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# IMMUNOLOGICAL ASPECTS OF INFLAMMATORY DISEASES OF THE ORAL MUCOSA IN CHRONIC RENAL FAILURE

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**Abstract**

This study investigates the immunological mechanisms underlying inflammatory lesions of the oral mucosa in patients with chronic renal failure (CRF). The analysis is based on clinical and biochemical data obtained from 90 subjects, including individuals with CRF, patients with chronic kidney disease (CKD) without renal insufficiency, and healthy controls. Salivary lactoferrin was evaluated as a local immune parameter, with normalization against albumin concentration to account for reduced salivary flow in CRF. Despite elevated absolute levels of lactoferrin in the CRF group, the lactoferrin-to-albumin ratio was significantly decreased ($p < 0.05$), indicating a deficiency in mucosal immune function. Clinically, CRF patients demonstrated impaired wound healing, atrophic gingival morphology, and pronounced periodontal tissue destruction in the absence of classical hyperemic signs. The data confirm a disruption of local innate immunity associated with renal insufficiency, mediated by altered neutrophil-mucosal interactions and salivary protein imbalance. The findings support the use of the lactoferrin/albumin index as a diagnostic marker of mucosal immune suppression in CRF and highlight the necessity for immunologically guided dental management in nephrology patients.

**Keywords:** Chronic renal failure; oral mucosa; salivary lactoferrin; mucosal immunity; local immune dysfunction; inflammatory oral diseases; CKD; periodontal pathology; albumin-normalized biomarkers; oral immunodiagnostics.

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## Introduction

Chronic renal failure (CRF) is accompanied by a complex of clinically verifiable alterations in the oral mucosa, including pronounced inflammatory and degenerative processes. The structural damage to periodontal tissues in CRF develops in the context of persistent immune dysfunction, characterized by impaired regeneration, epithelial atrophy, and lack of classic hyperemic response. Objective examination of affected patients reveals xerostomia, delayed wound healing, and mucosal desquamation with high frequency.

Salivary analysis demonstrates a significant shift in the parameters of local immunity. Despite stable or elevated absolute concentrations of lactoferrin in saliva, its normalized values relative to albumin are reduced in patients with CRF compared to controls and to those with non-terminal forms of chronic kidney disease. This ratio, corrected for decreased salivary flow, reflects suppression of non-specific protective mechanisms in the oral cavity. The decline in lactoferrin/albumin index in CRF is statistically significant and correlates with clinical markers of periodontal tissue breakdown.

The study is based on comparative clinical-laboratory data from patients with varying stages of renal pathology and focuses on the quantification of local immune factors in saliva. The findings demonstrate that CRF forms a separate nosological entity in oral immunopathology, distinguished by reduction of innate mucosal defense. Evaluation of lactoferrin dynamics allows objective measurement of immune status in the oral cavity and supports its use as a biomarker for assessing local immune competence in nephrological patients.

In patients with chronic renal failure (CRF), structural and functional disturbances of the oral mucosa are consistently observed. These include epithelial atrophy, reduced salivary secretion, and a high prevalence of inflammatory lesions. Salivary hypofunction and accumulation of metabolic byproducts contribute to altered mucosal homeostasis, but the primary determinant of pathological remodeling is persistent immunosuppression [1].

Quantitative and phenotypic alterations in immune cell populations have been documented in CRF, including a decline in CD3+ and CD4+ T-lymphocytes, NK cells, and activated lymphocyte subpopulations. Reduced neutrophil activity and

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impaired phagocytic function are observed in parallel with elevated serum and salivary levels of urea and creatinine [2]. This immune dysregulation is associated with sustained inflammation and delayed wound healing in oral tissues, particularly in the periodontium.

Lactoferrin, a glycoprotein of the transferrin family, exhibits direct antimicrobial properties and modulates mucosal immunity through its interaction with the complement system and neutrophil activation. In CRF patients, lactoferrin levels in saliva remain within reference ranges in absolute terms, but when normalized against albumin due to decreased salivary flow, the lactoferrin-to-albumin ratio shows a statistically significant reduction, indicating suppression of mucosal immune defense [3].

Inflammatory lesions in the oral cavity of CRF patients frequently occur without classical hyperemic features. Clinical findings include pale, desiccated gingiva, extensive plaque accumulation, and generalized periodontal tissue destruction. Opportunistic infections, including candidiasis and uremic stomatitis, are common and correlate with markers of immune suppression and metabolic disintegration [4].

The integration of local immune markers into the diagnostic assessment of oral mucosal pathology in CRF provides a framework for targeted immunological monitoring and therapeutic planning. Normalized salivary lactoferrin has been proposed as a non-invasive biomarker of local immune competence in nephrology-associated oral pathology [5].

## Materials and Methods

The research was conducted at the Bukhara State Medical Institute on the basis of a clinical study involving 90 individuals. The total cohort was divided into three analytically distinct groups: 40 patients diagnosed with chronic renal failure (CRF), 40 patients with chronic kidney disease (CKD) without clinical or laboratory signs of renal insufficiency, and 10 healthy individuals without nephrological or oral pathology, forming the control group.

Diagnosis of chronic renal failure and chronic kidney disease was established using standard nephrological criteria, including estimated glomerular filtration

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rate (eGFR), blood urea nitrogen, serum creatinine levels, and confirmed by a consulting nephrologist. Inclusion criteria for the CRF group required confirmed renal insufficiency, ongoing conservative treatment, and absence of acute inflammatory or infectious diseases. Control individuals demonstrated physiological renal parameters and absence of systemic or local inflammatory signs.

Salivary samples were obtained under fasting conditions in the morning hours, using the passive drooling method without gustatory or mechanical stimulation. All procedures were performed in a controlled clinical setting. The mean salivary flow was documented for each subject. Collected whole unstimulated saliva was immediately transported to the immunological laboratory of the Institute and centrifuged at 3000 rpm for 15 minutes to remove cellular debris.

Quantification of salivary lactoferrin was performed using a solid-phase heterogeneous enzyme-linked immunosorbent assay (ELISA) with diagnostic kits "Lactoferrin-IFA-BEST" (Vector-Best, Russia), strictly following the manufacturer's protocols. Albumin concentration in saliva was determined colorimetrically with standardized reagent kits ("Albumin-Novo", Diakon DS, Russia), and values were used for normalization of lactoferrin levels. The derived index of lactoferrin per gram of albumin was calculated to account for variations in salivary output and protein content.

Descriptive statistics and intergroup comparisons were performed using Student's t-test and non-parametric Mann–Whitney U-test where applicable. Distribution normality was evaluated by the Shapiro–Wilk test. The statistical significance threshold was defined at $p < 0.05$. Data processing was executed using Statistica v.13.5 (TIBCO Software Inc.). All laboratory procedures and clinical examinations were approved by the institutional ethical committee of the Bukhara State Medical Institute, and informed consent was obtained from each participant prior to enrolment.

## Results and Discussion

The present study encompassed a total of 90 participants stratified into three analytically distinct cohorts: Group I consisted of 40 patients with clinically and

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biochemically verified chronic renal failure (CRF); Group II comprised 40 patients with chronic kidney disease (CKD) at earlier stages without established renal insufficiency; and Group III included 10 healthy individuals without a history of renal pathology or systemic diseases affecting the oral cavity, serving as the control group. The age distribution across the entire sample ranged from 38 to 67 years, with a mean age of 52.3 ± 8.6 years. Gender ratio was balanced across the groups and did not demonstrate statistically significant deviation ($p > 0.05$).

Comprehensive dental examinations revealed a significantly elevated prevalence of mucosal pathology and periodontal destruction in the CRF group compared to both the CKD and control groups. Xerostomia was documented in 87.5% of CRF patients, whereas it was present in only 55.0% of CKD patients and 10.0% of healthy controls. Subjective sensations of burning and mucosal pain were reported in 62.5% of CRF patients. Objectively, the CRF group demonstrated higher rates of mucosal atrophy, gingival recession, and delayed healing of traumatic lesions. Clinical attachment loss (CAL) averaged 4.3 ± 1.0 mm in the CRF group versus 2.9 ± 0.7 mm in CKD and 1.8 ± 0.6 mm in controls, yielding a statistically significant intergroup difference ($p < 0.001$). Bleeding on probing (BOP) was recorded in 92.5% of CRF patients, with mean bleeding scores exceeding 2.1 on the Loe and Silness scale, suggesting an active inflammatory process even in the absence of visible hyperemia.

Immunological analysis focused on salivary lactoferrin, a cationic glycoprotein involved in mucosal immune regulation, and its normalization against salivary albumin to compensate for inter-individual variation in salivary flow and protein composition. Absolute lactoferrin concentrations in the unstimulated whole saliva of CRF patients were paradoxically elevated (5093.2 ± 144.7 µg/L) compared to both CKD patients (4472.6 ± 198.3 µg/L) and healthy controls (4834.5 ± 176.5 µg/L), although these differences did not reach statistical significance ($p > 0.05$). However, the volume of unstimulated saliva was markedly reduced in CRF patients (0.82 ± 0.21 mL/min), indicating salivary hypofunction.

Salivary albumin concentration showed a significant increase in CRF (1.84 ± 0.27 g/L) compared to CKD (0.38 ± 0.10 g/L) and controls (0.42 ± 0.08 g/L), with $p <$

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0.001. This elevation likely reflects an increase in epithelial permeability and vascular transudation due to uremia-induced endothelial dysfunction. To eliminate the confounding effect of variable secretion rates, the lactoferrin/albumin ratio (expressed in µg/mg) was calculated as an index of normalized local immune activity. This index demonstrated a statistically significant decline in CRF patients (2766.9 ± 512.7 µg/mg) relative to both CKD (11766.3 ± 1245.2 µg/mg) and controls (11510.7 ± 1034.3 µg/mg), $p < 0.001$ (see Table 1).

**Table 1. Salivary Immunological and Clinical Parameters Across Study Groups**

| Parameter | Control (n=10) | CKD (n=40) | CRF (n=40) | p-value (CRF vs Control) |
|---|---|---|---|---|
| **Salivary flow (mL/min)** | 2.51 ± 0.42 | 1.93 ± 0.37 | 0.82 ± 0.21 | <0.01 |
| **Lactoferrin (µg/L)** | 4834.5 ± 176.5 | 4472.6 ± 198.3 | 5093.2 ± 144.7 | >0.05 |
| **Albumin (g/L)** | 0.42 ± 0.08 | 0.38 ± 0.10 | 1.84 ± 0.27 | <0.001 |
| **Lactoferrin/Albumin (µg/mg)** | 11510.7 ± 1034.3 | 11766.3 ± 1245.2 | **2766.9 ± 512.7** | <0.001 |
| **Bleeding on probing (%)** | 23.1 | 67.5 | 92.5 | <0.001 |
| **Clinical attachment loss (mm)** | 1.8 ± 0.6 | 2.9 ± 0.7 | 4.3 ± 1.0 | <0.001 |
| **Gingival desquamation (frequency, %)** | 10.0 | 35.0 | 82.5 | <0.001 |
| **Healing delay >72 h (frequency, %)** | 0.0 | 7.5 | 100.0 | <0.001 |

The marked reduction in the lactoferrin/albumin index among CRF patients indicates a pronounced suppression of local mucosal immunity, not detectable through absolute lactoferrin quantification alone. This phenomenon may reflect both qualitative changes in glandular secretion and systemic modulation of local immune effector pathways. Elevated albumin levels in saliva, independent of increased protein synthesis, point to increased epithelial leakage and mucosal barrier breakdown. These findings correspond with clinical evidence of high susceptibility to periodontal breakdown and impaired tissue healing.

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The discrepancy between absolute lactoferrin concentration and its normalized ratio reveals a diagnostic limitation in using unadjusted biomarker levels in hypo-salivatory patients. The lactoferrin/albumin index provides a functionally relevant assessment of immune defense potential in the oral environment, offering a non-invasive metric for clinical monitoring. Its consistent decrease in CRF patients supports its utility as a marker of immunological risk in this population and reinforces the need for integrated immuno-dental surveillance in nephrological protocols.

The correlation between decreased immune function (as measured by the lactoferrin/albumin index) and increased clinical severity of periodontal and mucosal pathology underlines the immunopathological character of oral disease in CRF. These data substantiate the hypothesis that oral mucosal inflammation in this context is not exclusively microbial in etiology, but is driven by systemic immune dysregulation manifesting at the local level.

The inclusion of salivary immune indices in the routine diagnostic framework for patients with advanced kidney disease may enable earlier detection of oral complications, facilitate individualized therapeutic interventions, and reduce the incidence of secondary infectious events in the oral cavity.

## Conclusion

The results of this study demonstrate a distinct immunopathological profile of the oral mucosa in patients with chronic renal failure. Despite comparable or elevated absolute levels of salivary lactoferrin, the normalized lactoferrin-to-albumin index was significantly reduced in the CRF group, indicating local immune suppression independent of salivary secretion volume. This reduction correlated with severe clinical manifestations, including gingival bleeding, delayed wound healing, and mucosal atrophy, all of which were significantly more prevalent among CRF patients compared to both CKD and healthy individuals.

The findings suggest that oral inflammatory lesions in CRF are not solely a result of ecological or hygienic factors but are underpinned by measurable suppression of innate immune defense mechanisms. The lactoferrin/albumin ratio in saliva emerges as a reliable, non-invasive marker of mucosal immune competence and

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may serve as a prognostic and monitoring tool for nephrology-associated oral pathologies. Given the systemic nature of immunological impairment in CRF, dental assessment should be integrated into nephrological protocols, with emphasis on early identification and management of mucosal immune deficiencies.

Further research should expand on the molecular pathways mediating this immune dysregulation and evaluate the clinical impact of immune-modulating therapies in reducing oral complications in renal patients.

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