Vol: 9 Issue: 1

EDJ

Assessment of Oral Manifestation and Inflammatory Markers (IL-17) in End Stage Chronic Kidney Disease Patients: A Cross Sectional Study

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ABSTRACT

Background and Objectives: Chronic kidney disease (CKD) is a progressive condition characterized by irreversible deterioration of kidney function, resulting in systemic complications that may adversely affect oral health. Patients undergoing hemodialysis frequently present with various oral manifestations due to metabolic disturbances, medication use, and altered immune responses. Interleukin-17 (IL-17) is an inflammatory cytokine involved in host defense against Candida albicans and may play a role in the oral health status of CKD patients. This study aimed to evaluate oral manifestations and serum IL-17 levels in patients with end stage chronic kidney disease undergoing hemodialysis.

Methods: A cross-sectional study was conducted on 60 participants, including 30 patients with CKD undergoing hemodialysis for more than six months and 30 healthy controls matched for sex. Clinical examinations included assessment of oral dryness, salivary flow rate (sialometry), periodontal status, halitosis, coated tongue, pale oral mucosa, and lip fissures. Serum IL-17 levels were measured using laboratory analysis. Data were analyzed using independent samples t-test and Chi-square test, with statistical significance set at $p < 0.05$.

Results: Dry mouth, pale oral mucosa, and lip fissures were significantly more prevalent among CKD patients than controls ($p < 0.05$). Salivary flow rate was significantly reduced, while periodontal disease severity was significantly increased in the CKD group. Although serum IL 17 levels were higher in CKD patients than in healthy controls, the difference was not statistically significant ($p = 0.182$).

Conclusion: Patients with chronic kidney disease undergoing hemodialysis exhibit a higher prevalence of oral manifestations and periodontal disease compared with healthy individuals. Regular oral healthcare and preventive dental measures are essential for improving oral health outcomes in this population.

Keywords: Chronic kidney disease, Hemodialysis, Oral manifestations, Interleukin-17, Periodontal disease, Xerostomia

Article Information

Submission Date: 23/7/2025
Revision date: 18/8/2025
Acceptance date: 19/10/2025
Publishing date: June 2026

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DOI: doi.org/10.15218/edj.2026.17

INTRODUCTION

The kidney is a vital organ that removes nitrogenous waste products and exogenous substances, such as drugs, from the bloodstream. It also maintains electrolyte balance, participates in erythropoietin synthesis, and contributes to insulin metabolism and clearance. Impaired kidney function results in the accumulation of nitrogenous waste products in the circulation, leading to renal failure. There are two major classifications of renal failure: acute and chronic kidney failure.[1] Acute kidney injury is considered a critical condition with a higher prevalence among older individuals and a greater incidence in males than females.[2] Chronic renal failure is characterized by a gradual decline in kidney function, leading to structural and functional abnormalities that affect body fluid volume and composition. It is diagnosed when kidney damage persists for at least three months or when the glomerular filtration rate falls below 60 mL/min/1.73 m². This condition may eventually require renal replacement therapy, including dialysis or kidney transplantation, and is referred to as end-stage renal disease (ESRD).[3] The causes of chronic kidney disease (CKD) are diverse. The most common causes include diabetes mellitus, hypertension, primary glomerulonephritis, hereditary or cystic kidney diseases, and plasma cell dyscrasias.[4] Additional risk factors include smoking, acute kidney injury, family history, obesity, and other metabolic disorders.[5,6] Dialysis is a renal replacement therapy that removes waste products and excess fluid from the blood when the kidneys can no longer perform their normal function. Two main types of dialysis are available: peritoneal dialysis and hemodialysis.[7] Hemodialysis is the most commonly used modality. During the procedure, blood is withdrawn through a vascular access site and passed through a dialysis machine where waste products and excess fluids are removed before the purified blood is returned to the body.[8] Chronic kidney disease is a major global health problem. Because the kidneys play essential physiological roles, their dysfunction can lead to bone metabolism disorders, hematological abnormalities, electrolyte disturbances, cardiovascular disease, and hypertension. Since oral health reflects systemic health, both CKD and its treatment can significantly affect the oral cavity.[9] Common oral manifestations of CKD include gingival enlargement, xerostomia, parotitis, enamel hypoplasia, delayed tooth eruption, oral mucosal lesions, lichenoid reactions, ulceration, angular cheilitis, candidiasis, uremic stomatitis, and taste disturbances. Uremic fetor, characterized by a fish-like odor of the breath, results from the breakdown of accumulated urea into ammonia. Uremic stomatitis is a rare condition that may occur in patients with markedly elevated blood urea levels.[10-12] Patients with CKD frequently experience xerostomia due to salivary gland dysfunction, elevated blood urea levels, electrolyte imbalances, medication use, mouth breathing, and fluid restriction.[13-15] Xerostomia may result in dry and fissured lips, oral discomfort, cervical caries, oral lesions, difficulty swallowing, and coated tongue formation.[16] Petechiae, bruising, and gingival bleeding may also occur in patients with renal failure due to platelet dysfunction, increased vascular fragility, and the use of anticoagulants during dialysis procedures.[13] Inflammatory markers are biological substances that indicate the presence of inflammation, autoimmune disorders, or chronic diseases.[18] Chronic kidney disease is recognized as a chronic pro-inflammatory condition associated with elevated levels of inflammatory cytokines.[19] Interleukin-17 (IL-17) plays an essential role in mucosal immunity against fungal infections, particularly Candida species. Defects in the IL-17 pathway are associated with chronic mucocutaneous candidiasis and recurrent fungal infections involving the oral mucosa, skin, and nails.[20]

METHODS

Study Design and Participants

This cross-sectional study was conducted between December 2024 and March 2025. Thirty patients diagnosed with chronic kidney disease (CKD) and undergoing hemodialysis for at least six months were recruited from the Dialysis Center at Erbil Teaching Hospital. Thirty healthy individuals, matched for sex and selected from the general population, were included as a control group. Participants who had received oral or dental treatment during the study period were excluded.

Clinical and Laboratory Assessment

For laboratory investigations, 3 mL of venous blood was collected from each participant for the assessment of serum interleukin-17 (IL-17) levels. Oral examinations were performed using disposable dental mirrors and periodontal probes. The evaluated oral manifestations included dry mouth, pale oral mucosa, lip fissures, coated tongue, and halitosis. Periodontal status was assessed using the Ramfjord Periodontal Disease Index (PDI). Sali-

vary flow rate was measured using the unstimulated whole saliva collection (spitting) method. Participants were instructed to refrain from eating and drinking for at least two hours before the test. Saliva samples were collected between 8:00 AM and 10:00 AM to minimize diurnal variation. The collected saliva was measured in a graduated tube, and the salivary flow rate was calculated in mL/min. An unstimulated salivary flow rate below 0.1 mL/min was considered indicative of hyposalivation.

Ethical approval

The ethics board of the Oral Diagnosis Department at Hawler Medical University College of Dentistry gave its approval to this study at scientific Committee Meeting Number: 0D6 Date April11,2024 and written consent that was informed was extracted from each participant in this research after explanation the aim of this research and he has choice to agree or not.

Statistical Analysis

Statistical analyses were performed using Microsoft Excel (Version 2210, Microsoft Corporation) and JASP software (Version 0.19.3.0). Descriptive statistics were expressed as mean ± standard deviation (SD). Independent-samples t-tests were used to compare continuous variables between groups, while the Chi-square test of independence was used to evaluate associations between categorical variables. Statistical significance was set at $p < 0.05$.

RESULTS

The study included a total of 60 participants, comprising 30 patients undergoing hemodialysis and 30 healthy controls. Both groups included male and female participants. The mean age of the patient group was 43.20 ± 9.80 years, whereas the mean age of the control group was 31.63 ± 8.05 years, as shown in Table 1.

Table 1. Demographic Characteristics of Healthy and Patient Groups

Patient Status	Gender		Mean Age (years)	St. Deviation	Maximum	Minimum
	Male	Female				
Healthy (n=30)	15	15	31.633	8.045	49.000	20.000
Patients (n=30)	17	13	43.200	9.803	62.000	26.000

An independent-samples t-test was used to compare serum IL-17 levels, salivary flow rate, and periodontal index between the two groups. IL-17 levels were slightly higher in the CKD group than in the control group; however, the difference was not statistically significant (t-test, $p = 0.182$). In contrast, significant differences were observed in salivary flow rate and periodontal status.

The mean salivary flow rate was significantly lower in CKD patients (1.295 ± 0.278) than in healthy controls (1.778 ± 0.278) (independent-samples t-test, $p < 0.001$). Similarly, the mean periodontal disease index (PDI) score was significantly higher in the CKD group (1.216 ± 0.689) than in the control group (0.588 ± 0.357), indicating more severe periodontal disease among hemodialysis patients (independent-samples t-test, $p < 0.001$). Effect size analysis demonstrated a large effect for both salivary flow rate (Cohen's d = 1.74) and periodontal index (Cohen's d = 1.13), whereas the effect size for IL-17 was small (Cohen's d = 0.35), as shown in Table 2.

The association between oral manifestations and CKD status was evaluated using the Chi-square test of independence. Dry mouth and pale oral mucosa were significantly associated with CKD ($\chi^2 = 60.00$, $p < 0.001$). Lip fissures were also significantly more frequent among CKD patients than controls ($\chi^2 = 7.20$, $p = 0.007$).

In contrast, coated tongue and halitosis showed no statistically significant association with CKD status. Coated tongue was observed in 9 CKD patients and 8 healthy controls ($\chi^2 = 0.082$, $p = 0.774$), whereas halitosis was present in 11 CKD patients and 13 controls ($\chi^2 = 0.278$, $p = 0.598$). These findings indicate that dry mouth, pale oral mucosa, and lip fissures are strongly associated with chronic kidney disease, whereas coated tongue and halitosis are not significantly associated with disease status (Table 3).

DOI: doi.org/10.15218/edj.2026.17

Table 2. Comparison of IL-17, Salivary Flow Rate, and Periodontal Index Between CKD Patients and Controls

	Patient group		Healthy group			
Variable	**Mean (uncontrol)**	**S.DEV. (uncontrol)**	**Mean (control)**	**S.DEV. (control)**	**P-value**	**Significant**
IL-17 (pg/ml)	13.7056	11.822	9.62016	11.5950	0.18184	*ns
Sialometry (ml/min)	1.295	0.2778	1.7783	0.2778	0.0000056	**s
Periodontal index	1.2157	0.6885	0.5882	0.3570	0.000042	**s

*ns = not significant
**s = significant

Table 3. Oral Manifestations Among CKD Patients and Controls

Variable	CKD Yes	CKD No	Control Yes	Control No	χ^2	p-value
Dry mouth	30	0	0	30	60.00	<0.001**
Pale mucosa	30	0	0	30	60.00	<0.001**
Lip fissure	11	19	2	28	7.20	0.007**
Coated Tongue	9	21	8	22	0.082	0.774*
Halitosis	11	19	13	17	0.278	0.5988*

*ns = not significant
**s = significant

DISCUSSION

Interleukin-17 (IL-17) is an important pro-inflammatory cytokine that plays a critical role in host defense against mucosal fungal infections, particularly Candida albicans. This cytokine is primarily produced by T helper 17 (Th17) cells and contributes significantly to the maintenance of oral mucosal immunity. Defects in the IL-17 signaling pathway have been associated with chronic mucocutaneous candidiasis and recurrent oral fungal infections.[23] In the present study, serum IL-17 levels were slightly higher in patients undergoing hemodialysis than in healthy controls; however, the difference was not statistically significant. These findings are consistent with previous studies that reported elevated inflammatory cytokine levels in CKD patients due to chronic low-grade inflammation and immune dysregulation.[25] The observed increase in IL-17 levels may reflect the inflammatory status associated with chronic kidney disease. Furthermore, the absence of oral candidal infections among the study participants may explain the lack of a statistically significant alteration in IL-17 levels.[26] Salivary gland hypofunction was significantly associated with CKD patients in the current study. Reduced salivary flow may result from elevated blood urea and creatinine levels, salivary gland dysfunction, fluid restriction, medication use, and electrolyte imbalances commonly observed in dialysis patients. Consequently, xerostomia and lip fissures were significantly more prevalent among CKD patients.[27] The findings also demonstrated a significantly lower salivary flow rate among hemodialysis patients compared with healthy controls. Previous studies have reported that salivary gland dysfunction in CKD patients may be related to metabolic disturbances, glandular atrophy, dehydration, altered blood osmolality, and reduced salivary gland secretion.[27,28] These factors contribute to oral dryness and adversely affect oral health and quality of life. Periodontal disease was significantly more severe among CKD patients than among healthy controls. This finding may be attributed to impaired immune function,

chronic systemic inflammation, poor oral hygiene, nutritional deficiencies, psychological stress, and the long-term effects of dialysis treatment. Similar findings have been reported in previous studies investigating periodontal conditions among patients with end-stage renal disease.[18,29] Pale oral mucosa was significantly associated with CKD patients. This clinical finding is most likely related to anemia, which is highly prevalent among patients receiving hemodialysis. Erythropoietin deficiency, reduced red blood cell survival, chronic inflammation, iron deficiency, and blood loss during dialysis procedures are recognized contributors to anemia in chronic kidney disease patients.[12] Halitosis is commonly associated with dialysis, tongue coating, xerostomia, periodontal disease, and the activity of Gram-negative bacteria. Elevated concentrations of urea and proteins in saliva are metabolized by oral microorganisms, resulting in the production of volatile sulfur compounds that contribute to oral malodor.[17] Coated tongue may develop as a consequence of poor oral hygiene, dehydration, smoking, and reduced salivary flow rate.[18,30] Although halitosis and coated tongue were more frequently observed among CKD patients, no statistically significant differences were detected between the study groups. This finding may be explained by the presence of additional contributing factors among healthy controls, including smoking habits, poor oral hygiene practices, and dental caries. The findings of the present study emphasize the importance of comprehensive oral healthcare for patients undergoing hemodialysis. Early diagnosis and management of oral manifestations may improve oral health status, reduce complications, and enhance the overall quality of life of patients with chronic kidney disease.

Limitations

This study has several limitations. First, the sample size was relatively small, which may have limited the statistical power to detect differences in certain variables, particularly serum IL-17 levels. Second, the mean age differed between the patient and control groups, which may have acted as a potential confounding factor. Finally, the cross-sectional design does not allow the establishment of causal relationships between chronic kidney disease, oral manifestations, and inflammatory markers.

CONCLUSION

Patients with chronic kidney disease undergoing hemodialysis exhibited a significantly higher prevalence of oral manifestations, particularly xerostomia, pale oral mucosa, lip fissures, and periodontal disease, compared with healthy controls. Salivary flow rate was significantly reduced in the CKD group, while periodontal disease severity was significantly increased. Although serum IL-17 levels were slightly elevated among CKD patients, no statistically significant difference was observed between patients and healthy controls. These findings highlight the importance of regular oral examinations and preventive dental care for patients undergoing hemodialysis. Early detection and management of oral manifestations may improve oral health status and enhance the overall quality of life of individuals with chronic kidney disease.

Acknowledgements

The authors would like to express their sincere gratitude to the College of Dentistry, Hawler Medical University, for its academic support. The authors also thank the staff of the Dialysis Center at Erbil Teaching Hospital and all participants who contributed to this study.

Conflict of Interest

The authors declare no conflicts of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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DOI: doi.org/10.15218/edj.2026.17

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