Evaluation of inflammatory biomarkers and biochemical indicators in patients with combined periodontal and upper respiratory tract diseases

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Periodontal diseases and chronic tonsillitis are among the most prevalent inflammatory conditions affecting the oral cavity and upper respiratory tract, respectively. Increasing evidence suggests a bidirectional relationship between oral and systemic health, with chronic infections contributing to systemic inflammatory burden. The present study aimed to comparatively evaluate clinical periodontal parameters, systemic inflammatory markers, and biochemical indicators in patients with coexisting stomatological and otorhinolaryngological diseases. A prospective comparative study was conducted involving 60 patients aged 18–45 years, divided into two groups: Group I (n=30) included patients with periodontitis and chronic tonsillitis, while Group II (n=30) consisted of patients with gingivitis and chronic tonsillitis. Clinical periodontal indices, including Gingival Index (GI), Plaque Index (PI), and Periodontal Pocket Depth (PPD), were assessed. Systemic inflammatory markers (CRP, WBC, ESR) and biochemical parameters (IL-6, TNF-α, total protein) were analyzed using standardized laboratory methods. The results demonstrated significantly higher clinical and laboratory parameters in patients with periodontitis compared to those with gingivitis ($p<0.05$). Group I exhibited markedly elevated levels of CRP, IL-6, TNF-α, WBC, and ESR, indicating a pronounced systemic inflammatory response. Additionally, total protein levels were significantly higher in this group, reflecting increased metabolic and inflammatory activity. These findings suggest a synergistic effect of coexisting periodontal and tonsillar inflammation, leading to amplification of systemic inflammatory processes. In conclusion, the coexistence of periodontitis and chronic tonsillitis is associated with a significantly increased systemic inflammatory burden compared to gingivitis. Cytokine profiles and biochemical markers may serve as reliable indicators of disease severity. A multidisciplinary approach integrating dental and ENT management is essential for early diagnosis, effective treatment, and reduction of systemic complications.

Keywords: *Periodontitis, gingivitis, chronic tonsillitis, inflammatory biomarkers, cytokines, C-Reactive Protein, interleukin-6, Tumor Necrosis Factor-alpha*

INTRODUCTION

Periodontal disease (PD) is a general term encompassing a group of inflammatory pathologies that mainly include gingivitis and periodontitis. It is particularly pervasive in adults, though is not uncommon in children. Indeed, PD is an often all-encompassing term used to refer to any of the wide spectrum of inflammatory diseases that can affect the periodontium. PD is

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often initiated by an uncontrolled inflammatory response to a slow and constant bacterial colonization of the tooth surface and soft gingival tissues – Gingivitis, but it is the host inflammatory response to the microbial challenge that is responsible for the degradation of the periodontium – i.e., Periodontitis (Martínez-García et al., 2021).

Previous studies have shown that periodontitis can cause reactions in the immune system and a variety of diseases, including IgA nephropathy and glycosylated hemoglobin leading to diabetes onset (Byun et al., 2020).

Gingivitis is a mild form of gum disease and when treated quickly and properly it is completely reversible. Periodontitis is an advanced and irreversible disease of the periodontium with periods of exacerbations, progressions and remission (Lasica et al., 2024).

Tonsils and all other epithelium-lined interface surfaces of the body are exposed to colonization by a wide range of micro-organisms.[1] In general, the established microbiota lives in harmony with the host because the constant renewal of the surfaces by shedding prevents the accumulation of large masses of micro-organisms.[2] In the mouth, however, teeth provide hard, nonshedding surfaces for the development of extensive bacterial deposits. This accumulation (plaque) or its calcified form, calculus, around the teeth is an indicator of poor oral hygiene and has been designated as the primary cause of caries, gingivitis, and periodontitis (Adetayo et al., 2021).

Priyadharshini et al. reported a case of tonsillar actinomycosis that was possibly due to infection from actinomycosis normally found in dental plaque. Similarly, Georgalas et al. reported a positive association between poor oral hygiene and tonsillar infection while examining 158 subjects in their prospective study (Adetayo et al., 2020).

A variety of systemic diseases and conditions can affect the course of periodontitis or have a negative impact on the periodontal attachment apparatus. Gingival recessions are highly prevalent and often associated with hypersensitivity, the development of caries and non-carious cervical lesions on the exposed root surface and impaired esthetics. Occlusal forces can result in injury to teeth and periodontal attachment apparatus (Jepsen et al., 2018).

Tonsillitis is an inflammation of the pharyngeal tonsils. The inflammation may affect other areas of the back of the throat, including the adenoids and the lingual tonsils. Acute tonsillitis is an infection of the tonsils triggered by one of the several types of bacteria or viruses, and peritonsillar abscesses can also occur. Chronic tonsillitis is a tenacious infection of the tonsils, which may result in tonsil stones. Recurrent tonsillitis ensues when an individual suffers from several incidents of tonsillitis per year (Abu Bakar et al., 2018).

The aim of this study was to evaluate and compare clinical periodontal parameters, systemic inflammatory markers, and biochemical indicators in patients with combined stomatological and otorhinolaryngological diseases – specifically periodontitis or gingivitis associated with chronic tonsillitis – and to assess the impact of disease severity on the systemic inflammatory response.

MATERIALS AND METHODS

This study was designed as a prospective comparative investigation aimed at evaluating inflammatory and biochemical parameters in patients with combined stomatological and otorhinolaryngological pathology. A total of 60 patients were enrolled in the study. All participants were recruited based on predefined inclusion and exclusion criteria and provided informed consent prior to participation.

The study population was divided into two groups according to their clinical diagnosis: Group I – 30 patients diagnosed with periodontitis in combination with chronic tonsillitis; Group II 30 patients diagnosed with gingivitis in combination with chronic tonsillitis. The age of the participants was between 18-45 years, with a mean age of 31.4±6.2 years. The gender distribution was relatively balanced, comprising 52% females and 48% males.

Inclusion criteria into research of patients were:

- Age between 18 and 45 years
- Presence of chronic tonsillitis confirmed by ENT examination
- Diagnosis of periodontitis or gingivitis

based on clinical periodontal criteria
- Absence of acute systemic diseases

The study exclusion criteria included the following:
- History of systemic inflammatory or autoimmune diseases
- Recent antibiotic or anti-inflammatory therapy (within the last 3 months)
- Pregnancy or lactation
- Previous periodontal or ENT surgical interventions.

A comprehensive clinical examination was performed for all patients. The following stomatological parameters were assessed:

Gingival Index (GI) – to evaluate the severity of gingival inflammation (Sanz et al., 2020).

Plaque Index (PI) – to assess oral hygiene status (Ceylan Şen et al., 2025).

Periodontal Pocket Depth (PPD, mm) – measured using a calibrated periodontal probe (Jabri et al., 2026).

Additionally, ENT-related parameters were evaluated, including the degree of tonsillar inflammation, which was determined based on a combination of subjective symptoms (e.g., sore throat, discomfort) and objective clinical findings (hyperemia, tonsillar hypertrophy, presence of exudate).

Venous blood samples were collected from all participants under standardized conditions. The following inflammatory markers were analyzed: C-reactive protein (CRP, mg/L), white blood cell count (WBC, $\times 10^9$/L), erythrocyte sedimentation rate (ESR, mm/hour).

In addition, the following biochemical parameters were measured: Interleukin-6 (IL-6, pg/mL), tumor necrosis factor-alpha (TNF-α, pg/mL), total protein (g/L).

These biomarkers were selected due to their established role in systemic inflammatory response and their relevance in both periodontal and tonsillar pathology.

Statistical analysis was performed using standard biomedical statistical methods. Continuous variables were expressed as mean±standard deviation (M±SD). Group comparisons were carried out using: Student's t-test for normally distributed data, Mann-Whitney U test for non-parametric data, Chi-square (χ^2) test for categorical variables. A p-value <0.05 was considered statistically significant. All analyses were conducted using appropriate statistical software, ensuring the validity and reliability of the obtained results.

RESULTS AND DISCUSSION

The comparative analysis of clinical periodontal parameters between the two study groups is presented in Table 1. Patients with periodontitis and chronic tonsillitis (Group I) demonstrated significantly higher values of all assessed indices compared to patients with gingivitis and chronic tonsillitis (Group II). Specifically, the Gingival Index (GI) was markedly elevated in Group I (2.4±0.3) compared to Group II (1.8±0.2), indicating more severe gingival inflammation ($p<0.001$). Similarly, the Plaque Index (PI) was significantly higher in Group I (2.6±0.4 and 2.1±0.3; $p=0.002$), reflecting poorer oral hygiene and increased plaque accumulation.

The most pronounced difference was observed in periodontal pocket depth (PPD), which was more than twice as high in Group I (5.2±0.8 mm) compared to Group II (2.3±0.5 mm; $p<0.001$). These findings clearly indicate that periodontal destruction is significantly more advanced in patients with periodontitis, which directly affects both local tissue integrity and functional status.

The analysis of systemic inflammatory markers revealed a significantly stronger inflammatory response in Group I (Table 2). The level of CRP was markedly elevated in patients with periodontitis (12.8±3.2 mg/L) compared to those with gingivitis (7.1±2.4 mg/L; $p<0.001$). In addition, WBC count was significantly higher in Group I (9.8±1.5×10⁹/L and 7.6±1.2×10⁹/L; $p=0.004$), indicating an intensified immune response.

The ESR also showed a statistically significant increase in Group I (24.5±5.1 mm/h and 16.2±4.3 mm/h; $p<0.001$), further confirming the presence of an active systemic inflammatory process. These results suggest that the coexistence of periodontitis and chronic tonsillitis leads to a synergistic enhancement of systemic inflammation.

Significant differences were also observed in

pro-inflammatory cytokines and biochemical markers (Table 3). The levels of IL-6 were substantially higher in Group I (18.4±4.6 pg/mL) compared to Group II (11.2±3.1 pg/mL; p<0.001). Similarly, TNF-α was elevated in Group I (22.7±5.2 pg/mL and 14.5±3.8 pg/mL; p<0.001).

Table 1. Comparative clinical parameters in the study groups

Indicator	Group I **(Periodontitis + Chronic Tonsillitis)**	Group II **(Gingivitis + Chronic Tonsillitis)**	p
GI	2.4±0.3	1.8±0.2	<0.001
PI	2.6±0.4	2.1±0.3	0.002
PPD (mm)	5.2±0.8	2.3±0.5	<0.001

Table 2. Comparative inflammatory marker levels in the study groups

Indicator	Group I **(Periodontitis + Chronic Tonsillitis)**	Group II **(Gingivitis + Chronic Tonsillitis)**	p
CRP (mg/L)	12.8±3.2	7.1±2.4	<0.001
WBC (×10⁹/L)	9.8±1.5	7.6±1.2	0.004
ESR (mm/hour)	24.5±5.1	16.2±4.3	<0.001

Table 3. Comparative biochemical parameters in the study groups

Indicator	Group I **(Periodontitis + Chronic Tonsillitis)**	Group II **(Gingivitis + Chronic Tonsillitis)**	p
IL-6 (pg/mL)	18.4±4.6	11.2±3.1	<0.001
TNF-α (pg/mL)	22.7±5.2	14.5±3.8	<0.001
Total protein (g/L)	73.2±4.1	70.1±3.7	0.041

The total protein level was also slightly but significantly higher in the I group (73.2±4.1 g/L vs 70.1±3.7 g/L; p=0.041), reflecting increased metabolic and inflammatory activity. These findings confirm that patients with periodontitis exhibit a more pronounced systemic inflammatory response mediated by cytokine activation.

The findings of this study demonstrate that the coexistence of periodontitis and chronic tonsillitis results in a significantly more severe inflammatory burden compared to gingivitis combined with chronic tonsillitis. Periodontitis, being a destructive inflammatory disease affecting the supporting structures of the teeth, contributes not only to local tissue damage but also to systemic inflammatory activation.

The elevated levels of CRP, IL-6, and TNF-α observed in the I group indicate a strong systemic inflammatory response, which is consistent with the concept of oral-systemic interconnection. These biomarkers are well-established mediators of inflammation and play a key role in both periodontal tissue destruction and systemic immune regulation.

In contrast, gingivitis is a reversible, more superficial inflammatory condition, which explains the lower levels of both clinical and laboratory parameters in the II group. The absence of deep periodontal pockets and limited tissue destruction in gingivitis reduces the systemic dissemination of inflammatory mediators.

The results also support the hypothesis that chronic infections of the oral cavity and upper respiratory tract may act synergistically, amplifying the overall inflammatory response. The presence of chronic tonsillitis may serve as an additional source of persistent infection, further exacerbating systemic inflammation in patients with periodontitis.

From a clinical perspective, these findings emphasize the importance of a multidisciplinary approach, integrating both dental and otorhinolaryngological management. Early diagnosis and combined treatment strategies may help reduce the systemic inflammatory load and improve overall patient outcomes.

CONCLUSIONS

- Patients with periodontitis combined with chronic tonsillitis exhibit significantly higher clinical, inflammatory, and biochemical parameters compared to those with gingivitis.
- Periodontitis is associated with a more

pronounced systemic inflammatory response, as evidenced by elevated CRP, IL-6, and TNF-α levels.
- Gingivitis, as a superficial inflammatory condition, has a limited systemic impact.
- The combination of stomatological and ENT pathologies leads to amplification of systemic inflammation.
- Cytokine levels can serve as reliable markers of disease severity and inflammatory activity.
- A comprehensive, multidisciplinary diagnostic and therapeutic approach is essential for effective management of such patients.

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CONFLICT OF INTEREST

The author declares no conflict of interest related to this study.

ETHICAL APPROVAL

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the relevant institutional ethics committee.

AUTHOR CONTRIBUTIONS

Narmina Gurskaya conceived and designed the study, coordinated patient recruitment, performed clinical periodontal assessments, and drafted the manuscript. Sariyya Puri-Zahidan contributed to clinical examinations, data collection, and interpretation of the dental findings. Sevda Elesgerova participated in laboratory investigations, analysis of inflammatory biomarkers, and manuscript revision. Sevinj Guliyeva performed statistical analyses, contributed to data interpretation, and critically reviewed the manuscript. All authors read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

AI STATEMENT

The authors declare that no artificial intelligence (AI) tools were used to generate, analyze, interpret, or validate the clinical, laboratory, or statistical data presented in this study. Any AI-assisted technologies, if used, were limited to language editing, grammar correction, or formatting support. The authors take full responsibility for the accuracy, originality, and integrity of the manuscript.

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