Comparative Evaluation of the Lipid Profile in the Serum of Patients with Type II Diabetes Mellitus and Healthy Individuals with Periodontitis

Abstract

Context: Periodontal disease is an immuno-inflammatory disease that is initiated by the interaction between microbial plaque and the periodontal tissues. The data available on the association of periodontal diseases with the lipid profile are conflicting. Therefore, a need for a study in this area was felt. Aims: To evaluate the lipid profile in the serum of patients with chronic periodontitis and chronic periodontitis with Type II diabetes mellitus (DM) patients and to compare it with healthy controls, to see whether they can serve as potential markers for chronic periodontitis and also to assess whether periodontitis can have systemic effects. Settings and Design: This study is a cross-sectional study. Subjects and Methods: This cross-sectional study was conducted involving 300 participants in the age group of 30–60 years from October 2010 to May 2015. Five milliliters of venous blood was collected from each of the study participants, from the antecubital vein. Lipid profile was assessed using the ERBA commercially available kit. Statistical Analysis: Statistical analysis was carried out using SPSS software version 17. Multigroup comparison was carried out using ANOVA. The honest significant difference Tukey’s test was used in conjunction with ANOVA to find means which are significantly different from each other. Results: When the lipid profile was estimated, total cholesterol (TC) levels were seen to be significantly higher (P < 0.001) in the DM with periodontitis group. High-density lipoprotein (HDL) levels were seen to be significantly higher (P < 0.001) in the control group. Mean serum low-density lipoprotein (LDL) and very LDL (VLDL) levels were seen to be significantly higher (P < 0.001) in the DM with periodontitis group. The triglyceride (TGL) values were also significantly higher (P < 0.001) in the DM with periodontitis group. The HDL and LDL levels were seen to be nonsignificant between chronic periodontitis and chronic periodontitis with diabetic group. Conclusions: The findings of the study showed that the lipid profile was significantly altered in patients with chronic periodontitis as compared to healthy controls. There was a potentiated difference in the values for TC, VLDL cholesterol, and TGL in patients with chronic periodontitis when compared to patients with Type II DM. HDL cholesterol and LDL cholesterol did not show a significant difference.

Keywords: High-density lipoprotein cholesterol, low-density lipoprotein cholesterol, total cholesterol, triglyceride, Type II Diabetes mellitus, very low-density lipoprotein cholesterol

Introduction

Periodontal disease is an immuno-inflammatory lesion occurring as a result of an interaction of the microbial plaque biofilm with the immune-inflammatory response of the host and the subsequent alterations in the homeostasis of the bone and connective tissues. Traditionally, it has been accepted that periodontitis is an oral disease, and the destruction of the tissues remains localized within the periodontium; however, current evidence suggests that periodontitis can produce alterations in systemic health.

Periodontitis has been recognized today as the 6th complication of diabetes mellitus (DM). Both the chronic disease conditions are said to have a bidirectional relationship. The two diseases have the capacity to induce an inflammatory response leading to the production of various mediators of inflammation. There is sufficient evidence available today to suggest that Type II DM is associated with an increased prevalence, extent, and severity of periodontal disease.

Hyperlipidemia is considered as one of the main risk factors for cardiovascular diseases. The currently accepted risk factors for hyperlipidemia include a diet that is rich in fats, lack of physical exercise, and genetics. Recent evidences suggest that periodontal diseases also could be a risk factor for hyperlipidemia although

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the results are conflicting with several studies showing no association.\cite{6,7}

It is postulated that periodontal infections can affect systemic health, considering the large number of microorganisms associated with the disease, its chronic nature and the local and systemic immunologic responses of the host. A possible suggested mechanism is that chronic oral inflammation may lead to increase in the levels of blood cholesterol; however, research on this has shown conflicting results. The sustained rise in levels of the pro-inflammatory cytokines in chronic periodontitis can lead to abnormal serum lipid levels which can cause a deleterious effect on the general systemic health.\cite{9}

The current data available on the effect of periodontal diseases in altering the lipid metabolism leading to hyperlipidemia are conflicting. Studies have shown that Type II DM is positively correlated with hyperlipidemia and periodontitis does not show a definite association;\cite{10,11} however, other studies have shown a positive association between periodontitis and hyperlipidemia.\cite{10,11}

A study was conducted to examine whether dyslipidemia is associated with periodontitis in a total of 18,210 adults, part of the 4th Korea National Health and Nutrition Examination Survey. Results showed that periodontitis was significantly associated with low high-density lipoprotein (HDL) and high triglyceride (TGL) levels.\cite{12}

Another study conducted to assess the relation between serum lipids and periodontal infection, included 8028 participants, part of the Health 2000, Health Examination Survey in Finland. Serum levels of TGL, HDL cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) were calculated. The study did not find any association between serum lipid levels and periodontal infections.\cite{13}

Taking into consideration the bidirectional relationship between DM and periodontal disease, patients suffering from Type II DM with chronic periodontitis were also included in this study, to see whether there is a potentiated effect on the alteration in lipid profile levels in patients suffering from both the diseases.

Thus, the present study was conducted to evaluate the lipid profile, total cholesterol (TC), (HDL-c, LDL-c and very LDL cholesterol (VLDL-c), and TGL of the groups to better understand the association between periodontal disease and dyslipidemia.

**Objective**

To evaluate the lipid profile, TC, HDL-c, LDL-c, VLDL-c, and TGL, in the serum of patients with chronic periodontitis and chronic periodontitis with Type II DM patients and to compare it with healthy controls, to see whether they can serve as potential markers for chronic periodontitis and also to assess whether periodontitis can have systemic effects.

**Subjects and Methods**

A cross-sectional study was conducted involving 300 participants from Coastal Karnataka and North Kerala in the age group of 30–60 years reporting to the Department of Periodontics, at A B Shetty Memorial Institute of Dental Sciences from October 2010 to May 2015.

The sample size was calculated based on the assessment of various studies conducted earlier and the expected mean differences. The power of the study was fixed at 80%, and error was fixed at 5%.

The ethical clearance was obtained from the Central Ethics Committee, Nitte University on September 13, 2010, before the start of the study. All the participants enrolled into the study were given a consent form, which was explained to them and a written consent was obtained. A case history was recorded for each participant enrolled in the study as per the case history format.

The body mass index (BMI) of all the 300 participants were also assessed according to the criteria by Nieto-García et al.\cite{14} and participants who had a BMI above 25, i.e. overweight and obese individuals were excluded from the study.

Only participants who were free of any systemic diseases were included in Group I and III, and participants who were free of any systemic diseases other than Type II DM were included in Group II. The participants in Group II were those who were under treatment for Type II DM and on oral diabetic drugs and dietary modifications for more than 1 year and <5 years.

Participants included in Group I and II had chronic generalized severe periodontitis, as per the American Academy of Periodontology/Centers for Disease Control and Prevention classification of periodontal disease given by Eke et al.\cite{15} The diagnosis of chronic generalized severe periodontitis was established based on the clinical findings of gingival inflammation and clinical attachment loss more than 5 mm, pocket depth more than 4 mm at 3 or 4 sites in more than four teeth in each quadrant with radiographic evidence of bone loss. Periodontal health was established as the absence of clinical signs of gingival inflammation and no evidence of bone loss in participants with good oral hygiene. All participants underwent periodontal examination by a single trained examiner. Aggressive periodontitis patients were excluded from the study.

Participants with a history of intake of antibiotics in the previous 4 weeks, and also a history of intake of vitamin and mineral supplements and any periodontal treatment during the past 6 months were excluded from the study.

Participants with a history of any form of tobacco usage and alcoholism and pregnant and lactating women were also excluded from the study.
The random blood sugar (RBS) and glycosylated hemoglobin assay were estimated, and participants with a RBS score of <120 and hemoglobin A1c score of <7 were included in the study. The periodontal status was also assessed before allotting the participants to the various groups. A single trained investigator screened and allotted the patients to all the three groups.

The lipid profile was determined using the standard estimation kits available. TC levels were determined using the cholesterol oxidase-peroxidase methodology, HDL-c by the phosphotungstic acid method, and TGL by the glycerol phosphate oxidase-Trinder method. LDL-c was calculated as TC− (HDL-c + VLDL-c) and VLDL-c was calculated as TC/5. The DNA damage was assessed using the alkaline single cell gel (comet) assay.

**Results**

For assessment of the lipid profile, TC, HDL, LDL, VLDL, and TGL values were estimated for all the three groups [Graph 1].

TC levels were seen to be highest in Group II (186.87 ± 25.02), lower in Group I (177.09 ± 26.31), and lowest in Group III (157.56 ± 30.31) [Table 1].

When the mean serum cholesterol levels were compared between Group I and II, it was found to be statistically significant (\( P = 0.032 \)). When comparing between Group I and III and Group II and III also, the values were found to be significant (\( P < 0.001 \)) [Table 2].

HDL levels were seen to be highest in Group III (41.75 ± 12.50), lower in Group I (34.11 ± 9.69), and lowest in Group II (31.70 ± 10.06).

When the mean serum HDL levels were compared between Group I and II, it was found to be nonsignificant (\( P = 0.260 \)). When comparing between Group I and III and Group II and III, the values were found to be significant (\( P < 0.001 \)).

LDL levels were seen to be highest in Group II (111.79 ± 19.50), lesser in Group I (107.49 ± 22.99), and least in Group III (92.82 ± 20.42).

When the mean serum LDL levels were compared between Group I and II, it was found to be nonsignificant (\( P = 0.318 \)).

### Table 1: Comparison of the lipid profile among the 3 groups using one-way ANOVA

|       | n  | Mean±SD         | Minimum | Maximum | F     | P         |
|-------|----|-----------------|---------|---------|-------|-----------|
| TC    |    |                 |         |         |       |           |
| Group 1 | 100 | 177.0970±26.31267 | 107.14  | 215.30  | 29.712 | <0.001    |
| Group 2 | 100 | 186.8714±25.02833 | 124.30  | 250.85  |       |           |
| Group 3 | 100 | 157.5695±30.31160 | 101.81  | 214.20  |       |           |
| HDL   |    |                 |         |         |       |           |
| Group 1 | 100 | 34.1134±9.69034  | 13.41   | 56.43   | 23.496 | <0.001    |
| Group 2 | 100 | 31.7073±10.06201 | 12.63   | 55.84   |       |           |
| Group 3 | 100 | 41.7570±12.50685 | 18.44   | 82.35   |       |           |
| LDL   |    |                 |         |         |       |           |
| Group 1 | 100 | 107.4916±22.99392 | 33.17   | 188.56  | 22.377 | <0.001    |
| Group 2 | 100 | 111.7974±19.50494 | 11.32   | 150.10  |       |           |
| Group 3 | 100 | 92.8247±20.42721 | 44.50   | 174.62  |       |           |
| VLDL  |    |                 |         |         |       |           |
| Group 1 | 100 | 35.5545±12.71797 | 11.45   | 62.71   | 37.900 | <0.001    |
| Group 2 | 100 | 42.7081±17.25553 | 12.50   | 90.59   |       |           |
| Group 3 | 100 | 25.5356±11.37914 | 11.24   | 70.77   |       |           |
| TGL   |    |                 |         |         |       |           |
| Group 1 | 100 | 133.6461±21.60974 | 89.71   | 184.70  | 79.729 | <0.001    |
| Group 2 | 100 | 145.3746±18.58275 | 103.11  | 182.30  |       |           |
| Group 3 | 100 | 110.7162±18.89432 | 14.61   | 149.20  |       |           |

TC: Total cholesterol; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; VLDL: Very low-density lipoprotein; TGL: Triglyceride; SD: Standard deviation
Comparison between Group I and III and Group II and III showed the values to be significant ($P < 0.001$).

VLDL levels were seen to be highest in Group II (42.70 ± 17.25), lower in Group I (35.55 ± 12.71), and least in Group III (25.53 ± 11.37).

When the mean serum VLDL levels were compared between Group I and II, it was found to be significant ($P = 0.001$). Furthermore, comparing between Group I and III and Group II and III, values were seen to be significant ($P < 0.001$).

TGL values were seen to be highest in Group II (145.37 ± 18.58), lower in Group I (133.64 ± 21.60), and least in Group III (110.71 ± 11.37).

When the mean serum TGL values were compared between Group I and II, a statistically significant result was obtained ($P < 0.001$). Similar results were obtained when comparing between Group I and III and also between Group II and III ($P < 0.001$)

**Discussion**

Periodontal disease is the second most common oral disease that is initiated by specific species of pathogenic microorganisms in the dental biofilm. Inflammation is the central cause for tissue destruction that occurs in chronic periodontitis. In the periodontal tissues, the inflammatory process starts with the penetration of the various bacterial toxins and enzymes through the lining epithelium. The inflammatory process becomes chronic when the pathogenic microorganisms continue to grow and cannot be eliminated by the host response. Thus, the inflammatory reaction persists leading to damage to the periodontal tissues. Chronic periodontitis is thus characterized by persistent gingival inflammation, fibrosis, and loss of periodontal tissues. If not treated, it results in apical migration of the junctional epithelium and destruction of the periodontal attachment apparatus including the alveolar bone.

This local disruption of the homeostatic balance within the periodontal tissues may not be confined to the periodontium alone. Currently, research shows that cells of the immune system can transmit inflammatory responses to other parts of the body when challenged by local periodontal stimuli.[10]

The two possible mechanisms suggested by which this can occur are by direct migration and colonization of the pathogenic microorganisms to distant organs, leading to an inflammatory reaction at sites distant from the point of infection, and also the systemic inflammation as a result of metastatic periodontal inflammation.

Hence, in this study, to assess the lipid profile in patients with chronic periodontitis, the serum of patients was chosen as compared to saliva or gingival crevicular fluid to better understand the hypothesis that chronic periodontal inflammation can be a contributing risk factor for systemic inflammation at distant sites.

However, the studies that have demonstrated the association between periodontitis and various systemic diseases have been mostly retrospective studies. They can help to identify a possible association, but retrospective studies cannot demonstrate causation. Hence, the evidence available currently is insufficient to establish the association between periodontitis and various systemic diseases.

Among all the systemic disease studied, for their association with periodontitis, most evidence is available for the possible association between DM and periodontal diseases.
Studies on patients with diabetes and periodontal disease have revealed that both diseases have a synergistic effect when they coexist in an individual. However, the exact mechanisms by which hyperglycemia can lead to increased periodontal tissue destruction is not yet fully understood. It is hypothesized that long-term hyperglycemia, seen in patients with diabetes, can lead to increased anaerobic infections in the periodontal tissues with a hyperactive immune response, which can cause chronic inflammation in various organ systems of the body including the periodontium.

Hence, in this study, patients with chronic periodontitis with Type II DM have been included as a separate group, to see the extent of the potentiated effect of the two diseases existing together on the lipid profile.

In our study, the lipid profile was assessed for all the three groups, taking into consideration recent data which suggested that periodontal disease could be a risk factor for hyperlipidemia. Studies by Katz et al.\[4\] and Lösche et al.\[5\] have suggested an association between hyperlipidemia and periodontal diseases although the data on this are conflicting with studies by Machado et al.\[6\], Khoshkhounejad et al.\[7\], not reporting an association.

Assessment of TC levels showed the values to be highest in Group II, lesser in Group I, and least in Group III. The difference between the three groups was found to be statistically significant. The results are in accordance with studies conducted by Henrich et al.\[17\] and Hamissi et al.\[18\] which showed that periodontal disease was significantly related to higher TC levels.

A study by Almeida Abdo et al.\[9\] showed that TC was significantly increased in patients with Type II DM; however, periodontal disease did not show any significant correlation. The results of this study are contrary to the findings of our study regarding periodontal diseases.

Serum HDL-c levels showed the values to be highest in Group III, lesser in Group I, and least in Group II. Comparing Group I and II, the values were seen to be nonsignificant, but it was significant between Group I and III and Group II and III. Serum LDL-c levels were seen to be highest in Group II, lesser in Group I, and lowest in Group III. The values were nonsignificant between Group I and II, but significant between Group I and III and Group II and III. The serum VLDL levels also showed a similar pattern between the three groups; however, it was significant between all the three groups.

When the TGL values were assessed, it was seen to be highest in Group II, lesser in Group I, and least in Group III. The values were significant between the three groups.

The results are in accordance with the study by Penumarthy et al.\[10\] which showed that LDL-c, TGL, and TC were high, and HDL-c levels lower in the periodontitis patients as compared to controls.

A study by Taleghani et al.\[11\] showed that TC and TGL levels were significantly higher, but HDL-c and LDL-c did not show any significant difference in periodontitis patients as compared to healthy controls. Another study by Hamissi et al.\[18\] showed that HDL-c, LDL-c, and TGL levels did not show any difference between periodontitis and healthy controls, and only TC levels were significantly elevated in periodontitis patients.

A study by Pushparani et al.\[19\] on patients with Type II DM with periodontitis showed increased values of serum cholesterol and LDL-c and decreased HDL-c in periodontitis patients with Type II DM. These results are in accordance with the results of our study.

This study was performed without any case–control assessment. Therefore, several confounding factors could affect the outcome, particularly high serum lipid levels, due to an inappropriate dietary regimen being included in the study. However, in our study, overweight and obese participants were eliminated which minimizes the possibility of participants with an inappropriate dietary regimen being included in the study.

Overall, the results of our study point to an association between chronic periodontitis and dyslipidemia with elevated values of TC, LDL-c, VLDL-c, and TGL and depressed values of HDL-c. The increased presence of pro-inflammatory cytokines seen in chronic periodontitis, which is a cause for increased oxidative stress can also be the possible cause for the increase in serum lipid levels.

Conclusions
The lipid profile analysis showed that all the parameters, i.e., TC, HDL-c, LDL-c, VLDL-c, and TGL were seen to be significantly altered when comparing the chronic periodontitis group to the healthy controls.

The lipid profile analysis also showed that TC, VLDL-c, and TGL were seen to be significantly altered when comparing the chronic periodontitis group to the chronic periodontitis with Type II DM group, whereas HDL-c and LDL-c were not significantly altered.

The present study supports and extends the view that assessment of the lipid profile can serve as a possible marker for chronic periodontitis and that periodontitis has systemic manifestations.

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Conflicts of interest
There are no conflicts of interest.
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