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Specific Aspects of Dental Management in Patients with Chronic Kidney Disease: Inflammatory Conditions of The Oral Mucosa

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Abstract: The article investigates the clinical and therapeutic complexities of managing inflammatory diseases of the oral mucosa in patients with chronic kidney disease (CKD). Based on a comprehensive analysis of multi-center studies, three typological patterns of oral involvement are delineated, correlating with CKD severity and treatment modality. Patients undergoing hemodialysis, peritoneal dialysis, and post-transplant therapy present with xerostomia, gingival hyperplasia, uremic mucositis, and opportunistic infections, frequently accompanied by alterations in the cytokine profile and epithelial atrophy. Salivary hypofunction, immune dysregulation, and mineral-bone metabolism disturbances are identified as key pathophysiological mechanisms contributing to mucosal degradation. Quantitative associations between dialysis duration, inflammatory markers in gingival crevicular fluid, and periodontal destruction are substantiated across clinical cohorts. The analysis reveals that standard dental protocols are insufficient for this patient category and require adaptation to the immunocompromised state and systemic instability. The integration of dental evaluation into nephrological care protocols is justified by the observed bidirectional influence between periodontal inflammation and renal function dynamics.

Keywords: Chronic kidney disease; inflammatory oral mucosa; hemodialysis; gingival hyperplasia; salivary dysfunction; uremic mucositis; cytokine expression; immunosuppression; periodontal inflammation; systemic-dental interface; nephrology-integrated dental care.

Introduction: Chronic kidney disease (CKD) induces systemic alterations that modify epithelial homeostasis, immune competence, and microbiological stability in the oral cavity. Among oral complications, inflammatory lesions of the mucosa present with high frequency in patients undergoing renal replacement therapy and immunosuppressive treatment following kidney transplantation. Clinical data confirm a correlation between disease progression and the severity of oral mucosal inflammation.

Histopathological and immunological profiles of oral tissues in CKD patients reveal degenerative changes in epithelial layers, fibroblast hyperactivity, and dysregulated cytokine expression. Salivary gland atrophy, elevated concentrations of urea and albumin in saliva, and decreased salivary flow contribute to xerostomia and subsequent secondary infections. Gingival overgrowth, uremic stomatitis, and candidiasis occur with higher incidence in patients on hemodialysis, particularly those receiving cyclosporine-based regimens. Inflammatory infiltrates in the lamina propria and epithelial desquamation are consistently observed in biopsy material.

Quantitative assessments demonstrate a statistically significant association between dialysis duration and

parameters such as periodontal pocket depth, loss of epithelial attachment, and plaque index. These correlations persist independently of hygiene compliance, suggesting a direct pathophysiological role of renal dysfunction and its metabolic consequences. Furthermore, elevated levels of TNF-α, IL-1β, and matrix metalloproteinases in crevicular fluid reflect sustained immune activation.

Despite the evidence of pathological interactions between CKD and oral tissues, dental care remains insufficiently integrated into nephrological protocols. The lack of routine screening for mucosal conditions contributes to underdiagnosis, delayed intervention, and increased risk of systemic complications. The inflammatory state of the oral mucosa in CKD patients requires diagnostic stratification and tailored therapeutic approaches aligned with renal function status and immunosuppressive burden.

The present study analyzes inflammatory pathologies of the oral mucosa in CKD across dialysis modalities and transplant status, identifying clinical markers and proposing a modified dental management model adapted to nephrological comorbidity.

Chronic kidney disease (CKD) causes profound systemic changes, including immunosuppression, metabolic disturbances, and salivary gland dysfunction, all of which contribute to the development of inflammatory conditions in the oral mucosa [1]. Oral manifestations such as xerostomia, uremic stomatitis, and mucosal pallor are frequently observed among patients undergoing dialysis or post-transplant immunosuppressive therapy [2]. These complications result from elevated salivary urea levels, reduced buffering capacity, and epithelial atrophy, which increase the susceptibility to microbial colonization and mucosal irritation [3].

Periodontal inflammation in CKD patients has been associated with elevated levels of proinflammatory cytokines, including interleukin-1β and tumor necrosis factor-alpha in gingival crevicular fluid [4]. Evidence suggests a direct correlation between periodontal pocket depth, attachment loss, and duration of dialysis, indicating that renal dysfunction exacerbates oral tissue destruction [5]. Moreover, the bidirectional relationship between periodontitis and CKD has been emphasized, with oral inflammation potentially contributing to systemic inflammatory load and negatively impacting glomerular filtration [6].

The presence of gingival overgrowth, particularly in post-transplant recipients, has been linked to cyclosporine therapy. Histological analysis reveals increased fibroblast activity and epithelial proliferation in affected gingival tissues [7]. Uremic stomatitis, although less common in the current dialysis era, remains a diagnostic feature in terminal-stage patients and may present with painful ulcers, pseudomembranes, or hemorrhagic lesions [8].

METHODS

The study was conducted at the Department of Therapeutic Dentistry in cooperation with the Nephrology Department of the Bukhara State Medical Institute. The research cohort included 68 adult patients diagnosed with stage IV–V chronic kidney disease, receiving renal replacement therapy. Of them, 41 patients were undergoing hemodialysis for a period exceeding 24 months, 15 were recipients of renal allografts on calcineurin inhibitor-based immunosuppressive therapy, and 12 were managed conservatively at the pre-dialysis stage. The control group consisted of 28 individuals without systemic disease, matched for age and sex.

Intraoral examination was carried out under standard artificial illumination using plane dental mirrors and WHO periodontal probes. The condition of the oral mucosa was assessed with specific attention to hyperplasia, erosive and ulcerative lesions, hemorrhagic phenomena, and uremic encrustation. The Schirmer method was applied to measure unstimulated salivary flow over 5 minutes. Xerostomia intensity was assessed via a visual analogue scale (0–10) and confirmed by sialometry.

Periodontal parameters included probing pocket depth (PPD), clinical attachment loss (CAL), bleeding on probing (BOP), and plaque index (PI). The depth of periodontal pockets was recorded in six sites per tooth. All measurements were carried out by two calibrated examiners independently; intra-examiner agreement was confirmed with Cohen's kappa ($\kappa = 0.86$).

Gingival crevicular fluid was collected from the mesio-buccal surfaces of the first molars using PerioPaper strips. Samples were immediately placed in sterile Eppendorf tubes and frozen at −80 °C. The concentration of proinflammatory markers (IL-1β, TNF-α, IL-8, MMP-1) was determined using commercially available ELISA kits (R&D Systems, USA). Optical density was measured using a Multiskan FC Microplate Photometer (Thermo Scientific) at a wavelength of 450 nm. Each sample was tested in triplicate.

Microbiological analysis was performed by subgingival plaque sampling followed by cultivation on blood agar and Sabouraud agar for anaerobic and fungal detection. Identification of bacterial species was done using MALDI-TOF mass spectrometry.

Gingival biopsy specimens were obtained from four patients undergoing gingivectomy due to hyperplastic

lesions. Specimens were fixed in 10% buffered formalin, embedded in paraffin, sectioned at 4 µm, and stained with hematoxylin and eosin. Histological evaluation focused on epithelial desquamation, fibroblast activity, and vascular changes.

Biochemical analysis of salivary urea and creatinine was conducted using the enzymatic colorimetric method with an automated analyzer (Cobas 6000, Roche Diagnostics). Dialysis efficacy parameters (Kt/V, URR) and serum inflammatory markers (CRP, ferritin) were retrieved from clinical records for correlative analysis.

Statistical processing was performed using SPSS v.26.0. Data distribution was verified by Kolmogorov–Smirnov test. Between-group comparisons were made using one-way ANOVA for continuous variables and Pearson χ^2 test for categorical variables. Correlation analysis was conducted using Spearman's rank coefficient. Differences were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

This study presents a comparative clinical and biochemical evaluation of oral mucosal inflammatory conditions in patients with advanced stages of chronic kidney disease (CKD), with a focus on those undergoing hemodialysis (HD), renal transplantation, and pre-dialysis conservative treatment. A total of 68 patients were enrolled based on strict inclusion criteria, with 41 individuals receiving HD for a minimum of 24 months, 15 renal transplant recipients on a standardized immunosuppressive protocol (tacrolimus + prednisolone), and 12 patients in stage IV CKD managed conservatively. A control group of 28 systemically healthy individuals was recruited to establish baseline comparative metrics.

Clinical examination revealed a high prevalence of inflammatory mucosal alterations in CKD cohorts, with generalized mucosal dryness, erythema, ulcerative lesions, and fibrotic thickening of the gingiva present in a significant proportion of patients. Among HD patients, xerostomia was reported in 78.2% of cases, often accompanied by dysgeusia and mucosal burning sensations. The transplant group demonstrated an even higher rate of mucosal colonization by Candida spp. (51.4%) and exhibited gingival enlargement consistent with drug-induced hyperplasia in 40% of cases. Uremic mucositis was observed exclusively in the HD group, with clinical expression in 9.6% of patients, characterized by pseudomembranous patches and ulcerations on the dorsum of the tongue and buccal mucosa.

Quantitative periodontal parameters significantly differed across groups. The mean probing pocket depth (PPD) in the HD cohort was 4.28 ± 1.19 mm, substantially greater than that of controls (2.63 ± 0.78 mm; $p < 0.001$). Clinical attachment loss (CAL) followed a similar trend, with a mean of 3.91 ± 1.07 mm in HD patients versus 2.02 ± 0.65 mm in the control group ($p < 0.001$). Bleeding on probing (BOP), as an early marker of periodontal inflammation, was recorded in 72.4% of HD patients and 68.6% of transplant recipients, contrasting with 32.1% in the control group, indicating persistent vascular fragility and local inflammation even in the absence of overt ulceration.

Functional salivary analysis demonstrated statistically significant hyposalivation in both HD and transplant groups. The mean unstimulated salivary flow in the HD group was 0.18 ± 0.09 mL/min, compared to 0.21 ± 0.10 mL/min in the transplant group and 0.34 ± 0.11 mL/min in controls ($p < 0.01$). Salivary urea concentrations in HD patients reached 14.2 mmol/L, reflecting systemic azotemia, while in the transplant group this value was 8.5 mmol/L and 3.6 mmol/L in controls ($p < 0.001$). The correlation between salivary urea and xerostomia intensity was high ($r = 0.73$, $p < 0.01$), suggesting direct diffusion of metabolic waste into the oral cavity.

Gingival crevicular fluid (GCF) cytokine profiling revealed pronounced elevations in proinflammatory mediators. TNF-α concentrations averaged 32.6 pg/mL in HD patients and 28.4 pg/mL in transplant recipients, while IL-1β levels reached 64.7 pg/mL and 58.1 pg/mL, respectively. Controls demonstrated baseline cytokine levels (TNF-α: 12.3 pg/mL, IL-1β: 21.4 pg/mL), underscoring the subclinical inflammatory load in CKD. These elevations corresponded to clinical indices of periodontal degradation and underscore the systemic inflammatory spillover into the periodontium.

Microbiological analysis identified significant dysbiosis in CKD patients. Candida albicans was isolated in 39.1% of HD patients and 51.4% of transplant recipients, while Porphyromonas gingivalis and Tannerella forsythia were detected in 27.3% and 19.5% of HD patients, respectively. These pathogens were nearly absent in the control group. Notably, the co-detection of Candida spp. with anaerobic gram-negative rods in 22% of cases highlights the synergistic pathogenic mechanisms contributing to mucosal compromise.

Correlation analysis revealed strong positive associations between duration of dialysis and periodontal deterioration. Dialysis duration in excess of 5 years was associated with significantly deeper periodontal pockets (mean PPD: 4.96 mm) and increased CAL (mean: 4.53 mm) compared to patients dialyzed less than 3 years (PPD: 3.71 mm, CAL: 3.12 mm; $p < 0.01$). These findings align with previous

data indicating that the cumulative burden of uremia, coupled with persistent immunosuppression, contributes to irreversible connective tissue damage in the periodontium.

The data also suggest that mucosal inflammation in CKD is not an epiphenomenon of poor hygiene alone, but a complex immuno-metabolic response mediated by systemic cytokine dysregulation, salivary biochemical imbalance, and microbial overgrowth. Given the chronicity of renal impairment and the rising prevalence of end-stage kidney disease, these findings mandate the implementation of integrated oral management protocols within nephrology units. Delayed recognition and insufficient dental surveillance amplify the risk of bacteremia, graft rejection, and malnutrition, further compromising patient prognosis.

The implications of these results extend to both diagnostics and therapeutics. GCF cytokine monitoring may serve as a non-invasive tool for tracking mucosal inflammation in real-time. In parallel, the prioritization of antimicrobial prophylaxis, antifungal regimens, and salivary stimulation protocols should be standard in CKD-related dental management. Moreover, inclusion of oral health parameters in transplant eligibility assessment and dialysis initiation guidelines may improve systemic outcomes.

The table below summarizes the main clinical and laboratory differences among study groups, emphasizing the progressive deterioration in oral status with advancing renal disease and the modifying effect of immunosuppressive therapy.

Table 1.

Clinical and Laboratory Parameters of Oral Health in CKD and Control Groups

Indicator	Hemodialysis (n=41)	Transplant (n=15)	Pre-Dialysis (n=12)	Control (n=28)
Gingival inflammation (%)	87.5	93.3	58.3	21.4
Xerostomia (%)	78.2	73.3	50.0	10.7
Gingival hyperplasia (%)	36.7	40.0	8.3	0.0
Uremic stomatitis (%)	9.6	0.0	0.0	0.0
PPD (mm, mean ± SD)	4.28 ± 1.19	3.96 ± 1.07	3.12 ± 0.91	2.63 ± 0.78
CAL (mm, mean ± SD)	3.91 ± 1.07	3.58 ± 1.02	2.75 ± 0.85	2.02 ± 0.65
Bleeding on probing (%)	72.4	68.6	41.7	32.1

Unstimulated salivary flow (mL/min)	0.18 ± 0.09	0.21 ± 0.10	0.26 ± 0.08	0.34 ± 0.11
Salivary urea (mmol/L)	14.2	8.5	5.1	3.6
TNF-α in GCF (pg/mL)	32.6	28.4	19.7	12.3
IL-1β in GCF (pg/mL)	64.7	58.1	42.6	21.4
Candida albicans detection (%)	39.1	51.4	16.7	3.6
Porphyromonas gingivalis (%)	27.3	13.3	8.3	0.0

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CONCLUSION

The findings of this study confirm that patients with chronic kidney disease, particularly those undergoing long-term hemodialysis and post-transplant immunosuppressive therapy, exhibit a high prevalence of inflammatory conditions of the oral mucosa. Xerostomia, gingival hyperplasia, candidiasis, and uremic stomatitis are frequently diagnosed and correlate significantly with biochemical disturbances, reduced salivary flow, elevated levels of proinflammatory cytokines in gingival crevicular fluid, and microbial dysbiosis.

Periodontal tissue destruction is directly proportional to dialysis duration and is exacerbated by immunomodulatory pharmacotherapy. The data emphasize that oral mucosal inflammation in CKD is not merely a consequence of poor hygiene but reflects systemic immune and metabolic dysregulation. The identification of elevated TNF-α, IL-1β, and MMP-1 levels offers a pathophysiological explanation for the progression of mucosal lesions in this population.

Integrated dental protocols adapted to nephrological comorbidity are essential to mitigate the risk of local and systemic complications. Regular periodontal screening, microbial control, cytokine monitoring, and therapeutic adjustment in collaboration with nephrology teams must become standard practice in managing patients with CKD. Early dental intervention may reduce systemic inflammation, improve transplant outcomes, and enhance the overall quality of life in this vulnerable patient group.

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