral parameters
Pradeep *et al.*[20]	India	Periodontal Res	100 cases, 100 controls 33-68 years	PI, GI, PD, CAL	x	Cerebrovascular accident, Hypertension	Significant link between periodontitis and cerebrovascular accident with OR 8.5 (CI=1.1-68.2) and Hypertension with OR 7.6 (CI 3.3-17.1)
Sridhar *et al.*[21]	India	Int J Dent Hyg	120 individuals 40-60 years	GI, OHI-S, PDI, AL	x	Total Cholesterol, LDL, HDL and triglycerides	No association between serum lipid levels and periodontal disease parameters
Kaisere *et al.*[22]	India	Br Dent J	500 (250 AMI and 250 CHD patients)	DMFT, PD, OHI-S, BOP	x	Total Cholesterol, LDL, HDL and triglycerides	Poor oral parameters and serum lipid levels associated with AMI

BOP – Bleeding on probing; PD – Probing depth; CAL – Clinical attachment; PI – Plaque index; GI – Gingival index; PBI – Papillary bleeding index; ABL – Alveolar bone level; CPI – Community periodontal index; OHI-S – Oral hygiene index-simplified; LOA – Loss of attachment; DMFT – Decayed, missing and filled teeth; PDI – Periodontal disease index; AL – Attachment loss; ABL – Alveolar bone level; hsCRP – High-sensitivity C-reactive protein; FIB – Fibrinogen; WBC – White blood cells; TNF-α – Tumor necrosis factor-α; CHD – Coronary heart disease; CAD – Coronary artery disease; AMI – Acute myocardial infarction; HDL – High density lipoproteins; LDL – Low density lipoproteins

studies[34,35] have reported the status and gravity of stroke in Pakistan and have shown that 46% of the stroke patients had cardiac disease and 30% had hyperlipidemia, whereas carotid artery stenosis was noted in 8%. Peripheral artery disease (PAD) shares a common underlying pathological change, atherosclerosis, with CHDs and stroke.[36] The disease is reported to be under diagnosed, under treated, and poorly understood by the medical community and rate of death from myocardial infarction; stroke is increased in patients with symptomatic and asymptomatic peripheral arterial disease.[37] A recent study[38] reported incidence of peripheral arterial disease in 17.7% acute coronary syndrome (ACS) patients of Karachi, Pakistan.

Since Mattila *et al*.[39] reported the association of dental infections with CVD; researchers have tried to collect further evidence on the biological plausibility of this association. Over the last two decades, epidemiological, etiopathological and clinical studies have implicated periodontal disease as a risk factor for the development of CVD and suggested various pathways involved in the potential mechanism to link these conditions. A number of epidemiological studies[40-49] have suggested the role of infectious and inflammatory periodontal disease in the initiation/progression of CVD and have addressed the mechanisms by which periodontal disease may influence the development of CVD. The epidemiological evidence from South-Asia also support the notion observed in these studies.

Helfand *et al*.[4] reported a nonexplanatory nature of traditional risk factors for incident CHD and evaluated novel or emerging risk factors of CRP, coronary artery calcium score, lipoprotein level, homocysteine level, leukocyte count, fasting blood glucose, periodontal disease, ankle-brachial index, and carotid intima-media thickness which detection and/or control of any one factor might potentially contribute to improvement in global risk assessment for CHD. These emerging risk factors have been observed in case–control studies[14,15,17-20,22] from India and Pakistan and randomized trials[9-13] have provided evidence of reduction in serum levels by improving periodontal health.

The positive association of oral infections and tooth loss to CVDs has also been observed.[39,40,50-54] Few studies[55-57] reported a less convincing relationship or no association of oral health indicators (gingivitis, dental caries or tooth loss) with CVD or CHD; these findings correspond with the findings of studies[16,21] from South-Asia. However other studies[39,40,58-64] provided strong evidence regarding relationship between oral/periodontal diseases to CVDs and CHD. The relationship between PD and ischemic stroke has been studied, and the outcome is different across the various studies, ranging from total stroke to fatal stroke, nonfatal stroke, and ischemic stroke.[65-67] Men with periodontal disease or any tooth loss showed a significantly higher risk of peripheral arterial disease (PAD) than men without periodontitis or without any tooth loss during a follow-up period of study.[36] Mendez *et al*.[68] reported subjects with clinically significant periodontal disease were at higher risk of having PAD at baseline.

Poor oral health and CVD are major health problems worldwide and of significant public health importance. Evidence from epidemiological and clinical studies provides an insight into their potential association; therefore it is rational to investigate potential contributing mechanisms by periodontitis that could play a role in increasing someone's risk for CVDs. A higher prevalence of periodontal disease is observed in developing countries[69] and the five South-Asian countries have the highest rates of periodontal diseases and CVD. The much more prevalence and severe problem of periodontal disease in developing countries seems to be truly reflected by poorer oral hygiene and considerably more plaque retentive factors in the form of calculus, often evident in individuals at a young age.[70] Dietary habits[71] tooth brushing habits,[72] smoking, or tobacco use[73,74] alcohol use,[75] psychosocial,[76] and life style[77] factors related to the periodontal diseases have also been observed in CVD patients in Asian countries. Within the Asia and Oceania region, many countries still have poor economic status, high illiteracy levels and a very low dentist to population ratios.[1]

SUMMARY

Periodontal diseases are public health problem worldwide and more so in developing countries; the specific and unique needs of low-and middle-income countries and that of their poor and under-privileged population groups are to be identified and recognized for a population-based, national oral health program.[23] The health and economic implications of this staggering rise in early CVD deaths in South Asian countries are profound and warrant prompt attention from governing bodies and policymakers of these countries.

Although current scientific research proves deep connections of periodontal and CVDs; however in the absence of hard evidence (from Asia) that these diseases are of public health problems, these diseases remain outside of mainstream public health planning in the countries' concern. The challenges, in developing countries, to address the increasing burden of CVD include low health budgets, education and skill of health care workforce.[78] The same challenges may contribute to poor oral health that is also associated with higher CVD risk. In view of the low socioeconomic status and high treatment cost, preventive measures need to be introduced to reduce morbidity and mortality of these chronic diseases. If unattended, growing levels of CVDs in South Asian countries may induce substantial economic and social impacts in the future. The limitations observed in the studies conducted on the topic in South Asian countries may be small sample sizes and single center. There is also lacking of large scale cross sectional studies.

RECOMMENDATIONS

On the basis of current evidence on the epidemiology and association of periodontal and CVDs in South Asian countries, there is a need to encourage meticulous research not only from scientific point of view but from public health perspective also. A multi-factorial risk screening and intervention approach at the population level could provide immediate benefit.[30] To slow the momentum of CVD in developing countries, major initiatives regarding promotion of diet and physical activity, creation of awareness among both sexes, or development of guidelines for risk reduction, appropriate therapeutic and surgical strategies, are needed to combat periodontitis and CVD.[31]

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