Volume 3, Issue 5, May 2025 ISSN (E): 2938-3765

THE RELATIONSHIP BETWEEN CHRONIC RENAL FAILURE AND INFLAMMATORY DISEASES OF THE ORAL MUCOSA: NEW THERAPEUTIC STRATEGIES

Sabirov Bobur Kadirbaevich
Khabibova Nazira Nasullaevna
Bukhara State Medical Institute

Abstract
Chronic renal failure (CRF) is associated with a high prevalence of inflammatory lesions in the oral mucosa, manifesting as a distinct spectrum of clinical and histopathological alterations. The progression of uremia correlates with a shift in local immune reactivity, endothelial dysfunction, and accumulation of metabolic byproducts in the oral cavity. The review integrates current clinical findings and mechanistic evidence linking salivary hypofunction, altered microbiocenosis, and immunosuppressive pharmacotherapy to the pathogenesis of oral mucosal diseases in CRF patients. Specific attention is given to xerostomia, uremic stomatitis, candidiasis, lichen planus, and vascular-associated mucosal bleeding. The article evaluates the limitations of symptomatic treatment in the context of sustained renal impairment and proposes novel therapeutic algorithms, including targeted antimicrobial regimens, cytokine-modulating agents, and pre-transplant oral rehabilitation protocols. Interdisciplinary coordination between nephrology and oral medicine is positioned as a critical component of patient management, particularly in pre-dialysis and post-transplant cohorts.

Keywords: Chronic renal failure; oral mucosa; mucosal inflammation; uremic stomatitis; xerostomia; hemodialysis; candidiasis; lichen planus; endothelial dysfunction; nephrology-oriented oral care.

Introduction

Inflammatory diseases of the oral mucosa in patients with chronic renal failure (CRF) constitute a polymorphic pathological cluster with a documented correlation to the severity and duration of uremia. Histopathological and clinical data confirm persistent mucosal degradation under conditions of azotemia, metabolic acidosis, and secondary immunodeficiency. Hemodialysis and continuous ambulatory peritoneal dialysis further modulate the oral environment, exacerbating epithelial atrophy, dysbiosis, and microvascular instability.

Current evidence demonstrates the predominance of xerostomia, gingival hemorrhagic phenomena, erosive lichenoid reactions, and candidiasis in CRF cohorts. These lesions are resistant to conventional therapy and display poor reversibility until the resolution of the underlying renal pathology. Uremic stomatitis, observed in patients with serum urea

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

concentrations exceeding 150 mg/dL, remains pathognomonic for terminal-stage nephropathy and is frequently accompanied by ulceronecrotic and hemorrhagic components.

Salivary compositional shifts, including elevated concentrations of ammonia, urea, and β2-microglobulin, create a proteolytic and inflammatory milieu, facilitating epithelial desquamation and impaired wound healing. Pharmacological suppression of immune surveillance—via corticosteroids, calcineurin inhibitors, or anti-proliferative agents—further predisposes to dysplastic transformation and opportunistic colonization.

The absence of protocolized oral diagnostic and therapeutic frameworks within nephrology underscores the necessity for evidence-based integration. This study systematizes current pathogenetic models of mucosal inflammation in CRF, critically reviews available therapeutic regimens, and proposes clinically applicable strategies for risk-adapted management in dialysis and pre-transplant populations.

Chronic renal failure (CRF) significantly affects the oral mucosa, leading to various inflammatory conditions. Patients with CRF often exhibit oral manifestations such as xerostomia, uremic odor, and mucosal lesions, which are attributed to metabolic imbalances and immunosuppression associated with renal dysfunction [1]. These oral conditions not only affect the quality of life but also pose challenges in the management of CRF patients.

The prevalence of oral mucosal lesions in CRF patients is notably higher compared to the general population. Studies have reported that conditions like uremic stomatitis, candidiasis, and mucositis are common in individuals undergoing hemodialysis [2]. The pathophysiology involves the accumulation of uremic toxins, altered salivary composition, and compromised immune responses, which collectively contribute to the development of these lesions [3].

Management strategies for these oral manifestations require a multidisciplinary approach. Regular dental evaluations and prompt treatment of oral infections are crucial. Additionally, addressing systemic factors such as maintaining optimal dialysis and controlling metabolic parameters can mitigate the severity of oral conditions [4].

Emerging therapeutic interventions focus on enhancing oral hygiene practices, utilizing antimicrobial mouthwashes, and implementing dietary modifications to reduce the burden of oral diseases in CRF patients. Furthermore, patient education on the importance of oral health and its impact on overall well-being is essential [5].

Materials and Methods

The study was conducted at the Department of Nephrology and Oral Pathology, Bukhara State Medical Institute. The research cohort included 68 patients with confirmed chronic renal failure at stages 4–5, undergoing maintenance hemodialysis for at least six months. The control group consisted of 20 systemically healthy individuals without renal pathology, matched by age and sex. Comprehensive intraoral examination was performed using a standardized clinical protocol in accordance with WHO diagnostic criteria for inflammatory diseases of the oral mucosa. The mucosal condition was classified into four clinical forms: erythematous, erosive, ulceronecrotic, and hyperplastic. Objective mucosal assessment included visual scoring, bleeding on palpation, localization mapping, and pain index on the VAS scale. Salivary flow rate was determined by the

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Navazesh method; biochemical parameters of saliva (urea, creatinine, calcium, phosphate) were quantified using spectrophotometric analysis on a Mindray BS-240 system.

Cytological samples were obtained from lesional and perilesional mucosa by scraping with a sterile cytobrush and stained using Romanowsky-Giemsa and Papanicolaou protocols. Cell morphology was evaluated under light microscopy with quantification of epithelial integrity, nuclear-cytoplasmic ratio, polymorphonuclear infiltration, and presence of dyskeratosis. All cytological analyses were interpreted blindly by two independent pathologists.

Microbiological identification was conducted from mucosal swabs cultured on chromogenic media for Candida spp. and Mitis Salivarius agar for streptococcal colonies. Colony-forming units were recorded after 48 hours of incubation at 37°C under aerobic and microaerophilic conditions. Identification was confirmed by VITEK 2 compact system. PCR-based verification of *Candida albicans*, *C. glabrata*, and *C. tropicalis* strains was performed in selected cases with persistent lesions.

Inflammatory and immunological profiles were assessed by quantifying IL-6, TNF-α, and salivary sIgA concentrations using ELISA (BioLegend, USA), with readings validated on a Thermo Fisher Multiskan FC reader. Serum urea, creatinine, and electrolytes were retrieved from the dialysis unit's automated analyzers (Roche Cobas 8000 series) and synchronized to the day of oral sampling. Hemostasis was evaluated through platelet count, PFA-100 bleeding time, and plasma fibrinogen concentration.

Statistical processing included Shapiro–Wilk normality testing, intergroup comparison using Mann–Whitney U test, Spearman rank correlation analysis, and multivariate logistic regression to assess predictors of mucosal pathology severity. Analytical processing was carried out in Stata 17.0. Statistical significance was set at $\alpha = 0.01$ for all tests.

Results and Discussion

The clinical investigation was conducted at the Department of Nephrology and Oral Medicine, Bukhara State Medical Institute. The primary cohort consisted of 68 patients diagnosed with end-stage chronic renal failure (CRF), all receiving thrice-weekly maintenance hemodialysis for a minimum of six months. The mean age was 54.1 ± 8.7 years. A control group of 20 systemically healthy individuals, matched by sex and age, was included for baseline comparison.

Inflammatory-destructive alterations of the oral mucosa were documented in 61 out of 68 CRF patients (89.7%), whereas mucosal lesions in the control group were observed in only 3 individuals (15%). Xerostomia was recorded in 76.4% of CRF patients, oral candidiasis in 54.4%, uremic stomatitis in 35.2%, and erosive lichen planus in 17.6%. The corresponding findings in the control group were limited to isolated cases of xerostomia (10%) without any confirmed mycotic or ulcerative pathology. The intergroup differences reached high statistical significance (χ^2, $p < 0.001$).

Salivary urea levels in CRF patients were elevated to 15.2 ± 2.9 mmol/L, compared to 5.8 ± 1.3 mmol/L in controls ($p < 0.001$), accompanied by a marked shift in pH toward acidification (6.03 ± 0.24 vs. 6.82 ± 0.12, $p < 0.001$). Cytological analysis identified inflammatory-desquamative changes in 87.1% of CRF cases with lesions, including epithelial atrophy, nuclear pyknosis, and

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

neutrophilic infiltration. Fungal colonization with *Candida spp.* was confirmed in 64.7% of CRF patients, while all control subjects tested negative on mycological culture.

Mean salivary interleukin-6 (IL-6) concentration in CRF patients presenting with mucosal inflammation was 32.8 ± 7.4 pg/mL, significantly exceeding the levels in healthy controls (13.5 ± 3.9 pg/mL, $p < 0.01$). A strong positive correlation was observed between IL-6 concentration and clinical mucosal severity score (Spearman's $\rho = 0.61$; $p < 0.001$). Stratified analysis revealed that patients with dialysis duration exceeding five years demonstrated an increased frequency of keratotic mucosal lesions (23.1%) and higher fungal burden, suggesting a cumulative immunological deterioration with prolonged extracorporeal treatment exposure.

Table 1. Comparative Clinical and Biochemical Parameters in Study Groups

Parameter	CRF Patients (n = 68)	Control Group (n = 20)	p-value
Prevalence of oral mucosal lesions (%)	89.7	15	< 0.001
Xerostomia (%)	76.4	10	< 0.001
Candidiasis (%)	54.4	0	< 0.001
Uremic stomatitis (%)	35.2	0	< 0.001
Salivary urea (mmol/L)	15.2 ± 2.9	5.8 ± 1.3	< 0.001
Salivary pH	6.03 ± 0.24	6.82 ± 0.12	< 0.001
IL-6 in saliva (pg/mL)	32.8 ± 7.4	13.5 ± 3.9	< 0.01
Positive *Candida* culture (%)	64.7	0	< 0.001

The data substantiate the hypothesis that CRF significantly predisposes patients to a broad spectrum of inflammatory and infectious oral mucosal disorders. The combination of nitrogenous metabolite accumulation, altered oral fluid biochemistry, salivary gland hypofunction, and systemic immunosuppression creates a sustained pathological environment favoring mucosal breakdown and microbial dysbiosis.

Elevated salivary IL-6 in affected patients suggests its utility as a non-invasive biomarker for active mucosal inflammation in the CRF population. Given the direct correlation with clinical symptomatology, IL-6 quantification may support early-stage screening and severity stratification within nephrology-dental co-management protocols.

Moreover, the cumulative dialysis duration appears to be a critical variable influencing not only lesion prevalence but also resistance to standard therapeutic interventions. These findings emphasize the necessity for integrated, duration-adjusted treatment frameworks combining antifungal prophylaxis, cytokine modulation, and epithelial repair strategies tailored to immunologically vulnerable patients.

The presented results warrant further validation in multicenter prospective trials to evaluate long-term efficacy of targeted interventions and to refine therapeutic algorithms for oral mucosal preservation in chronic renal failure.

Conclusion

The findings of this study confirm a high prevalence of inflammatory and infectious lesions of the oral mucosa among patients with chronic renal failure, particularly those undergoing long-term

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

hemodialysis. The presence of xerostomia, uremic stomatitis, oral candidiasis, and keratotic lesions is closely associated with elevated levels of salivary urea, reduced pH, and increased local expression of proinflammatory cytokines such as interleukin-6. The statistical correlation between salivary biomarkers and clinical severity indicates a strong systemic-to-local pathophysiological link. Moreover, the duration of dialysis emerges as a key determinant of both lesion complexity and therapeutic resistance.

These results reinforce the necessity of integrating oral health protocols into nephrology practice. Biomarker-driven diagnostics, combined with stratified therapeutic approaches—including antifungal management, topical immunomodulation, and salivary gland support—should be prioritized in the care of CRF patients. Future research must explore interventional efficacy and develop standardized oral monitoring frameworks within dialysis programs and pre-transplantation pathways.

References

1. Proctor R., Kumar N., Stein A. et al. Oral and dental aspects of chronic renal failure. J Dent Res. 2005;84(3):199–208.
2. Dencheva M., Ivanov I. Oral findings in patients with replaced renal function – a pilot study. Journal of IMAB. 2010;16(4):54–57.
3. Torkzaban P., Khoshhal M. Periodontal status in patients undergoing hemodialysis. DJH. 2009;1(1):7–10.
4. Klassen J.T., Krasko B.M. The dental health status of dialysis patients. J Can Dent Assoc. 2002;68(1):34–38.
5. Cerveró A., Bagán J.V., Roda R.P. Dental management in renal failure: patients on dialysis. Med Oral Patol Oral Cir Bucal. 2008;13:E419–E426.
6. Chuang S.F., Sung J.M., Kuo S.C. Oral and dental manifestations in diabetic and nondiabetic uremic patients receiving hemodialysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005;99:689–695.
7. Davidovich E., Schwarz Z., Davidson T. Oral findings and periodontal status in children and young adults with renal failure. J Clin Periodontol. 2005;32(11):1076–1082.
8. Antoniades D.Z., St. Louis B. Ulcerative uremic stomatitis associated with untreated CRF: case report and literature review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101(5):608–613.
9. Uenotsuchi T., Nakagawa H., Nagai Y. Cutaneous and lingual papules as a sign of β2-microglobulin-derived amyloidosis in a long-term hemodialysis patient. Eur J Dermatol. 2003;13(4):393–395.
10. Locatelli F., Canaud B., Eckardt K.U. Oxidative stress in end-stage renal disease: emerging threat to patient outcomes. Nephrol Dial Transplant. 2003;18(7):1272–1280.
11. Ferrario V.F., Tartaglia G.M., Dellavia C. Abnormal variations in the facial soft tissues of adult uremic patients on chronic dialysis. Angle Orthod. 2005;75(3):312–317.
12. Summers S.A., Tilakaratne W.M., Fortune F. Renal disease and the mouth. Am J Med. 2007;120(7):568–573.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

13. Bastos J.A., Dias C.R., Garcia M.V. Assessment of knowledge toward periodontal disease among nephrology personnel. J Bras Nefrol. 2011;33(4):431–435.
14. Teschner M., Heemann U., Pavenstädt H. Incidence and spectrum of malignant disease among dialysis patients in North Bavaria. Dtsch Med Wochenschr. 2002;127(47):2497–2502.
15. Yaşar F., Aydın B., Topaloğlu B. Oral health status and salivary parameters in hemodialysis patients. Clin Oral Investig. 2021;25(2):535–543.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5