Effect of Periodontal Inflammation on Haematological and Liver Function Parameters - A Comparative Clinical Study from Uttar Pradesh, India

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ABSTRACT

BACKGROUND
Periodontitis is an inflammatory disease of periodontium. The inflamed and ulcerated epithelium allows the entry of oral microorganisms, bacterial endotoxins, proinflammatory immune mediators, like Interleukin-1 (IL-1), Interleukin-6 (IL-6), tumour necrosis factor (TNF-α) and prostaglandin E2 (PGE2) into the systemic circulation, which may produce systemic effects. The present study was conducted to evaluate the effect of periodontal inflammation on haematological and liver function parameters.

METHODS
The clinical study was conducted among 30 patients with periodontal inflammation. Clinical parameters [plaque index (PI), gingival index (GI), probing pocket depth (PPD)], haematological [RBC count, haemoglobin (Hb) concentration, total leucocyte count and differential leucocyte count] and liver function parameters [alanine aminotransferase (ALT), aspartate aminotransferase (AST) & alkaline phosphatase (ALP)] were recorded at baseline and after 1 month of scaling and root planning (SRP).

RESULTS
There was significant improvement in clinical parameters (P-value < 0.001), haematological parameters (P-value < 0.001), except eosinophils (P = 0.303) and basophils (P = 0.860). Changes in liver function test (LFT) parameters were found to be significant (P < 0.05) after SRP.

CONCLUSIONS
There is an association between periodontal inflammation and systemic parameters.

KEY WORDS
Periodontal Inflammation, Haematological, LFT.

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BACKGROUND

An association between oral infections and systemic diseases has been suspected for centuries. Over the past decade, scientific evidence suggests an association between oral infection and systemic diseases such as atherosclerosis, cardiovascular diseases (CVDs), cerebrovascular disease, premature and low birth weight and pulmonary diseases. It is because the microbes associated with the periodontal disease process invoke an inflammatory response which leads to release of various cytokines. These cytokines and other inflammatory mediators reach to the distant sites via the vascular circulation and play a key role in the pathogenesis of its systemic effects.1

The adult human body consists of 1013 somatic cells and 1014 normal or commensal microbes. These commensal bacteria reside on the surfaces of teeth in the form of complex ecosystem termed as biofilm and on the mucosal lining of oral cavity, respiratory tract, oesophagus, gastrointestinal tract and urinary tract. Under some conditions, these microorganisms become opportunistic and are associated with local or systemic infections.

Evidence shows that oral bacteria contribute to systemic diseases. One of the best documented examples is involvement of the gram-positive Streptococcus sanguis and Streptococcus oralis in infective endocarditis.1 Leukocytes are an integral part of the innate immune system; these cells are recruited at higher levels during episodes of bacteremia in periodontitis into the systemic circulation.2 The higher number of leukocytes increase the blood rheology, make the blood more viscous and also cells may adhere to the endothelial lining of the blood vessels causing decrease in the blood flow. Reduced blood flow could play a role in relation to CVDs, especially in narrow or partly blocked arteries. So, the blood count can give a definite hint about underlying disease.3,4

The systemic effects of periodontal diseases are known to be caused by bacteremia arising from diseased periodontal tissues and the resultant inflammatory response. This inflammatory response can lead to changes in commonly assessed blood parameters i.e. RBC count, haemoglobin concentration, total leukocyte count, differential leukocyte count and liver function test parameters.5,6,7,8

Periodontitis is an inflammatory disease of periodontium that contributes to an increase in cytokines including tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hs-CRP). These cytokines defend the body against infection. However, they can also affect normal body functions such as it may interfere with production and normal activity of erythropoietin and iron absorption resulting in decreased RBC count and haemoglobin concentration.

Inflammatory reaction affects erythrocyte sedimentation rate by increasing concentrations of fibrinogen and alpha globulins. Increase in white blood cell (WBC) count is known as leucocytosis and is a frequent sign of an inflammatory response.9,10

Aspartate Aminotransferase is a soluble cytosolic enzyme which is restricted to the cell cytoplasm. It is released into extracellular fluid upon cell death. Similarly, Alanine Aminotransferase is also associated with cell injury and cell death.

METHODS

The present clinical study was carried out among 30 systemically healthy patients aged between 18 to 60 years selected from Outpatient Department of Periodontology, Uttar Pradesh University of Medical Sciences Saifai, Etawah, U.P. India. Sample size was taken based on the convenience of the study.

Study was conducted from January 2018 to June 2019. The research protocol was submitted to the institutional ethical committee & review board and ethical approval obtained.

All patients were verbally informed about the study protocol and a written informed consent was obtained. Patients were selected on the basis of following criteria.

Inclusion Criteria

- Presence of at least 20 teeth
- Probing pocket depth (PPD) ≤ 5 mm at least 30 % sites
- Gingival index (GI) ≤ 2

Exclusion Criteria

- Individuals suffering from any systemic disease.
- History of periodontal treatment or use of any drug for at least 3 months prior to the study.
- Individuals with history of malaria or jaundice in the last 1 year.
- Smokers, tobacco chewers and alcohol abuse.
- Pregnant and lactating female.
Study Parameters
All the selected patients were evaluated for the following parameters.

Clinical Parameters
Periodontal status of patients included in the study was recorded using following periodontal parameters.
- Plaque index - Is measuring of dental plaque in area adjacent to gingival margin.
- Gingival index
- Probing pocket depth using UNC-15 probe (Hu Friedy), the probe is placed onto the tooth and the distance between cement-enamel junction and the gingival margin is measured.

Haematological Parameters
- Red blood cell (RBC) count
- Haemoglobin concentration
- Total leucocyte count
- Differential leucocyte count

Liver Function Test Parameters
- Alanine aminotransferase
- Aspartate aminotransferase
- Alkaline phosphatases

Statistical Analysis
The results were analysed using descriptive statistics and making comparisons among the various groups. Discrete (categorical) data was summarized as in proportions and percentages (%). The normality of data is tested by Kolmogorov test and according to data, nature parametric or non-parametric tests were applied. The following statistics were calculated in the present analysis. The test applied
1. Arithmetic Mean
2. Standard deviation (σ)
3. Paired t test
4. Wilcoxon signed rank test

Statistical Significance
In testing a given hypothesis, the maximum probability with which we would be willing to take risk is called level of significance of the test.
- P-value ≥ 0.05 - Non-significant
- P-value < 0.05 - Significant
- P-value < 0.01 - Highly Significant

RESULTS
The present study was done to assess the effect of periodontal inflammation on haematological and liver function parameters. A total of 30 patients were included in the study fulfilling the inclusion criteria.

Observations for the clinical parameters i.e. PI, GI, PPD, haematological parameters i.e. RBC, Hb conc, TLC, DLC and liver function parameters i.e. AST, ALT and ALP were made at baseline and after 1 month of SRP.

| Age (in Years) | No. of Patients | Percentage (%) |
|---------------|-----------------|----------------|
| 18 - 24       | 11              | 36.7           |
| 25 - 34       | 11              | 36.7           |
| 35 - 44       | 5               | 16.7           |
| 45 - 60       | 3               | 10.0           |
| Total         | 30              | 100.0          |

Table 1. Age Wise Distribution of Patients

| Clinical Parameters | Mean | SD | Mean Diff. | SE (Diff) | t-Value | P-Value |
|---------------------|------|----|------------|-----------|---------|---------|
| Plaque Index        |      |    |            |           |         |         |
| Baseline            | 1.27 | 0.37 | 1.60 | 0.09 | 17.97 | <0.001 |
| 1 month             |      |    |            |           |         |         |
| 0.57 | 0.23 |         |         |         |         |         |
| Gingival index      |      |    |            |           |         |         |
| Baseline            | 2.03 | 0.31 | 1.48 | 0.07 | 20.83 | <0.001 |
| 1 month             |      |    |            |           |         |         |
| 0.55 | 0.22 |         |         |         |         |         |
| Probing pocket depth|      |    |            |           |         |         |
| Baseline            | 3.86 | 0.45 | 0.02 | 0.08 | 12.08 | <0.001 |
| 1 month             |      |    |            |           |         |         |
| 2.94 | 0.37 |         |         |         |         |         |

Table 2. Assessment of Plaque Index / Gingival Index / Probing Pocket Depth, at Baseline and after 1 Month of Scaling and Root Planning

| Haematological Parameters | Mean | SD | Mean Diff. | SE (Diff) | t-Value | P-Value |
|---------------------------|------|----|------------|-----------|---------|---------|
| RBC count                 |      |    |            |           |         |         |
| Baseline                  | 20.83 | 2.13 | -0.15 | 1.72 | 20.83 | <0.001 |
| 1 month                   |      |    |            |           |         |         |
| 2.09 | 0.33 |         |         |         |         |         |
| Haemoglobin               |      |    |            |           |         |         |
| Baseline                  | 13.85 | 1.19 | -0.35 | 1.72 | 20.83 | <0.001 |
| 1 month                   |      |    |            |           |         |         |
| 13.49 | 1.16 |         |         |         |         |         |
| Alkaline phosphatases     |      |    |            |           |         |         |
| Baseline                  | 1.86 | 0.22 | -0.43 | 0.35 | 20.83 | <0.001 |
| 1 month                   |      |    |            |           |         |         |
| 1.86 | 0.22 |         |         |         |         |         |

Table 3. Assessment of Red Blood Cell Count (10^6 / µl) / Haemoglobin (Hb) Concentration (g / dl) / Total Leucocyte Count (10^9 / µl) at Baseline and after 1 Month of Scaling and Root Planning

| Liver Function Parameters | Mean | SD | Mean Diff. | SE (Diff) | z-Value | P-Value |
|---------------------------|------|----|------------|-----------|---------|---------|
| Alanine                   |      |    |            |           |         |         |
| Aminotransferase          |      |    |            |           |         |         |
| Baseline                  | 36.27 | 17.11 | 2.87 | 1.69 | 1.97 | 0.049 |
| 1 month                   |      |    |            |           |         |         |
| 33.40 | 17.58 |         |         |         |         |         |
| Aspartate                 |      |    |            |           |         |         |
| Aminotransferase          |      |    |            |           |         |         |
| Baseline                  | 31.13 | 8.69 | 2.90 | 1.39 | 2.09 | 0.046 |
| 1 month                   |      |    |            |           |         |         |
| 28.23 | 7.48 |         |         |         |         |         |

Table 4. Assessment of Alanine Aminotransferase / Aspartate Aminotransferase (IU / l) at Baseline and after 1 Month of Scaling and Root Planning

| Differential Leukocyte Count | Mean | SD | Mean Diff. | SE (Diff) | 2-Value | P-Value |
|------------------------------|------|----|------------|-----------|---------|---------|
| Neutrophil count             |      |    |            |           |         |         |
| Baseline                     | 0.20 X 10^3 | 0.38 X 10^3 | 0.20 X 10^3 | 0.09 X 10^3 | 3.96 | <0.001 |
| 1 month                      |      |    |            |           |         |         |
| 0.44 X 10^3 | 0.80 X 10^3 |         |         |         |         |         |
| Lymphocyte count             |      |    |            |           |         |         |
| Baseline                     | 0.30 X 10^3 | 0.50 X 10^3 | 0.30 X 10^3 | 0.09 X 10^3 | 3.96 | <0.001 |
| 1 month                      |      |    |            |           |         |         |
| 0.22 X 10^3 | 0.28 X 10^3 |         |         |         |         |         |
| Monocyte count               |      |    |            |           |         |         |
| Baseline                     | 0.35 X 10^3 | 0.50 X 10^3 | 0.35 X 10^3 | 0.09 X 10^3 | 3.96 | <0.001 |
| 1 month                      |      |    |            |           |         |         |
| 0.30 X 10^3 | 0.31 X 10^3 |         |         |         |         |         |
| Basophil count               |      |    |            |           |         |         |
| Baseline                     | 0.01 X 10^3 | 0.01 X 10^3 | 0.01 X 10^3 | 0.01 X 10^3 | 3.96 | <0.001 |
| 1 month                      |      |    |            |           |         |         |
| 0.01 X 10^3 | 0.01 X 10^3 |         |         |         |         |         |

Table 5. Assessment of Differential Leukocyte Count (10^9 / µl) at Baseline and after 1 Month of Scaling and Root Planning

# Wilcoxon signed rank test
After scaling and root planning, changes in the clinical parameters and haematological parameters were found to be highly significant (P < 0.01) except eosinophils (P = 0.303) and basophils (P = 0.860). Changes in LFT parameters were found to be significant (P < 0.05) after SRP (Table 6 & Graph 1).

Periodontal inflammation may affect haematological parameters via the release of various cytokines into the systemic circulation. In present study, mean value of RBC count and haemoglobin concentration were 4.27 X 10^12 /μl and 13.05 ± 2.13g /dl respectively at baseline and the level improves to 4.60 X 10^12 /μl and 13.49 ± 1.86 g /dl after resolution of periodontal inflammation and these mean increases were found to be highly significant. These findings of present study were in favour of research work carried out by Agarwal N et al.19

Seigel EH20 had reported a depression in the number of erythrocytes in presence of periodontal disease and their elevation after the pathological process arrest. Thomas B et al.21 showed that periodontitis patient has a lower haematocrit, lower number of erythrocytes, lower haemoglobin levels and higher erythrocyte sedimentation rates. Whereas, the studies by Wakai K et al.22 and Havemose-Poulsen A et al.23 failed to show any association between haemoglobin level and periodontal status.

In present study the mean values of ALT & AST level at baseline were 36.27 ± 17.11 IU / L & 31.13 ± 8.69 IU / L respectively which reduced to 33.40 ± 17.58 IU / L & 28.23 ± 7.48 IU / L respectively after 1 month of scaling and root planing. The mean reduction in ALT & AST after scaling and root planing were 2.87 ± 1.69 IU / L & 2.90 ± 1.39 IU / L respectively. These reductions were statistically significant. This reflects that the AST & ALT release is associated with periodontal inflammation. Khatavkar PR et al.24 in their study found that AST & ALT levels were reduced significantly after treatment suggesting that AST and ALT level decreases when periodontal status improves is in accordance with present study. The relationship of ALT & AST level with periodontal parameters via the release of various cytokines into the systemic circulation. In present study, mean value of RBC count and haemoglobin concentration were 4.27 X 10^12 /μl and 13.05 ± 2.13g /dl respectively at baseline and the level improves to 4.60 X 10^12 /μl and 13.49 ± 1.86 g /dl after resolution of periodontal inflammation and these mean increases were found to be highly significant. These findings of present study were in favour of research work carried out by Agarwal N et al.19

![Graph 1. Mean Change in All the Parameters](image)

**Table 6. Conclusive Results of Changes in the Included Parameters**

| Type     | Parameter | Mean Diff. SE (Diff) | P-Value Significance |
|----------|-----------|----------------------|----------------------|
| Clinical | PI        | 1.60                 | 0.09                 | < 0.001 HS |
|          | GI        | 1.48                 | 0.07                 | < 0.001 HS |
|          | PPD       | 0.92                 | 0.08                 | < 0.001 HS |
|          | RBC Count | -0.33 x 10^10        | 0.08 x 10^10         | < 0.001 HS |
|          | Hb        | -0.43                | 0.15                 | 0.009 HS   |
|          | Neutrophils| 0.76 x 10^9          | 0.20 x 10^9          | 0.002 HS   |
|          | Lymphocyte| 0.39 x 10^9          | 0.09 x 10^9          | < 0.001 HS |
|          | Monocyte  | 0.17 x 10^10         | 0.10 x 10^10         | < 0.001 HS |
|          | Eosinophils| 0.26 x 10^9          | 0.15 x 10^9          | 0.303 NS   |
|          | Basophils | -0.003 x 10^10       | 0.01 x 10^10         | 0.860 NS   |
|          | ALT (IU/L)| 2.87                 | 1.69                 | 0.049 S    |
|          | AST (IU/L)| 2.90                 | 1.39                 | 0.046 S    |
|          | ALP (IU/L)| 24.33                | 11.81                | 0.048 S    |

**DISCUSSION**

The present study was carried out to evaluate the effect of periodontal inflammation on haematological and liver function parameters. All clinical periodontal examinations were performed by single examiner to minimize the inter-examiner variations. To assess the effect of SRP, the changes in the periodontal parameters were evaluated at baseline and 30 days after SRP. Statistically highly significant reduction were found in mean value of PI (2.17 ± 0.37 at baseline, 0.57 ± 0.23 after 1 month), GI (2.03 ± 0.31 at baseline 0.55 ± 0.22 after 1 month) and PPD (3.86 ± 0.45 mm at baseline, 2.94 ± 0.37 mm after 1 month) suggesting that SRP and motivation for oral hygiene measures helped in improving the periodontal health thus reducing the periodontal inflammation of patients. The similar findings were also observed by Patel MD et al.18 in their study.

![Graph 1. Mean Change in All the Parameters](image)
CONCLUSIONS

The result of present study shows a correlation between periodontal inflammation and haematological & liver function parameters. The levels of haematological parameters; RBC count, Hb concentration were increased and TLC & DLC decreased without significant change in the eosinophil & basophil count. The liver function parameters (ALT, AST & ALP) reduced once the periodontal inflammation resolved. This reflects that the levels of serum enzymes ALT, AST & ALP are related to periodontal inflammation. Thus, periodontal inflammation has systemic effects as the chemical mediators involved in inflammation are same for any systemic inflammatory disease. However, further longitudinal clinical studies with larger sample size are needed to validate the association among the periodontal inflammation and systemic parameters.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com. Financial or other competing interests: None.

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