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LIPID PROFILE AND MARKER OF INFLAMMATION IN CHRONIC PERIODONTITIS

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ABSTRACT

Periodontal infections are the most important oral health burdens faced by both developed and developing countries of the world. These, predominantly gram negative infections cause systemic inflammation and have been implicated in the development of hyperlipidaemia, which is an important risk factor for development of cardiovascular diseases. However, some studies in recent times have found contradictory results. In this cross-sectional study, we measured levels of C - Reactive Protein (CRP) and lipid profile. We found that as compared to controls, patients with chronic periodontitis had higher mean CRP levels, total cholesterol, serum triglycerides and lower HDL cholesterol. Results of this study supports the hypothesis that localized inflammation, such as that in periodontitis, may result in systemic inflammation which may play an important role in the pathogenesis of many adverse systemic conditions such as atherosclerosis and cardiovascular complications.

KEY WORDS: Periodontitis, Inflammation, lipid profile, cardiovascular diseases, C – Reactive Protein.

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INTRODUCTION

Periodontitis is defined as a chronic inflammatory disease of the periodontium occurring in response to bacterial plaque on the adjacent teeth, characterized by gingivitis, destruction of alveolar bone and periodontal ligament, apical migration of the epithelial attachment resulting in the formation of periodontal pockets and ultimately loosening and exfoliation of teeth.[1] Periodontitis is found in 10-15% of the adult population worldwide.[2] It definitely would be much more in the developing countries of the world. Early studies done in India indicate that the population is highly susceptible to periodontitis. However, very limited studies provide prevalence data because of non-availability of standardized population-based studies.[3] Periodontitis is definitely one of the most significant oral health burdens faced by the world. In the recent times, increasing number of studies have focused their attention on the association between periodontal infections and systemic diseases. Many studies in literature provide clinching evidence to support the role of periodontal organisms in the development and progression of diseases and conditions like Diabetes Mellitus, Metabolic Syndrome, coronary heart disease (CHD), atherosclerosis, stroke, chronic obstructive pulmonary disease, adverse pregnancy outcomes, kidney diseases, etc.[4-9,10(Fig 1)] Hosts' response to the organisms causing periodontitis varies between individuals. Certain systemic disorders and conditions alter host tissues and physiology which may impair host barrier integrity and host defense to periodontal infection resulting in more destructive disease. [11] Various independent studies have revealed that localized inflammation within the oral cavity has systemic implications causing release of cytokines and acute phase proteins like C-reactive protein (CRP), haptoglobin, fibrinogen, etc. Chronic inflammation in the body is measured by the elevated levels of inflammatory markers and CRP is the marker of choice in monitoring the acute phase response as it increases to a relatively high concentration compared to basal concentration.[12] A bidirectional relationship may exist between periodontitis and systemic conditions, as both are inflammatory in nature. Some of these diseases share common risk factors with periodontitis like smoking, diabetes, genetic predisposition, low socioeconomic status, etc. Hyperlipidemia involves various disturbances of cholesterol and triglyceride levels, many forms of which are recognized risk factors for cardiovascular diseases. A lipid profile or lipid panel is a panel of blood tests that serves an as initial broad medical screening tool for abnormalities in lipids. There is abundant literature delving into the influence of periodontal diseases on hyperlipidaemia.[13] Lately, many questions are being asked about this association by the medical fraternity and some studies have also reported the lack of correlation between periodontitis and altered lipid profile.[14-15] Therefore, there is still debate regarding potential relationships between the two conditions. We therefore set out to explore whether there is any association between periodontal infection, CRP levels and lipid profile of the patients. An added objective of this research was to analyze the correlation between severity of periodontal inflammation and its effect on CRP and lipid profile levels.

MATERIALS AND METHODS

This cross-sectional study (Case Control) was conducted from Jan 2011 to Jun 2012 after the protocol was approved by the Institutional Ethics Committee of MGV's KBH Dental College and Hospital, Nasik and Human Ethics Committee, UDIRT, MUHS, Nasik.

Periodontal parameters

A full-mouth periodontal examination was performed by a single examiner (N.D). The patients were classified as having mild, moderate or severe periodontitis on the basis of extent and severity index.[16]

The following periodontal parameters were assessed using a graduated UNC15 probe at 6 sites per tooth i.e. mesio-buccal, mid-

buccal, disto-buccal, mesio-lingual, mid-lingual and disto-lingual:

1. Probing Pocket Depth (PPD)
2. Clinical Attachment Loss (CAL)
3. Bleeding on probing (BOP)

Inclusion criteria

1. CONTROL GROUP (CG)

a. Included both, periodontally healthy and patients with gingivitis.
b. At least 14 teeth in mouth.
c. BOP at sites with PPD of 1-3mm.

2. STUDY GROUP (SG) Patients with periodontitis

a. At least 14 teeth in mouth,
b. CAL of 1mm or more with BOP, at more than 30% of all sites in the mouth.

Exclusion criteria

1. Unfavourable systemic conditions (rheumatic fever, heart problems, diabetes, hypertension, liver or kidney diseases, etc.
2. Any infection requiring prophylactic antibiotic treatment.
3. Pregnant and lactating women, women on hormonal contraceptives or on HRT
4. Patients taking steroids or NSAID (for previous 3 months) or vitamin supplements.
5. Persons who have undergone scaling/root planing in the past 6 months.

150 subjects in the age group of 18-70 years with chronic periodontitis and 150 healthy controls, satisfying the inclusion and exclusion criteria, became part of the study. Patients' enrollment was done so that in the study group, we had 50 patients each with mild, moderate and severe periodontitis. They were recruited from the Out Patient Department of MGV's KBH Dental College & Hospital, Nashik. Prior to enrollment in the study, patients/candidates were given detailed oral information about the study. A Patient Information Sheet (PIS) was handed over to them and written informed consent obtained.

Physical parameters

Physical examinations included Blood Pressure, weight, height and BMI assessments. BMI was calculated as weight (Kg)/ height in (m^2)

Biochemical parameters

5 ml blood sample was collected by venipuncture from the median cubital vein and was transferred in plain bulb. Sample was allowed to clot at room temperature before centrifugation to collect serum. These were analyzed the same day for the following parameters

1. Total Cholesterol and HDL- Cholesterol estimation. (Enzymatic Diagnostic kit from Accurex Biomedical Pvt. Ltd.,Thane, India)
2. Estimation of serum triglycerides. (Enzymatic Diagnostic Kit from Accurex Biomedical Pvt. Ltd., Thane, India)
3. C-Reactive Protein Estimation (Immunoturbidometric Method using Turbilyte CRP kit from Tulip Diagnostic (P) Ltd., Goa, India.

RESULTS

Statistical analysis

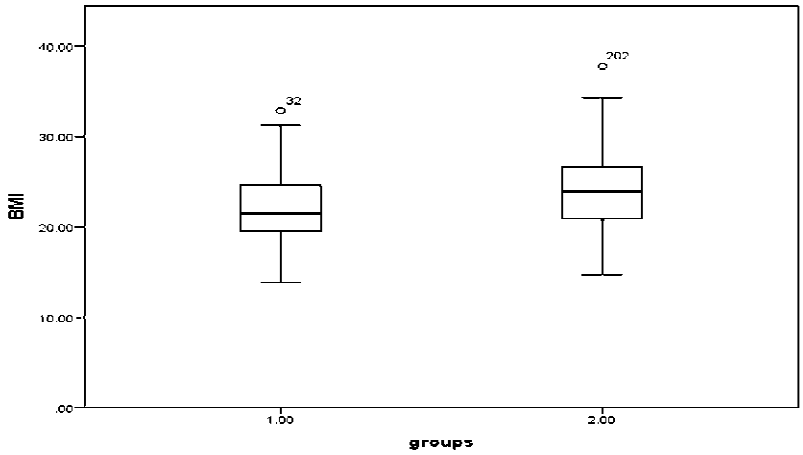
Statistical analysis was done by using students't' test and the data was expressed as mean ± standard deviation. Probability values of <0.05 were considered to be statistically significant. The comparison of control group was carried out with the study group with respect to mean value and standard deviation. Two sample't' test was applied at 299 degrees of freedom and 95% confidence interval. For comparison of parameters between controls and various categories of periodontitis, one-way ANOVA was applied. The results obtained are tabulated. (table 1 & 2)

Table 1
Comparison of mean values of the various parameters in both groups

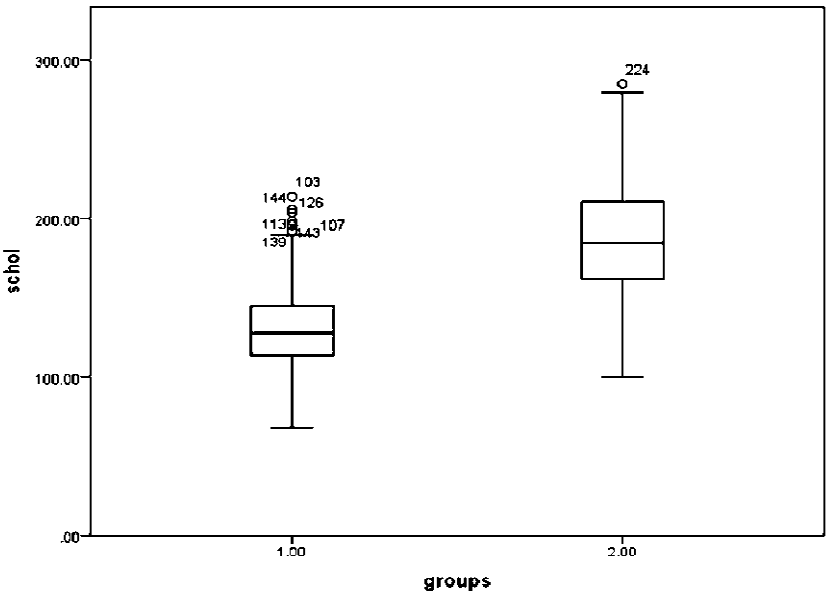
Parameter	Control Gp(1)	Study Gp(2)	P value
No. of Cases	150	150	
Females	30	36	
Males	120	114	
Mean Age	34.18±12	41±12.24	<0.001*
Mean BMI	22.12±3.72	24.09±4.22	<0.001*
S. Chol	131.09±28.62	185.24±36.74	<0.001*
HDL Chol	45.26±7.04	38.18±8.62	<0.001*
S TG	80.57±28.21	133.52±48.88	<0.001*
CRP	0.28±0.37	1.62±1.17	<0.001*

significant

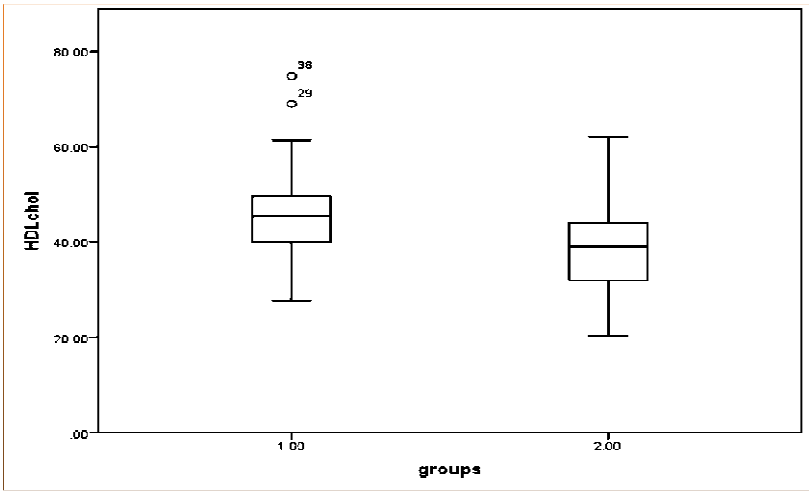
Graph 1
Box-plot showing mean BMI in controls and cases



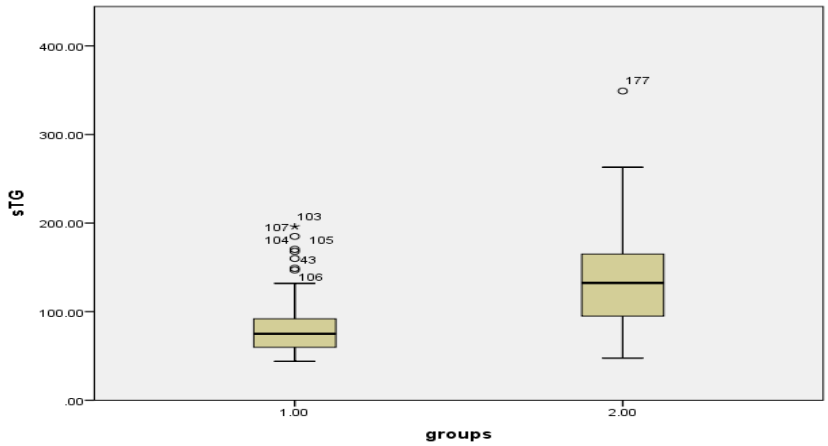
Graph 2
Box-Plot depicting mean serum cholesterol in controls and cases



Graph 3
Box-plot showing mean HDL Cholesterol in controls and cases



Graph 4
Box-Plot showing mean Serum Triglycerides in controls and cases



Graph 5
Box-Plot comparing mean CRP values in controls and cases

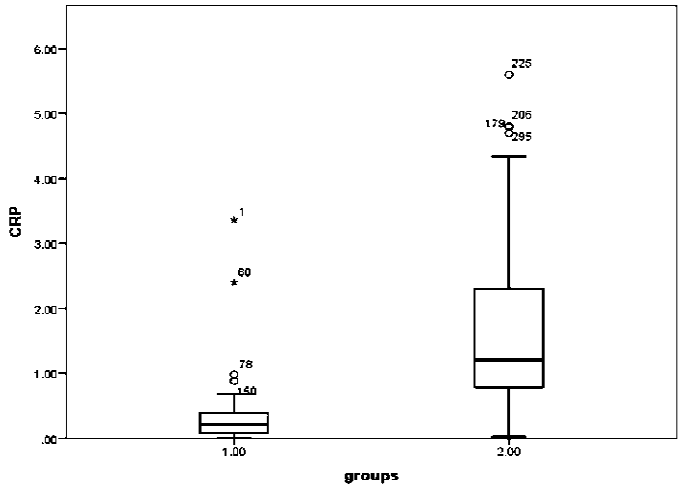


Table 2
Comparison of mean values of various parameters with controls after stratification

Parameter	Control	Mild	Moderate	Severe	p value
S Chol	131.09±28.62	170.60±33.81	190.88±36.96	193.83±35.61	<0.001*
HDL Chol	45.26±7.05	39.31±7.36	37.11±8.11	38.16±10.15	<0.001*
STG	80.57±28.21	121.24±53.10	128.72±42.61	150.45±46.71	<0.001*
CRP	0.283±0.37	1.059±0.94	1.736±1.23	2.058±1.10	<0.001*

Table 1 depicts the baseline characteristics for the 150 patients with periodontitis and 150 controls. Patients with periodontitis were significantly older than healthy controls. (34.18±12 versus 41.00±12.24 years, P< 0.001). It indicates that risk of periodontitis increases with increasing age. Significant difference was found between the mean BMI of controls and that of patients with periodontitis. The results of the present study seem to indicate that patients with moderate to severe periodontitis have significantly higher BMI than controls. (22.12±3.72 versus 24.09±4.22) The lipid profile of patients with periodontitis exhibited significantly higher levels of total cholesterol (p< 0.001) and serum triglycerides (p<0.001) and lower HDL cholesterol (p< 0.001) as compared to healthy controls. In our study, we found that controls have lower mean CRP values as compared to study group (0.28±0.37 versus 1.62± 1.17). Graphs 1-5 are box plots depicting mean values of controls (1) versus cases (2) with respect to BMI, total cholesterol, HDL cholesterol, serum triglycerides and CRP respectively.

Table 2 depicts the comparison of mean values of CRP and lipid profile after one-way ANOVA was applied to control, mild, moderate and severe categories. After stratification of patients on the basis of increasing severity of periodontitis, there still was significant difference in the mean total cholesterol and serum triglyceride values between the various categories. Similarly, CRP values also increased in a dose-response manner with severity of periodontitis.

DISCUSSION

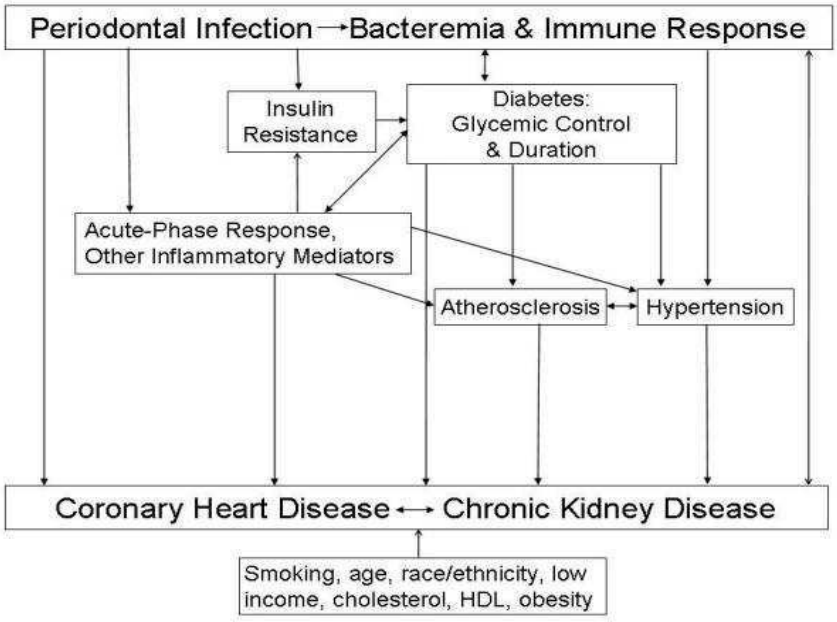
Patients were screened and included in the study when they came to the hospital for treatment. Hence, prior short-listing to have equal number of males and females was not possible. It was also not possible to have age and sex matched controls. We got considerably lesser number of women as compared to men in both the categories. Not much of importance can be attributed to this except that number of female patients visiting the OPD was considerably lesser than that of males. With this data it is difficult to say whether females have lesser dental problems as compared to males or if women tend to postpone dental visits till it becomes inevitable. Chronic inflammation in the body is measured by the elevated levels of inflammatory markers like CRP. Most of the studies available in literature are unanimous in their opinion that there is a positive association between periodontitis and CRP levels.[17-18] On the other hand, Kshirsagar et al found no association of severe periodontitis with CRP when they studied patients on hemodialysis.[19] Our results of the association of periodontitis and altered lipid profile are in agreement with Joshipura et al[20] who too found significant association of periodontal disease with biomarkers of endothelial dysfunction and dyslipidemia. Low grade chronic inflammation causes endothelial cell activation which is an early event in atherogenesis which in turn poses increased risk of atherosclerotic cardiovascular disease.[21] The extent of increase in CRP levels in periodontitis patients depends on the severity of the disease after adjusting for age, smoking, body mass index, triglycerides, and cholesterol. Localized inflammation caused by periodontal pathogens ultimately causes systemic inflammation. This positive correlation between CRP and periodontal disease might be a possible underlying pathway in the association between periodontal disease and the observed higher risk for CVD in these patients.[22] Iacopino and Cutler[23] say that there appears to be more than a casual relationship between serum

lipid levels and systemic health (particularly CVD, diabetes, tissue repair capacity, and immune cell function), susceptibility to periodontitis, and serum levels of pro-inflammatory cytokines. They say that it is possible that periodontitis-induced changes in immune cell function cause metabolic dysregulation of lipid metabolism through mechanisms involving proinflammatory cytokines. Uchiumi et al[24] carried out subcutaneous and continuous administration of lipopolysaccharide (LPS) in rats, which was considered to mimic chronic infection such as periodontal disease, and investigated its effect on the serum levels of TG, total cholesterol (TC) and free fatty acids (FFA) and cytokines. They found that serum FFA increased only slightly, whereas serum TC levels did not change appreciably. There was a significant increase in the levels of serum TG leading the authors to conclude that periodontal disease induces hypertriglyceridemia that increases the risk of atherosclerotic cardiovascular disease. Nibali et al[25] examined 302 patients with severe periodontitis and 183 controls to investigate differences in inflammatory and metabolic markers. After correcting for differences in age, gender, smoking and ethnicity, periodontitis subjects exhibited a low-grade systemic inflammation, dyslipidemia (lower HDL- cholesterol & higher LDL- cholesterol) and increased non-fasting glucose levels when compared to controls. A trend for a dose dependent effect of the number of periodontal pockets on the tested inflammatory and metabolic markers was observed suggesting a possible link between severe generalized periodontitis, systemic inflammation and a dysmetabolic status in otherwise healthy individuals. Losche W et al[26] also found similar results in their study of 39 subjects with moderate periodontal disease. Not only were total cholesterol, LDL cholesterol and TG significantly higher in periodontally diseased subjects, but there were also significantly higher frequency of pathological lipid profiles in the patient group. Similar results were also obtained by Moeintaghavi et al.[27] They found patients with periodontitis to have higher total cholesterol and triglycerides than controls but HDL and LDL cholesterol did not show significant differences. Taleghani et al[28] also found higher levels of TG and significantly higher levels of serum cholesterol in patients with periodontitis. Though they agree that patients with chronic periodontitis are more susceptible to hyperlipidemia, they express doubts about periodontitis being the cause for this increase. But, according to Tandon et al,[29] low level, chronic exposure to gram negative microorganisms and/ or their LPS can manifest a state of altered lipid metabolism; the main features of which are hypertriglyceridemia and lipid oxidation. The underlying mechanism for these alterations is the release of cytokines like TNF-α and IL which in turn affect lipid metabolism by influencing the production of other cytokines thus altering hemodynamics/ amino acid utilization of various tissues involved in lipid metabolism or modifying the hypothalamic-pituitary-adrenal axis, increasing plasma concentrations of adrenocorticotropic hormone, cortisol, adrenaline, nor-adrenaline and glucagon. The above modifications in turn, lead to enhanced hepatic lipogenesis, increased synthesis or reduced clearance of triglycerides and reduced clearance of LDL due to reduced lipoprotein lipase activity.

Page and Schroeder[30] gave insight into the pathogenesis of human periodontitis. Bacterial products like-LPS have the ability to initiate destructive processes. Microorganisms like *Porphyromonas gingivalis*, *Tannerella forsythia* (formerly *Bacteriodes forsythus*) and *Aggregatibacter actinomycetemcomitans*(formerly *Actinobacillus actinomycetemcomitans*), etc. produce enzymes that breakdown extracellular matrix such as collagen host cell membrane to produce nutrients for their growth and further tissue invasion, thereby initiating an immune and inflammatory process which stimulates the host to release various pro-inflammatory cytokines, Matrix metalloproteinases (MMP), prostaglandins(PGs) and host enzymes. The periodontal pocket serves as a portal of entry for pathogenic bacteria and their products into systemic circulation. In patients with moderate or severe periodontitis, the large surface area of the periodontal lesion serves as a significant source of inflammation. Periodontitis causes elevations of serum

proinflammatory cytokines such as IL-1 beta and TNF-α, which have been demonstrated to cause hyperlipidemia. Hence periodontitis may play a role in increasing serum lipids and proinflammatory cytokines leading to systemic complications arising out of this situation.[31] Conclusive evidence in this regard was provided by D' Aiuto et al[32] when they showed in their studies that there are significant reductions in inflammatory markers in response to non-surgical periodontal therapy. A Brazilian study assessed whether periodontal inflammation and tissue destruction are associated with CRP and lipids in stable heart disease patients. They found high levels of periodontal inflammation and tissue destruction with significantly higher triglyceride and VLDL cholesterol levels in their study group. Higher CAL and presence of severe periodontitis were significantly associated with higher CRP concentrations and pathological lipid profile.[33] In our study, we have found a possible association between periodontitis, inflammation and hyperlipidemia. Inflammation and hyperlipidemia may put the patients with periodontitis at a higher risk for development of cardiovascular diseases. We have also been able to rediscover that abnormal lipid profile and increased CRP are associated with increasing severity of periodontitis However, this being a cross-sectional study, we cannot show cause- effect relation between periodontitis and lipid profile. More studies are needed to provide concrete evidence to confirm if periodontitis is an independent risk factor for development of pathological lipid profiles. But the results definitely seem to indicate that oral health and treatment of periodontal diseases should be given utmost importance for improving the overall health of the individual.

Figure 1
Association between periodontal infection and systemic conditions[10]



REFERENCES

1. Stedman's Medical Dictionary, 28th Edition, Copyright@ 2006_Lippincott Williams & Wilkins. Available at http://dictionary.webmd.com/terms/periodontitis accessed 26 Jul 2012.
2. Eke PI, Dye BA, Wei L, Thornton- Evans GO, Genco RJ, Beck J, et al, Prevalence of periodontitis in adults in the United States: 2009 and 2010. J Dent Res, 91(10): 914-920, (2012 Oct)

3. Shaju JP, Zade RM, Das M, Prevalence of periodontitis in the Indian Population: a literature review. Journal Indian Soc of Periodontol, 15(1): 29-34, (2011)
4. Iacopino AM, Periodontitis and Diabetes interrelationships: role of inflammation. Ann. Periodontol., 6(1): 125-137, (2001 Dec)
5. Bullon P, Morillo JM, Ramirez-Tortosa MC, Quiles JL, Newman HN, Battino M, Metabolic syndrome and periodontitis: Is oxidative stress a common link. J. Dent Res., 88(6): 503-518, (2009 Jun)
6. Amar S, Gokce N, Morgan S, Loukideli M, Van Dyke TE, Vita JA, Periodontal disease is associated with brachial artery endothelial Dysfunction and Systemic Inflammation. Arteriosclerosis, Thrombosis and Vascular Biology, 23: 1245-1249, (2003)
7. Offenbacher S, Jared HL, O,Reilly PG, Wells SR, Salvi GE, Lawrence HP, et al, Potential pathogenic Mechanisms of periodontitis associated pregnancy complications. Annals of periodontology, 3(1): 233-250, (1998 Jul)
8. Kshirsagar AV, Moss KL, Elter JR, Beck JD, Offenbacher S, Falk RJ, Periodontal disease is associated with renal insufficiency in the Atherosclerosis Risk in Communities (ARIC) Study. Am J Kidney Dis., 45(4): 650-657, (2005 Apr)
9. Mealey BL, Klokkevold PR. Periodontal Medicine: Impact of Periodontal Infection on Systemic Health. In: Newman, Takei, Klokkevold, Carranza (eds), *Carranza's Clinical Periodontology,* 10th Edition, Saunders Elsevier, South-Asia Edition, New Delhi, 2006, pp. 313.
10. Fisher MA, Borgnakke WS, Taylor GW, Periodontal disease as a risk marker in coronary heart disease and chronic kidney disease. Curr Opin Nephrol Hypertens., 19(6): 519-526, (2010 Nov) Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC3084591/figure/F1/ (accessed 15 Aug 13)
11. Sreeram M, Suryakar A, Dani N, Khedkar S, Periodontal disease and its association with chronic disease: A Literature Review. Int J Pharm Bio Sci, 3(3): B82-89. (2012 Jul)
12. Ramamoorthy RD, Nallasamy V, Reddy R, Esther N, Maruthappan Y,A review of C-reactive protein: A diagnostic indicator in periodontal medicine. Journal of Pharmacy and BioAllied Sciences, 4(6): 422-426, (2012)
13. Macoveri-Surdu A, Rudnic I, Martu I, Solomon S, Pasarin L, Martu S, Studies regarding the bidirectional relationship between the periodontal disease and hyperlipidaemia. Romanian Journal of Oral Rehabilitation, 5(1): 77-82, (2013 Jan-Mar)
14. Bagavad Gita, Sajja C, Padmanabhan P, Are lipid profiles true surrogate biomarkers of coronary heart disease in periodontitis patients?: A case- control study in a south Indian population. J Indian Soc Periodontol.,16(1): 32-36, (2012 Jan-Mar)
15. Hamissi J, Shahsavarani MT, Hamissi H, A Comparison of Serum Lipid Profile between Periodontitis Patients and Healthy Individuals. Iranian Red Crescent Medical Journal,13(4): 283-284, (2011 Apr)
16. Beck JD, Arbes Jr SJ. Epidemiology of Gingival and Periodontal Diseases. In: Newman, Takei, Klokkevold, Carranza (eds), *Carranza's Clinical Periodontology,* 10th Edition, Saunders Elsevier, South-Asia Edition, New Delhi, India, 2006, pp. 121.
17. Gomes-Filho IS, Frietas C JM, da Cruz SS, Passos JS, Teixeira de Freitas CO, Aragao Farias NS, et al, Chronic periodontitis and C-Reactive Protein levels. J Periodontol., 82(7): 969-978, (2011 Jul)
18. Thakare KS, Deo V, Bhongade ML, Evaluation of the C-Reactive Protein serum levels in periodontitis patients with or without atherosclerosis. Indian J Dent Res., 21(3): 326-329, (2010 Jul-Sep)
19. Kshirsagar AV, Craig RG, Beck JD, Moss K, Offenbacher S, Kotanko P, et al, Severe periodontitis is associated with low serum albumin among patients on maintenance hemodialysis therapy.

Clin J Am Soc Nephrol., 2(2): 239-244, (2007 Mar)
20. Joshipura KJ, Wand HC, Merchant AT, Rimm EB, Periodontal disease and biomarkers related to cardiovascular disease. Journal of Dental Research, 83(2): 151-155, (2004 Feb)
21. Cleland SJ, Sattar N, Petrie JR, Forouhi NG, Elliott HL, Connell JM, Endothelial dysfunction as a possible link between C-reactive protein levels and cardiovascular disease. Clin Sci (Lond)., 98(5):531-535, (2000 May)
22. Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, De Nardin E, Periodontal infections contribute to elevated systemic C-reactive protein level. J Periodontol., 72(9): 1221-1227, (2001 Sep)
23. Iacopino AM, Cutler CW, Pathophysiological relationships between periodontitis and systemic disease: recent concepts involving serum lipids. J Periodontol., 71(8): 1375-1384, (2000 Aug)
24. Uchiumi D, Kobayashi M, Tachikawa T, Hasegawa K, Subcutaneous and continuous administration of lipopolysaccharide increases serum levels of triglyceride and monocyte chemoattractant protein-1 in rats. J Periodontal Res., 39(2): 120-128,(2004 Apr)
25. Nibali L, D'Aiuto F, Griffiths G, Patel K, Suvan J, Tonetti MS, Severe periodontitis is associated with systemic inflammation and a dysmetabolic Status: a case-control study. J Clin Periodontol., 34(11): 931-937, (2007 Nov)
26. Losche W, Karapetow F, Pohl A, Pohl C, Kocher T, Plasma lipid and blood glucose levels in patients with destructive periodontal disease. J Clin Periodontol., 27(8): 537-541, (2000 Aug)
27. Moeintaghavi A, Haerian-Ardakani A, Talebi-Ardakani, Tabatabaie I, Hyperlipidemia in patients with periodontitis. J Contemp Dent Pract, 6(3): 78-85, (2005 Aug)
28. Taleghani F, Shamaei Mahmoud, Shamaei Masoud, Association between Chronic Periodontitis and Serum Lipid Levels. Acta Medica Iranica, 48(1): 47-50, (2010)
29. Tandon Shruti, Dhingra MS, Lamba AK, Verma M, Munjal A, Faraz F, Effect of Periodontal Therapy on Serum Lipid Levels. Indian Journal of Medical Specialities, Doi: http://dx.doi.org/10.7713/ijms.2010.0005 , (2010 May) (accessed 16 Aug 2013)
30. Page RC, Schroeder HE, Pathogenesis of inflammatory periodontal diseases. A summary of current work. Lab Invest, 34(3): 235-249, (1976 Mar)
31. Seymour RA, Is gum disease killing your patient? Br Dent J, 206(10): 551-552. Doi 10.1038/sj.bdj.2009.472, (2009 May)
32. D'Aiuto F, Parkar M, Andreou G, Suvan J, Brett PM, Ready D, Tonetti MS, Periodontitis and systemic inflammation: Control of the local infection is associated with a reduction in serum inflammatory markers. Journal of Dental Research, 83(2): 156-160, (2004 Feb)
33. Flores MF, Montenegro MM, Furtado MV, Polancezyk CA, Rosing CK, Haas AN, Periodontal Status Affects C-Reactive Protein and Lipids in Stable Heart Disease Patients From a Tertiary Care Cardiovascular Clinic. Journal of Periodontol Online, Doi:10.1902/jop.2013.130255, (2013 Jun)