Innovative Journal of Medical Health Science

IJMHS 9 (8), 566–577 (2019) ISSN (O) 2277:4939 | (P) 2589:9341

# EFFECTS OF PERIODONTAL THERAPY ON SERUM LIPID LEVELS: A PROSPECTIVE INTERVENTIONAL TRIAL

Rajendra Kumar Meena[1], Swarga Jyoti Das[2]*

[1]*MDS (Periodontics), Medical Officer (Dental), CHC Mandawari, Lalsot, Dausa- 30504, Rajasthan, India*

[2]*MDS (Periodontics) PhD (Clinical Dentistry) (London), Professor and Head of Periodontics, Regional Dental College, Guwahati-781032, Assam, India*

Reviewed By: Dr. Daniel V.
Department: Medical

## ABSTRACT

**Background:** In periodontitis, the inflammatory cells synthesized and secreted proinflammatory mediators, namely interleukin 1α and β, and tumour necrosis factor α, interleukin 6, prostaglandins. A great interest has been developed regarding the systemic effect of these proinflammatory cytokines. Evidence suggests that they cause a state of altered lipid metabolism, manifested as dyslipidemia, either of heperlipidemia or hypolipidemia. Thus, a close association of periodontal disease and systemic conditions related to dyslipidemia is suggested, though not established yet.

**Objectives:** The present study was designed to evaluate the effects of non-surgical periodontal therapy on serum lipid levels in the subjects with moderate to severe generalized chronic periodontitis by comparing the serum levels of total cholesterol, triglyceride, LDL and HDL before and after periodontal therapy.

**Materials and Methods:** The selected subjects (n= 40) were randomly divided into two groups: Treatment group (treated with scaling and root planing + systemic Doxycycline (200 mg first day orally followed by 100 mg daily for 14 days) and Control (received no treatment). The periodontal parameters considered were gingival index, probing pocket depth and clinical attachment level, while the metabolic parameters were serum triglyceride, cholesterol, LDL cholesterol, HDL cholesterol (together called as serum lipid levels). The parameters were recorded on 0 day and 90.

**Results:** Serum triglyceride, serum cholesterol and LDL cholesterol levels were reduced with significant improvement in gingival health, pocket depth and clinical attachment level after periodontal therapy.

**Conclusion:** Periodontal therapy is effective in reducing the serum lipid levels, thereby reduces the risk of associated systemic diseases.

**Key words:** Cytokines, Periodontitis, Serum Cholesterol, Triglycerid, Prostaglandin, Pocket Depth, Clinical Attachment Level

*Corresponding author.
†Email: swargajyoti_das2@rediffmail.com.

## INTRODUCTION:

In periodontitis, the inflammatory cells especially the macrophages in response to the bacterial endotoxins, namely lipopoplysaccharides (LPS) synthesize and secrete a wide array of molecules including the inflammatory cytokines, proinflammatory mediators, namely interleukin (IL) -1α and β, and tumour necrosis factor α (TNF-α), IL- 6, prostaglandins (PG), particularly PGE2 and hydrolytic enzymes (*e.g*. matrix metalloproteinases), which are responsible for the periodontal breakdown [1, 2, 3]. However, these proinflammatory mediators are balanced by antiinflammatory cytokines and lipoxins [4]. Imbalance in between the activity of proinflammatory and antiinflammatory mediators is a major determinant of periodontal destruction [5]. Thus, both proinflammatory and antiinflammatory cytokines initiate, mediate and control immune and inflammatory responses.

Recently, great interest has been developed regarding the systemic effect of the proinflammatory cytokines potentially elevated in periodontitis. Evidence suggests that chronic exposure of host to Gram-negative microorganisms and /or LPS results in release of TNF-α and IL-1β which causes a state of altered lipid metabolism, manifested as hypertriglyceridemia and lipid oxidation. Again, TNF-α and IL-1β affect lipid metabolism through the production of other cytokines [2], by altering the hemodynamics and amino acid utilization of various tissues involved in lipid metabolism [6] or by modifying the hypothalamic-pituitary-adrenal axis via increasing the plasma concentration of adrenocorticotropic hormone (ACTH), cortisol, adrenaline, nor-adrenaline and glucagon [7, 8]. These cytokines further inhibit the adipose tissue lipoprotein lipase that results in decreased clearance of lipoproteins, which leads to enhanced hepatic lipogenesis [9], increased synthesis or reduced clearance of triglyceride (TG) and low density lipoprotein (LDL) [10 - 13] (Figure 1). This may be manifested as dyslipidemia, disorders in lipoprotein metabolism leading either to hyperlipidemia or hypolipidemia[14].

In 1991, the National Heart, Blood and Lung Institute under National Cholesterol Education Program (NCEP) proposed a diagnostic criterion for hyperlipidemia through lipid profile test (Table 1). Lipid profile refers to the concentration of LDL, HDL, triglycerides and total cholesterol in blood. LDL is responsible for diseases like atherosclerosis, while HDL carry cholesterol away from the tissues. Triglycerides and total cholesterol level refer to the lipid status and metabolic disorders.

Significantly higher plasmatic concentration of total cholesterol, LDL and triglyceride has been shown in the subjects with periodontal disease than in the subjects without periodontal disease [15. 16]. Again, reduced serum lipid levels with resolution of periodontal inflammation after periodontal therapy have been observed in few studies [17-19]. Thus, a close association of periodontal inflammation and cholesterol metabolism is suggested. However, Kamil *et al.*, in (2011) reported no effect of periodontal therapy on serum lipid parameters in the subjects with advanced periodontitis [20]. Thus, association between the periodontal disease and serum lipid levels still appears as a controversial issue. Hence, the present study was designed to evaluate the effects of non-surgical periodontal therapy on serum lipid levels in healthy subjects with moderate to severe generalized chronic periodontitis by comparing the blood serum levels of total cholesterol, triglyceride, LDL and HDL before and after periodontal therapy.

## MATERIALS AND METHODS:

The present study was carried out in the Department of Periodontics, Regional Dental

College, Guwahati, Assam, India to correlate the periodontal therapy and serum lipid levels, involving 40 subjects having moderate to severe periodontitis. Written consent was obtained from each participants.

**Inclusion criteria:**

- Subjects with minimum of 24 teeth, 35-55 years old with moderate to severe periodontitis
- Subjects with the probing pocket depth of 5 mm or more and clinical attachment loss of ≥ 3 mm, at least at 30% sites

**Exclusion criteria:**

- Subjects with known systemic ailments or other oral lesions
- Subjects with history of any periodontal therapy / administration of antibiotics in the past three months
- Pregnant and lactating mother
- Heavy smokers

The subjects were randomly categorized into two groups, comprising of 20 in each, based on the treatment provided:

- Group A (Treatment group): Subjects were instructed oral hygiene procedure. scaling and root planing followed by systemic Doxycycline (Cipla Ltd., Mumbai) (200 mg in two divided doses orally on day 1 followed by 100 mg once daily for 14 days).
- Group B (Control group): received no oral hygiene instruction, medications and periodontal therapy.

The following metabolic parameters (fasting serum lipid profile) were recorded:

- Triglycerides
- Total Cholesterol
- HDL cholesterol
- LDL cholesterol

To evaluate the periodontal status, following clinical parameters were recorded:

- Gingival index ( Silness and Loe, 1963) [1]
- Probing pocket depth ( PPD)
- Clinical attachment level (CAL)

Both metabolic and clinical parameters were recorded on day 0 (baseline) and at the end of 3 months.

**Gingival index (Loe and Silness, 1963):**

The gingival health status was assessed using a mouth mirror and a periodontal probe at four areas of each tooth: distofacial, facial, mesiofacial and lingual surfaces. It was scored on a numerical scale, according to the following criteria:

- **Score 0:** Normal gingiva
- **Score 1:** Mild inflammation, slight change in color, slight edema, no bleeding on probing
- **Score 2**: Moderate inflammation, redness, edema, and glazing; bleeding on probing
- **Score 3**: Severe inflammation, marked redness and edema, ulceration; tendency to spontaneous bleeding

The Gingival score for a tooth was obtained by dividing the sum of scores obtained at four areas by four. Then scores of each tooth are added and divided by the number of teeth examined to acquire gingival index scores for an individual. The oral cavity is rated as excellent (score 0), good (score 0.1 to 1.0), fair (score 1.1 to 2.0), and poor (score 2.1 to 3.0).

**Probing Pocket Depth:**

Probing pocket depth was measured using the UNC -15 periodontal probe, which is a 15 mm long probe with markings at each mm and color coding at $5^{th}$, $10^{th}$, and $15^{th}$ mm. Pocket depth was measured from gingival margin to base of the pocket, at four specific points in relation to a tooth: distofacial, facial,

mesiofacial, and lingual surfaces. Occlusal stent was used to confirm the same point and direction of measurement at various time point. Probing pocket depth of each subject was determined by adding all the individual scores and then dividing this by the number of surfaces recorded.

**Clinical Attachment level:**

Clinical attachment level is measured from a fixed point to the base of the pocket in mm using UNC -15 periodontal probe. Fixed reference point refers the occlusal stent here. It was measured at four points in relation to a tooth: distofacial, facial, mesiofacial, and middle of the lingual surfaces. Clinical attachment level for each subject was determined by adding all the individual scores and then dividing this by the total number of surfaces recorded.

**Method of blood collection:**

For blood collection, the subjects were called after 12 hours of fasting. A tourniquet was placed on the region of median cubital vein of the upper arm and the anticubital region was palpated. The skin around the area was wiped off with an alcohol swab and a syringe with the needle (bevel facing upward) was used to draw 4ml. of venous blood. The tourniquet was removed then. The blood was then placed immediately into an EDTA vial (BD Vacutainer$^{R}$ serum), shaked well and then process for the estimation of serum lipid profile levels.

The blood samples were centrifuged at 2500-3000 rpm for 8-10 minutes to separate serum from the blood. Separated serum was collected and stored at room temperature 18-28°C (64-82° F) in containers with lids to avoid contamination and evaporation. Serum levels of total cholesterol, triglyceride (TG) and HDL cholesterol were estimated by an enzymatic calorimetric method using VITROS 5600 Integrated System (J & J Ltd, Mumbai, India), while LDL cholesterol was calculated using the Friedewald formula as follows [21]:

LDL = Total cholesterol - (HDL-triglyceride /5)

After obtaining demographic data and history, all the clinical as well as the metabolic parameters were estimated on day 0.

All the subjects in treatment group (group A) were educated and motivated for proper oral hygiene maintenance. Plaque control measures were demonstrated. Periodontal therapy comprising of a pre procedural mouth rinse with 10 ml of 0.2% chlorhexidine for a minute and thorough scaling of all the teeth using ultrasonic scaler was executed. In contrast, the subjects of control group (group B) were not given any oral hygiene instructions, periodontal therapy and any medications.

On day 90, both periodontal and metabolic parameters were repeated in both the groups.

## RESULTS:

**Gingival index:**

The mean gingival index in group A was 1.87 ± 0.09 (range of 1.63 - 2.04) and 0.93 ± 0.05 (range of 0.85 - 1.01) on day 0 and 90, respectively (Table 2); thus the mean gingival index was reduced by 0.94 (50.26%) after 3 months following periodontal therapy. This difference was found to be very highly significant ($p < 0.001$). As shown in Table 2, the mean gingival index in group B was 1.82 ± 0.27 (range of 1.03 - 2.48) and 1.86 ± 0.21 (range of 1.42 - 2.42) on day 0 and 90, respectively. In contrast of group A, the mean GI was found to be increased by 0.04 (2.50%) after 3 months, though not significant statistically ($p > 0.05$).

**Probing Pocket Depth (in mm):**

The mean probing pocket depth in group A was 4.41 ± 0.45 (range of 3.62 - 5.35) and 2.60 ± 0.34 (range of 1.89 - 3.03) on day 0 and 90,

respectively; thus, the mean PPD was reduced by 1.81 (41.13%) after periodontal therapy (Table 2), which was very highly significant statistically ($p < 0.001$). As shown in Table 2, the mean PPD in group B was 4.65 ± 1.04 (range 3.61 - 8.33) and 4.71 ± 1.01 (range 3.63-8.21) on day 0 and 90, respectively; thus, the mean PPD was increased by 0.06 mm (1.24%), though not significant statistically ($p>0.05$).

**Clinical Attachment Level (in mm):**

The mean Clinical Attachment Level in group A was 11.36 ± 1.31 (range of 8.40 - 14.00) and 9.36 ± 1.19 (range of 6.53 - 11.90) day 0 and 90, respectively; thus the mean CAL is gained by 2.00 mm (17.64%) after periodontal therapy (Table 2), which was very highly significant statistically ($p < 0.001$). In group B, the mean CAL was 11.40 ± 0.93 (range 8.70 - 12.60) and 11.47 ± 0.81 (range 9.10 - 12.45) on day 0 and 90, respectively; thus, the mean CAL was increased by 0.07 mm (0.68%), though not significant statistically ($p > 0.05$).

**Serum Triglycerides (in mg/dL)**

The mean serum triglyceride in group A was 151.45 ± 62.28 (range of 48 - 277) mg/dL and 131.00 ± 61.11 (range of 44-297) mg/dL on day 0 and day 90, respectively. Thus, serum triglyceride level was reduced by 20.45 mg/dL (13.50%) after periodontal therapy, which is very highly significant statistically ($p <0.001$), while, in group B, serum triglyceride was increased by 0.79 (0.61%), from 127.77 ± 58.71 (range of 60 - 182) mg/dL on day 0 to 128.56 ± 57.51 (range of 83 - 181) mg/dL on day 90, though not significant statistically ($p >0.05$) (Table 3).

**Serum Cholesterol (mg/dL)**

As shown in Table 3, the mean serum cholesterol in group A was 177.80 ± 53.57 (range of 112 - 316) mg/dL and 160.75 ± 50.29 (range of 105 - 314) mg/dL on day 0 and day 90, respectively; thus, serum cholesterol was reduced by 17.05 mg/dL (9.85%) after periodontal therapy, which was very highly significant statistically ($p < 0.001$). In group B, serum cholesterol level was found to be 175.44 ± 34.39 (range of 131 - 259) mg/dL and 175.95 ± 34.12 (range of 145-261) mg/dL on day 0 and day 90, respectively. Though serum cholesterol in group B was e increased by 0.51 (0.29%) on day 90, it was not significant statistically ($p >0.05$).

**Serum HDL Cholesterol (mg/dL)**

The mean serum HDL cholesterol in group A was 39.40 ± 10.39 (range of 23 - 56) and 39.55±10.39 (range of 25-60) mg/dL on day 0 and 90, respectively; thus the serum HDL cholesterol was increased by 0.15 (0.38%) following periodontal therapy, though not significant statistically ($p>0.05$) (Table 3). In contrast, the serum HDL cholesterol in group B was found to be reduced by 0.37 (0.96%) on day 90 (39.10 ± 9.35; range being 25 - 59) mg/dL compared to that of the day 0 (39.48 ± 9.44; range being 25 - 61) mg/dL, though not significant statistically ($p >0.05$).

**Serum LDL Cholesterol (mg/dL)**

The mean serum LDL cholesterol in group A was 106.30 ± 41.11 (range of 47 - 206) and 94.95 ± 40.31 (range of 28 -198) on day 0 and 90, respectively; thus, the serum triglyceride was decreased by 11.35 (10.67%) after 3 month (Table 3), which was found to be very highly significant statistically ($p < 0.001$). Whereas, the serum LDL cholesterol in group B was increased by 1.05 (0.95%) on day 90 (111.45 ± 28.53; range of 83-181) compared to that of the day 0 (110.40 ± 28.99; range of 68 - 182), which is not significant statistically ($p >0.05$).

***Table 1. NCEP Criteria for the diagnosis of the hyperlipidemia***

| | Desirable (mg/dL) | Borderline (mg/dL) | Undesirable (mg/dL) |
|---|---|---|---|
| Total cholesterol | < 200 | 200 - 239 | > 240 |
| Triglyceride | < 150 | 150 - 199 | > 200 |
| HDL | > 60 | 40 - 59 | < 40 |
| LDL | < 110 | 110 - 129 | >130 |

***Table 2. Changes in Clinical parameters at different time points***

| Groups | Gingival Index | | | Probing Pocket Depth (in mm) | | | Clinical Attachment Level (in mm) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean ± SD (Range) | | | Mean ± SD (Range) | | | Mean ± SD (Range) | | |
| | Day 0 | Day 90 | Day 0 vs 90 | Day 0 | Day 90 | Day 0 vs 90 | Day 0 | Day 90 | Day 0 vs 90 |
| A (n = 20) | 1.87 ± 0.09 (1.63 - 2.04) | 0.93 ± 0.05 (0.85 - 1.01) | 0.94 *** | 4.41 ± 0.45 (3.62 - 5.35) | 2.60 ± 0.34 (1.89 - 3.03) | 1.81*** | 11.36±1.31 (8.40-14.00) | 9.36±1.19 (6.53-11.90) | 2.00*** |
| B (n = 20) | 1.82 ± 0.27 (1.03 - 2.48) | 1.86 ± 0.21 (1.42 - 2.42) | - 0.04 ns | 4.65 ± 1.04 (3.61 - 8.33) | 4.71 ± 1.01 (3.63 - 8.21) | - 0.06 ns | 11.40±0.93 (8.70-12.60) | 11.47±0.81 (9.10-12.45) | -0.07 ns |

***p < 0.001, very highly significant

ns = not significant (p > 0.05)

***Table 3. Changes in metabolic parameters at different time points***

| Days | Serum Triglycerides (mg/dL) Mean ± SD (Range) | | Serum Cholesterol (mg/dL) Mean ± SD (Range) | | Serum HDL Cholesterol (mg/dL) Mean ± SD (Range) | | Serum LDL Cholesterol (mg/dL) Mean ± SD (Range) | |
|---|---|---|---|---|---|---|---|---|
| | Group A (n= 20) | Group B (n= 20) | Group A (n= 20) | Group B (n= 20) | Group A (n= 20) | Group B (n= 20) | Group A (n= 20) | Group B (n= 20) |
| Day 0 | 151.45 ± 62.28 (48 - 277) | 127.77 ± 58.71 (60 - 182) | 177.80 ± 53.57 (112 – 316) | 175.44 ± 34.39 (131 - 259) | 39.40 ± 10.39 (23 - 56) | 39.48 ± 9.44 (25 - 61) | 106.30 ± 41.11 (47 - 206) | 110.40 ± 28.99 (68-182) |
| Day 90 | 131.00 ± 61.11 (44 - 297) | 128.56 ± 57.51 (83 - 181) | 160.75 ± 50.29 (105 - 314) | 175.95 ± 34.12 (145-261) | 39.55 ± 10.39 (25 - 60) | 39.10 ± 9.35 (25 - 59) | 94.95 ± 40.31 (28 - 198) | 111.45 ± 28.53 (83 - 181) |
| Day 0 vs 90 | 20.45 *** | - 0.79 ns | 17.05*** | 0.51 ns | -0.15 ns | 0.37 ns | 11.35*** | - 1.05 ns |

***p < 0.001, very highly significant

ns = not significant (p > 0.05)

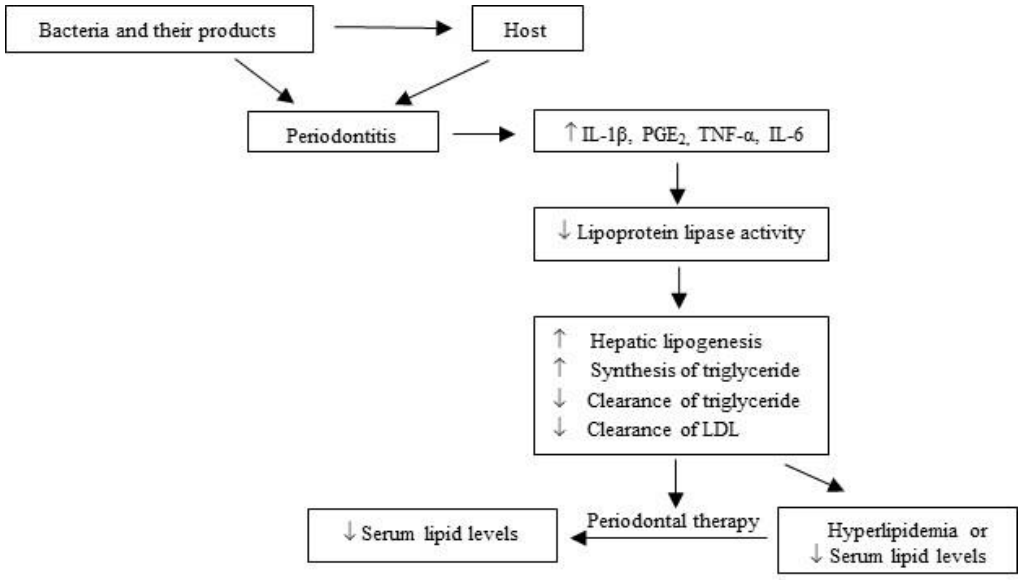


***Figure 1. Probable interrelationship between periodontal disease and serum lipid profile***

## DISCUSSION:

Recent evidences have shown that periodontitis affects the general health of an individual through increased serum levels of various inflammatory markers [22 - 24]. Similarly, association of various serum proinflammatory cytokines and systemic diseases, particularly cardiovascular disease, diabetes has also been shown by various investigators. Since periodontitis is associated with an increased levels of serum proinflammatory cytokines, there is a possibility that periodontitis affects the serum cholesterol level as well [25].

Acute systemic or chronic local infection induces change in the plasma concentration of cytokines and hormones, which determine the alteration in the lipid metabolism. An increased level of triglycerides in rats has been reported after induction of periodontitis by *Porphyromonas gingivalis* [26 - 27] and endotoxins [9]. These observations propose a similar systemic response to periodontal disease which occurs due to chronic exposure to microorganisms and endotoxins. A number of studies have stated that subjects with chronic periodontal disease show increased levels of serum triglyceride, total cholesterol and LDL cholesterol, and decreased level of serum HDL cholesterol compared to that of the subjects without periodontal disease [15, 25, 28, 29, 30]. Again, reductions in those parameters were reported following periodontal therapy [31-32]. However, few other studies have failed to observe such positive correlation between periodontitis and serum lipid levels [20, 34, 35]. Thus, association of periodontal diseases and serum lipid levels remains controversial. Considering this, the present study was carried out to determine the effects of periodontal therapy on serum lipid levels in healthy subjects with moderate to severe chronic periodontitis, using gingival index, probing pocket depth, clinical attachment level as clinical parameters and triglyceride, total cholesterol, HDL and LDL cholesterol as metabolic parameters, which were measured on day 0 and 90.

In the present study, subjects above the age of 35 years were considered because periodontitis is more prevalent in adults and regarded as generalized when it is prevalent in more than 30% sites [1, 35]. Subjects with systemic diseases and smokers were not included, as systemic diseases and smoking influence the periodontal destruction [36, 37]. Doxycycline,

prescribed as an adjunctive therapy, is a semisynthetic tetracycline, which is bacteriostatic in nature and is also a host modulatory agent. It also acts as tissue inhibitor of matrix metalloproteinases in spite of their antimicrobial activity [38]. It suppresses the bone growth and causes brown discolouration and malformation of deciduous teeth [39], that's why, pregnant and lactating mothers were excluded.

The index used for estimation of gingival health was based on an objective sign *i.e.* the bleeding on probing. Inflamed gingiva bleeds on gentle probing because of the ulcerations in the pocket epithelium and the fragility of the underlying vasculature. The percentage of sites that exhibit bleeding on probing at initial examination, prior to the treatment is a clinically useful piece of information for diagnosis and treatment planning. Clinical attachment level measurement is also referred to as one of the best way to assess the presence or absence of additional periodontal damage [40]. Probing pocket depth is considered as an important parameter for evaluation of the success of periodontal therapy, as it forms a baseline before therapy. In the present study, probing pocket depth was assessed on day 0 before therapy and on day 90 following periodontal therapy. Various opinions are prevailed in the literature regarding the timing of assessment of healing response following nonsurgical periodontal therapy. Morrison *et al*., (1980) suggested a period of 1 month after therapy as an ideal time for reassessment of probing pocket depth [42], while Badersten *et al*., (1981) opined that most of the changes occur in the first 4-5 months of therapy in periodontal pockets of 4-7 mm depth, while little changes occur next 13-months of observation period [43]. Considering this, in the present study the response to therapy was evaluated on day 90.

Probing pocket depth and gingival inflammation were significantly reduced on day 90 compared to that of day 0, while these are increased in control group, though not significant statistically. Again, there was significant gain in clinical attachment level after periodontal therapy in the treatment group (2.00 mm), in contrast of loss in clinical attachment level in the control group with time, though not significant statistically. Thus, the findings of the present study support the previous observations [43 44, 31, 32, 45].

The present study showed significant reduction in the serum triglyceride, overall cholesterol and LDL cholesterol levels in the treatment group. In contrast, triglyceride level was found to be increased in control group with time though not significant statistically. Similar observation was reported previously [46, 47, 31, 48, 32,]. However, the finding of the present study is not supporting the observation of Kamil *et al.*, (2011) [20]. This may be related to the variations in food habits, socioeconomic conditions, and lifestyle of the participants. Again, serum HDL cholesterol level was increased after periodontal therapy in the treatment group. It is noted that HDL is beneficial to the host, as it is considered as antiatherogenic lipoprotein because of its direct role in neutralising LPS in circulation, protecting LDL against oxidation as well as its role in reverse cholesterol transport [49]. Based on the findings of the present study, we may suggest a strong association of moderate to severe chronic periodontitis and serum lipid levels.

Certain variables like food habits, socioeconomic conditions, and lifestyle, which are difficult to control and may influence the results. Small sample size, follow-up of short duration are the shortcomings of the present study. Hence, long term studies with a larger sample size are recommended to determine the effect of periodontal therapy on the serum lipid levels.

## CONCLUSIONS:

We may conclude from the findings of this study that periodontal therapy is effective in reducing the serum triglyceride, serum cholesterol and LDL and in raising the level of HDL (good cholesterol), which is beneficial to the host.

Thereby, we may in proposition that periodontal therapy may reduce the risk of certain systemic diseases associated with periodontal inflammation.

**ACKNOWLEDGEMENT**

Does not arise

**CONFLICTOF INTEREST DISCLOSURE:**
The authors declare that there are not conflicts of interest.

## REFERENCES:

1. Newman MG, Takei HH, Klokkevold PR, Carranza FA. Carranza's Clinical Periodontology, Saunders Pub. 2007.
2. Socransky SS, Haffajee AD. The bacterial etiology of destructive periodontal disease: current concepts. Journal of Periodontology. 1992; 63: 322-31.
3. De Nardin E. The role of inflammatory and immunological mediators in periodontitis and cardiovascular diseases. Annals of Periodontology. 2001; 6: 30-40.
4. Van Dyke TE, Serhan CN. Resolution of inflammation: a new paradigm for the pathogenesis of periodontal diseases. Journal of Dental Research. 2003; 82: 82-90.
5. Page RC. Milestones in periodontal research and the remaining critical issues. Journal of Periodontal Research. 1999; 34:331-339.
6. Fukushima R, Saito H, Taniwake K. Different roles of IL-1 and TNF on hemodynamics and interorgan amino acid metabolism in awake dogs. American Journal of Physiology. 1992; 262: E275-281.
7. Imura H, Fukata J, Mori T. Cytokines and endocrine function: An interaction between the immune and neuroendocrine systems. Clinical Endocrinology. 1991; 35: 107-115.
8. Chrousos GP. The hypothalamic-pituitary-adrenal axis and immune-mediated inflammation. New England Journal of Medicine. 1995; 332: 1351-1362.
9. Feingold KR, Grunfeld C. Tumor necrosis factor alpha stimulates hepatic lipogensesis in the rat *in vivo*. Journal of Clinical Investigation. 1987; 80: 184-190.
10. Divertie GD. Jensen MD, Miles JM. Stimulation of lipolysis in humans by physiological hypercortisolemia. Diabetes. 1991; 40: 1228-1232.
11. Kurpad A, Khan K, Calders AG, Coppack S, Frayn K, Macdonald I, Elia M. Effect of noradrenaline on glycerol turnover and lipolysis in the whole body and subcutaneous adipose tissue in humans *in vivo*. Clinical Science. 1994; 86: 177-184.
12. Fried SK, Zechner R. Cachectin/tumor necrosis factor decreases human adipose tissue lipoprotein lipase mRNA levels, synthesis, and activity. Journal of Lipid Research. 1989; 30: 1917-1923.
13. Rosato EF, Vemulapalli P, Lang CH, Lanza-Jacoby S. Insulin stimulates lipoprotein lipase activity and synthesis in adipocytes from septic rats. Journal of Surgical Research. 1997; 73: 73 - 79.
14. Jacobson MS. Heart healthy diets for all children: no longer controversial. Journal of Pediatrics. 1998; 133: 1-2.
15. Cutler CW, Shinedling EA, Nunn M, Jotwani R, Kim BO, Nares S, Iacopino AM. Association between periodontitis and hyperlipidemia: cause or effect? Journal of Periodontology. 1999; 70: 1429-34.
16. Losche W, Karapetow F, Pohl A, Pohl C, Kocher T. Plasma lipid and blood

glucose levels in patients with destructive periodontal disease. Journal of Clinical Periodontology. 2000; 27:537-541.
17. Meurman JH, Sanz M, Janket SJ. Oral health, atherosclerosis, and cardiovascular disease. Critical Reviews in Oral Biology and Medicine. 2004; 15: 403-413.
18. Losche W, Marshal GJ, Apatzidou DA, Krause S, Kocher T, Kinane DF. Lipoprotein-associated phospholipase A2 and plasma lipids in patients with destructive periodontal disease. Journal of Clinical Periodontology. 2005; 32: 640-644.
19. Tandon S, Dhingra MS, Lamba AK, Verma M, Munjal A, Faraz F. Effect of periodontal therapy on serum lipid levels. Indian Journal Medical Specialities. 2010; 1:19-25.
20. Kamil W, Al Habashneh R, Khader Y, Al Bayati L, Taani D. Effect of nonsurgical periodontal therapy on C-reactive protein and serum lipids in Jordanian adults with advanced periodontitis. Journal of Periodontal Research. 2011; 46: 616-21.
21. Subramanian K, Shriraam M, Bharath R, Muthukumaran J, Kumaravel V. LDL-cholesterol: Friedewald calculated versus direct measurement-study from a large Indian laboratory database. Indian Journal of Endocrinology and Metabolism. 2014; 18: 502–504.
22. Ebersole JL, Machen RL, Steffen MJ, Willmann DE. Systemic acute-phase reactants, C-reactive protein and haptoglobin, in adult periodontitis. Clinical and Experimental Immunology. 1997; 107: 347-352.
23. Loos BG, Craandijk J, Hoek FJ, Wertheim PM, Velden U. Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. Journal of Periodontology. 2000; 71: 1528-1534.
24. Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, DeNardin E. Periodontal infections contribute to elevated systemic c-reactive protein level. Journal of Periodontology. 2001; 72: 1221-1227.
25. Katz J, Flugelman MY, Goldberg A, Heft M. Association between periodontal pockets and elevated cholesterol and low density lipoprotein cholesterol levels. Journal of Periodontology. 2002; 73:494-500.
26. Memon RA, Grunfeld C, Moser AH, Feingold KR. Tumor necrosis factor mediates the effects of endotoxin on cholesterol and triglyceride metabolism in mice. Endocrinology. 1993; 132: 2246-2253.
27. Doxey DL, Cutler CW, Iacopino AM. Diabetes prevents periodontitis–induced increases in gingival platelet derived growth factor-B and interleukin-1 beta in a rat model. Journal of Periodontology. 1998; 69: 113-119.
28. Marita M, Horiuchi M, Kinoshita Y, Yamamoto T, Watanabe T. Relationship between blood triglyceride levels and periodontal status. Community Dental Health. 2004; 21: 32-36.
29. Sharma S, Lamsal M, Sharma SK, Niraula SR, Koirala B. Association of serum LDL cholesterol level with periodontitis among patients visiting a tertiary-care hospital. Journal of the Nepal Medical Association. 2011; 51: 104-108.
30. Sangwan A, Tewari S, Singh H, Sharma RK and Narula SC. Periodontal status and hyperlipidemia: statin users *versus* non-users. Journal of Periodontology. 2013; 84: 3-12.
31. Duan JY, Ou-Yang XY, Zhou YX. Effect of periodontal initial therapy on the

serum levels of lipid in the patients with both periodontitis and hyperlipidemia. Journal of Peking University. 2009; 41: 36 - 39.

32. Rao NS, Bajaj P, Naik SB, Pradeep AR. Effect of non surgical periodontal therapy on serum lipid levels in chronic periodontitis. Archives of Oral Sciences and Research. 2011; 1: 60-64.
33. Machado AC, Quirino MR, Nascimento LF. Relation between chronic periodontal disease and plasmatic levels of triglycerides, total cholesterol and fractions. Brazilian Oral Research. 2005; 19: 284 - 289.
34. Valentaviciene G, Paipaliene P, Nedzelskiene I, Zilinskas J, Anusevicien OV. The relationship between blood serum lipids and periodontal condition. Stomatologija, Baltic Dental and Maxillofacial Journal. 2005; 8: 96-100.
35. Flemmig TF. Periodontitis. Annals of Periodontology. 1999; 4: 32-38.
36. Page RC. The pathobiology of periodontal diseases may affect systemic diseases: inversion of a paradigm. Annals of Periodontology. 1998; 3: 108-120.
37. Johnson GK, Slach NA. Impact of tobacco use on periodontal status. Journal of Dental Education. 2001; 65: 313-321.
38. Golub LM, Ryan ME, Williams RC. Modulation of the host response in the treatment of periodontitis. Dentistry Today. 1998; 17:102-109.
39. Tripathi KD. Essentials of Medical Pharmacology, Jaypee brothers medical publishers (p) Ltd. 2008.
40. Armitage GC. The complete periodontal examination. Periodontology 2000. 2004; 34: 22-33.
41. Morrison EC, Ramfjord SP, Hill RW. Short-term effects of initial, nonsurgical periodontal treatment (hygienic phase). Journal of Clinical Periodontology.1980; 7:199-211.
42. Badersten A, Nilveus R, Egelberg J. Effect of nonsurgical periodontal therapy I. Moderately advanced periodontitis. Journal of Clinical Periodontology. 1981; 8: 57-72.
43. 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. 2004; 83:156-160.
44. Offenbacher S, Lin D, Strauss R, McKaig R, Irving J, Barros SP, Moss K, Barrow DA, Hefti A, Beck JD. Effects of periodontal therapy during pregnancy on periodontal status, biologic parameters, and pregnancy outcomes: a pilot study. Journal of Periodontology. 2006; 77: 2011-2024.
45. Radafshar G, Torabi F, Mirfarhadi N. Short-term effects of intensive non-surgical periodontal therapy and low-dose doxycycline on serum levels of IL-6, TNF-α and lipid profile in advanced periodontitis. African Journal of Microbiology Research. 2012; 6: 355-360.
46. D'Aiuto F, Nibali L, Parkar M, Suvan J, Tonetti MS. Short-term effects of intensive periodontal therapy on serum inflammatory markers and cholesterol. Journal of Dental Research. 2005; 84: 269-273.
47. Oz SG, Fentoglu O, Kilicarslan A, Guven GS, Tanrtover MD, Aykac Y, Sozen T. Beneficial effects of periodontal treatment on metabolic control of hypercholesterolemia. Southern Medical Association Journal. 2007; 100: 686-691.
48. Fentoglu O, Sozen T, Oz SG., Kale B, Sonmez Y, Tonguc MO, Gurgan CA,

Aykaç Y, Kirzioğlu FY. Short-term effects of periodontal therapy as an adjunct to anti-lipemic treatment. Oral Disease. 2010; 16: 648-654.

49. Pussinen PJ, Jauhiainen M, Rautiainen TV, Sundvall J, Vesanen M, Mattila K, Palosuo T, Alfthan G, Asikainen S. Periodontitis decreases the antiatherogenic potency of high density lipoprotein. Journal of Lipid Research. 2004; 45: 139-147.

## AUTHOR BIOGRAPHY

**Rajendra Kumar Meena,** MDS (Periodontics), Medical Officer (Dental), CHC Mandawari, Lalsot, Dausa-30504, Rajasthan, India

**Swarga Jyoti Das,** MDS (Periodontics) PhD (Clinical Dentistry) (London), Professor and Head of Periodontics, Regional Dental College, Guwahati-781032, Assam, India