Review

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Oral Surgery and Dental Implants in Patients with Chronic Kidney Disease: Scoping Review for Oral Health Status

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The number of chronic kidney disease (CKD) patients requiring renal replacement therapy is increasing, often exhibiting oral manifestations including periodontal disease, gingival hyperplasia, altered saliva composition, and uremic stomatitis. Uremic stomatitis, xerostomia, and candidiasis are very frequent, particularly among patients undergoing dialysis or kidney transplant recipients. CKD patients also experience profound alterations in bone metabolism inherent in the homeostasis of calcium, phosphorus, vitamin D, parathyroid hormone, and fibroblast growth factor (FGF). These alterations lead to demineralization of the jaw bones, reduced bone trabeculae, reduced cortical bone thickness, fibrocystic bone lesions, bone fractures, and delayed wound healing post-tooth extraction. Consequently, oral health management of elderly hemodialysis patients poses serious clinical problems. This review focused on the oral health and rehabilitation of patients with CKD or on dialysis.

Keywords: oral health; dialysis; tooth extraction; complication; oral surgery; dental implant; periimplantitis

Introduction

The relationship between dental and periodontal health in chronic kidney disease (CKD) patients represents a debated topic in the literature, with limited clinical studies available. However, emerging evidence suggests that dialysis onset significantly exacerbates oral health issues, affecting around 90% of cases with morpho-functional alterations. CKD involves profound alterations in bone metabolism that provoke jaw bone demineralization, decreased bone trabeculae, reduced cortical bone thickness, fibrocystic bone lesions, bone fractures, and delayed wound healing following tooth extraction. The most common oral manifestations described in current literature are periodontal disease, gingival hyperplasia, alterations in saliva secretion and composition, and uremic stomatitis [1,2]. Lichenoid lesions associated with pharmacological immunosuppression are frequently present. Moreover, uremic stomatitis, xerostomia [3], and candidiasis [4] are very common in patients undergoing dialysis or kidney transplants [2]. CKD-associated mineral and bone disorder (CKD-MBD) is a common complication, particularly in cases of renal insufficiency, impacting bone and mineral metabolism systemically and affecting the composition and function of jaw bones. Consequently, it is important to recognize these pathological illnesses as they can affect implant therapy or oral surgery in CKD patients, and it is appropriate to customize treatment with targeted measures to prevent clinical complications for implant survival, osseointegration, and the success of regeneration therapy. This includes patients undergoing renal transplants who are subjected to immunosuppressive therapy and complex medical/pharmacological treatments [5].

Oral Involvement of CKD

CKD patients often present significant alterations in bone metabolism, impacting calcium and phosphorus homeostasis, vitamin D, parathyroid hormone, and fibroblast growth factor 23 (FGF23). This clinical scenario results in various changes, such as demineralization of the jaw bones, reduced bone trabeculae, reduced cortical bone thickness, metastatic soft tissue calcifications, fibrocystic bone lesions, bone fractures, and delayed wound healing after tooth extraction [1,6].

The most common dental tissue alterations include delayed dental eruption, enamel hypoplasia, lamina dura loss,

Table 1. Synthesis of the main complications connected with CKD.

Mucocutaneous manifestations	Uremic stomatitis
	Aphthous ulcerations
	Glossitis and cheilitis
	Lichenoid reaction
	Burning mouth syndrome
	Petechiae and bruising
Caries	Increase in dental plaque
	Poor oral hygiene
Periodontal disease	Periodontal aggressive bacteria in the gingival pockets
	Gingival hyperplasia and gingivitis
Salivation	Xerostomia
	Chronic sialadenitis
	Increase of bacteria in saliva
	Reduced buffer capacity of saliva
Dental anomalies	Delayed dental eruption
	Hypoplasia of the enamel
	Loss of lamina dura
	Extension of lesions in the periodontal ligament
	Destruction of the periodontium
	Dental mobility
	Calcification of the dental pulp and narrowing of the pulp chamber
Maxillary and mandibular bone anomalies	Reduced bone trabeculae and reduced thickness of the cortical bone
	Metastatic calcifications of soft tissues
	Fibrocystic bone lesions
	Bone fractures
	Impaired wound healing after tooth extraction
	Calcification of the temporomandibular joint
Painful syndromes	Odinophagy
	Dysphagia
Oral infections	Candidiasis
	Viral infections in patients on immunosuppressive therapy: *Cytomegalovirus* (CMV), *Herpes Simplex Virus* (HSV), *Epstein Barr* (EBV)
Neoplasms	Squamous oral carcinoma

CKD, chronic kidney disease.

inflammatory lesions within the periodontal ligament, increased teeth mobility, dental pulp calcification, and narrowed pulp chamber [7]. The main CKD clinical manifestations in the oral cavity are presented in Table 1 [7].

The treatment of oral diseases in patients with CKD is quite complex considering the comorbidities, such as diabetes and immunosuppression, as well as medications such as anticoagulants, antiplatelet agents, and antihypertensive agents [8]. According to a recent report from the Maximize Market Research (MMR) Institute [9], the global drug market in 2021 includes beta-blockers, ACE inhibitors, calcium channel blockers, erythropoiesis-stimulating agents (ESAS), diuretics, and angiotensin-II receptor blockers, due to an increasing prevalence of hypertension, interstitial nephritis, glomerulonephritis, cardiovascular diseases, such as heart disease, and stroke. In contrast, the prescribed medications for CKD subjects require careful consideration of potential adverse effects and nephrotoxicity in dental healthcare practice [10]. For instance, tetracyclines are characterized by a renal accumulation tendency, aggravating both azotemia and blood urea nitrogen levels. Moreover, non-steroidal anti-inflammatory drugs (NSAIDs) are associated with nephrotoxicity and different forms of renal illnesses, particularly with prolonged use, potentially causing hypertension, hyperkaliemia, and increased sodium/water retention. While penicillin antibiotics typically do not require dosing adjustments, overdosing could produce potentially nephrotoxic side effects. Sedatives are not indicated in the case of a glomerular filtration rate $<$50 mL/minute [10].

In addition, chronic renal failure associated with congenital/inherited factors must be considered. X-chromosome-related hypophosphatemia, Fraser syndrome, and the FAM20A mutation are well-known illnesses associated with severe renal compromise. In these patients, operative and subsequent rehabilitation management most often requires a complex, multidisciplinary approach [5,11].

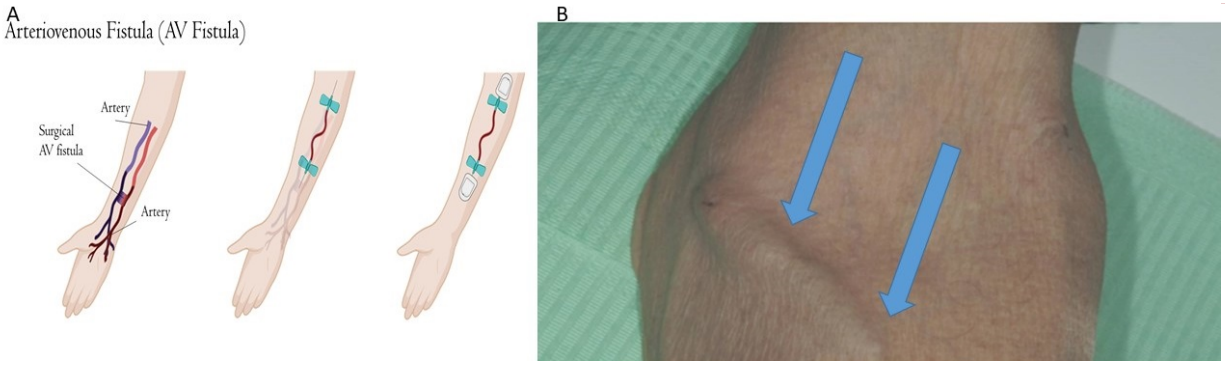

Fig. 1. Fistula. (A) Fistula pattern. The image was created by BioRender.com (Retrieved from https://app.biorender.com/biorender-templates). (B) Fistula (Arrows). The picture was obtained from the Department of Innovative Technologies in Medicine and Dentistry, and informed consent was obtained from the patients.

Gürkan *et al*. [12] investigated 145 CKD patients, revealing a prevalent trend towards poor daily oral hygiene (85.7%) and high levels of plaque and tartar (93.7%), often due to incorrect brushing and inaccurate hygiene practices. In this study, all of the patients were referred to a dentist for professional oral care [12]. The development of oral diseases, including periodontal illnesses, is frequently associated with symptoms such as pain and tenderness, gum swelling, and tooth loss, which can impair chewing function, especially among elderly individuals. Moreover, psychological factors such as stress, anxiety, and depression may exacerbate oral health issues which are further compounded by dialysis [13]. Souza *et al*. [14] reported on 286 Brazilian patients, including 13 in pre-dialysis, 158 in hemodialysis, 23 in peritoneal dialysis, and 92 under kidney transplants. The authors found poor oral conditions in 83% of subjects, with a high prevalence of dental tartar (87%) in patients under hemodialysis, especially in those patients taking calcium carbonate, and an insufficient oral hygiene level [14]. Furthermore, bad breath was found in 55% of the studied population. Dialysis patients often exhibit reduced salivary secretion accompanied by salivary gland atrophy and fibrosis, which may be asymptomatic. Additionally, there is a notable increase in urea-lytic organisms, leading to the formation of ammonium and subsequent halitosis [14]. Souza *et al*. [14] also noted an increased prevalence of dental caries in CKD patients compared to hemodialysis subjects, which may be attributed to the urea antibacterial effect and increased tartar formation. In fact, the Decayed, Missing, and Filled Permanent Teeth (DMFT) index for the CKD population was 20.6 compared to 13.9 in the healthy population [14]. The prevalence and severity of caries are expressed with the DMFT index according to Klein and Palmer classification, which represents the average number of decayed (D), missing elements (M), and filled (F) teeth (T) [14]. More recent studies reported that the incidence of end-stage renal failure (ESRD) is increasing in industrialized countries [15]. In clinical practices, the frequency of patients undergoing kidney transplantation, hemodialysis, and peritoneal dialysis is increasing. Dentists must consider the general health status and the relationships between oral pathologies and systemic concerns associated with renal compromissions [15]. Renal functions play an important role in various physiological processes, including the excretion of metabolic products like urea, blood volume regulation, electrolyte balance, erythropoiesis through erythropoietin secretion, and calcium homeostasis through the hydroxylation of vitamin D3 [16]. Pathological processes can induce a decrease in renal function, generating negative effects on multiple organs. In advanced stages of kidney disease, patients may require dialysis or kidney transplantation, requiring the administration of immunosuppressive drugs, corticosteroids, calcineurin inhibitors, and leukocyte proliferation inhibitors [4]. Alterations in calcium homeostasis can induce secondary hyperparathyroidism with an inflammatory state of the oral mucosa aggravated by uremia, resulting in impaired function of lymphocytes and monocytes, as well as progressive alveolar bone atrophy [17]. Immunosuppressive drugs produce periodontal tissue illnesses, with severe gingival hyperplasia occurring in 22–58% of cases, particularly with the use of calcineurin inhibitors and calcium antagonists [18]. The severity of this effect is often dose-dependent and correlated with the presence of tartar and plaque, although meticulous oral hygiene practices can mitigate its occurrence [18]. A recent study proposed a genetic predisposition mediated by the TGF-β1 factor as a contributing factor to this type of gingival hyperplasia. Atherosclerotic complications such as myocardial infarction, cardiac arrest, and arrhythmias represent the main causes of mortality, especially at a young age, and are highly associated with inflammation levels, detected by the C-reactive protein (CRP). Elevated CRP serum levels have been observed in individuals with moderate to severe periodontal disease, suggesting a correlation between CRP levels and the severity of periodontal disease [19]. Additionally, patients undergoing periodontal therapy showed decreased CPR and lower risk of heart complications [19]. Deschamps *et al*. [20] conducted a

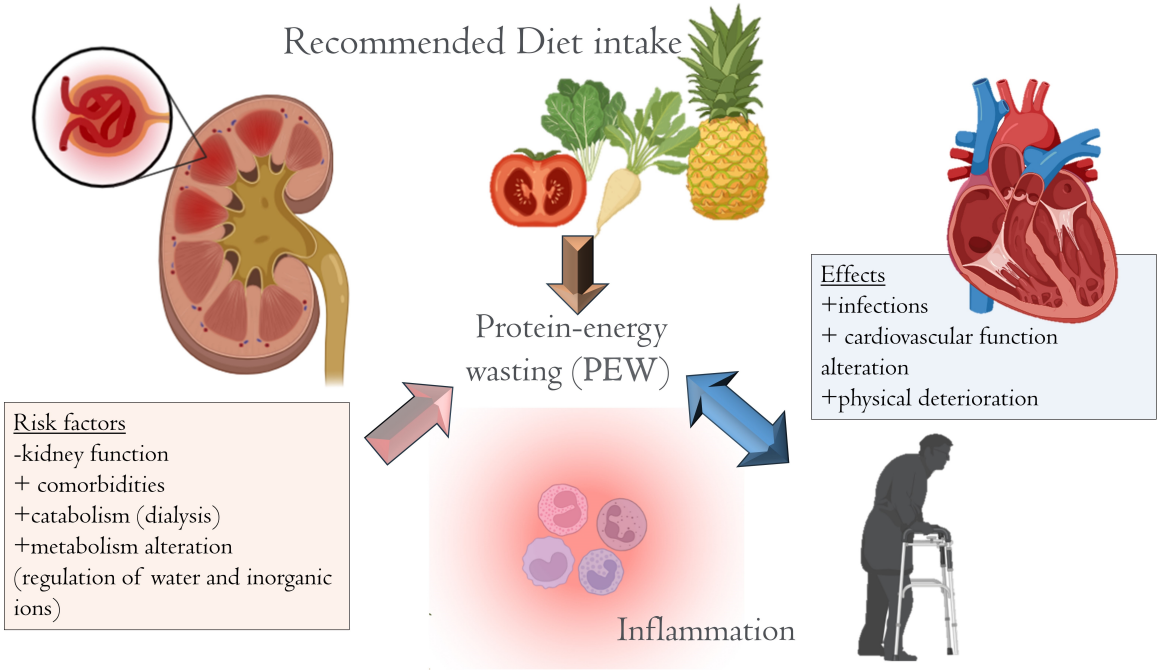

Fig. 2. Summary of the implications of protein energy wasting (PEW) in chronic renal failure. The image was created with BioRender.com (Retrieved from https://app.biorender.com/biorender-templates).

systematic review and meta-analysis to evaluate the association between periodontitis (PD) and CKD to investigate the potential influence of periodontal treatment in CKD patients. Most studies indicated an increased incidence of PD in patients with CKD. For example, a meta-analysis showed an association between CKD and PD, with an increased association in cases of severe PD (OR = 2.39 (1.70–3.36). The association remained observable after adjustment for major risk factors for CKD or the use of precise diagnostic criteria (OR = 2.26 for severe PD (1.69–3.01)) [20]. Although very few randomized controlled clinical trials validate the efficacy of periodontal therapy in preventing cardiovascular disease, careful monitoring of the periodontal conditions of CKD patients is useful, prescribing adequate antibiotic prophylaxis and accounting for possible alterations in the metabolism of CKD patients. Dialysis subjects need sturdy blood vessels that can be used regularly for hemodialysis. Consequently, the dialysis patient undergoes arm surgery to create a large, sturdy blood vessel that can be used regularly for hemodialysis (arteriovenous fistula) [21]. In dialysis patients, the dentist should know that the arm with the fistula cannot be used to administer intravenous drugs [21] (Fig. 1).

Clinical Implications of Periodontal Disease

Bacterial spread and cytokine modulation from the periodontal pocket into the bloodstream can affect both endothelial and renal function [8,13]. In fact, inflammation is a well-known risk factor for CKD. The hypothesis of a bidirectional link between the two pathologies has been proposed due to the evidence of various biological mechanisms associated with kidney disease that could aggravate periodontitis [22,23]. For example, high uremia increases susceptibility to opportunistic infections that can produce changes in urea concentration and salivary pH [24,25]. Study data have demonstrated the beneficial effects of periodontal therapy on renal function, due to the improvement of glomerular filtration rate (eGFR) and creatinine associated with the under-expression of inflammatory markers such as IL-6 and CRP [8,13]. Improvements in endothelial function have also been documented, which can contribute to the increase in renal microcirculation and, therefore, to a more effective filtration process [8,13]. Furthermore, it is believed that periodontal treatment mitigates the progression of kidney disease, cardiovascular risk, and various systemic conditions, including diabetes which exacerbates kidney dysfunction [26]. Oral diseases also contribute to the high incidence of protein energy wasting (PEW) in CKD patients, causing both inflammation and PEW. In fact, numerous studies associate the accumulation of proinflammatory cytokines with different aspects of PEW, including anorexia, muscle wasting, low anabolic hormones, increased energy expenditure, insulin resistance, dry mouth, anorexia, and nutritional deficiencies [27] (Figs. 2,3). Cengiz *et al.* [28] reported that changes in periodontal pocket depth and periodontal and gingival indexes became more frequent after a 5-year observation period, suggesting a progressive deterioration in health status associated with CKD.

Studies suggest that edentulous individuals tend to have an inappropriate dietary intake, characterized by low

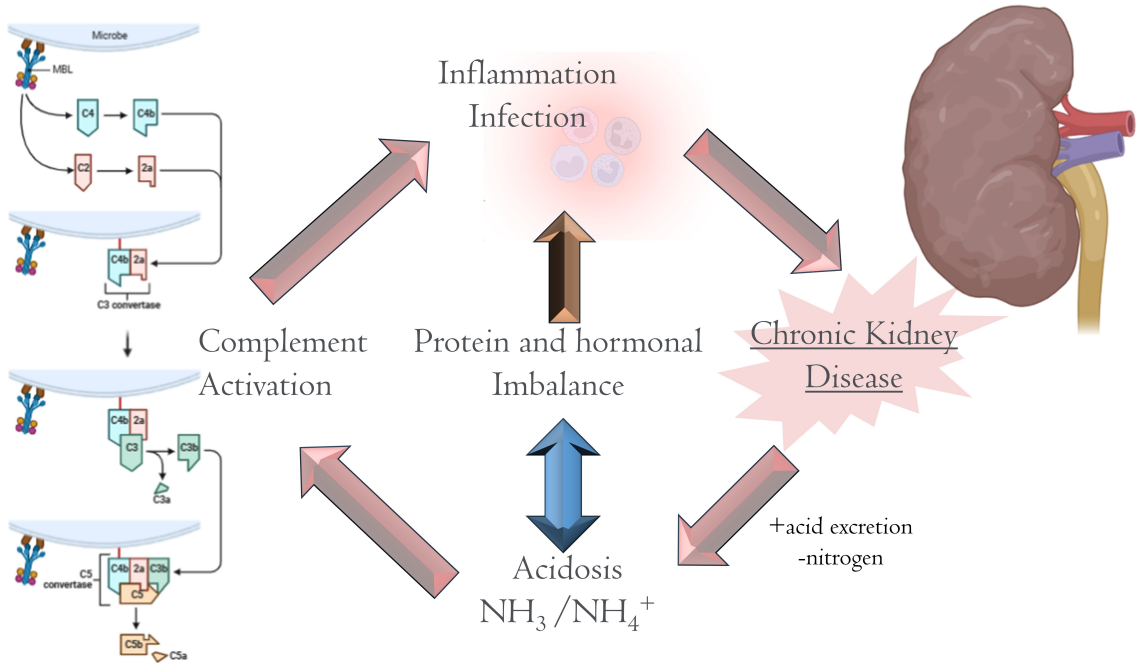

Fig. 3. Interconnection of Kidney Disease (KD) progression with metabolic acidosis, hormonal resistance, inflammation, and protein catabolism. The image was created with BioRender.com (Retrieved from https://app.biorender.com/biorender-templates).

protein levels and higher consumption of high-calorie, high-fat foods compared to the general population. Additionally, studies have highlighted a correlation between the severity of renal dysfunction and the presence of dental tartar, which reflects impaired calcium-phosphorus homeostasis. This association has been observed in pediatric patients with CKD at various stages, including those in pre-dialysis, undergoing dialysis, or after kidney transplantation, when compared to healthy children as a control [29]. Dialyzed children exhibited the most abundant levels of dental tartar and salivary urea rates among the studied groups. These patients showed increased oral mucosa pH levels, correlated to abundant salivary urea. Bacterial hydrolysis leads to the release of ammonia, increasing pH levels in dental plaque and promoting calcium and phosphorus precipitation [29]. Furthermore, dialysis patients exhibited lower salivary concentrations of magnesium, which may contribute to the amplification of tartar formation observed in this group considering magnesium's ability to inhibit the calcification process [29]. Severe periodontitis and poor dental status have been associated with low serum albumin and PEW in both adult hemodialysis (HD) and peritoneal dialysis patients. A recent study in HD mental illness patients described signs of poor oral health in HD hemodialysis, where 80% of patients reported severe periodontitis associated with both poor nutritional status and systemic inflammation [28]. Certain medications such as antidepressants, antipsychotics, antiemetics, and antihistamines can reduce salivary flow and xerostomia [3]. The risk of xerostomia increases with increasing reliance on medications, especially in geriatric subjects. The saliva lubricates and protects soft and hard oral tissues, helps soften foods, and facilitates swallowing. The reduction of salivary flow likely contributes to thirst and difficulty swallowing, both of which affect satiety [30]. Oral dryness and thirst decrease while salivary flow increases after transplant [30]. The severity of PEW in ESRD patients may also be aggravated by temporomandibular joint disorders, which are also more common in dialysis patients as a consequence of renal osteodystrophy [30] (Figs. 4,5,6,7).

Oral Health in CKD Patients

The increase in dental sensitivity induces the patient to prefer soft foods at normal temperatures. Additionally, xerostomia and halitosis, characterized by dry mouth and an unpleasant taste, contribute to reduced food intake. Taste alterations and aversions to certain foods further exacerbate this issue [3]. Approximately 30% of patients with advanced chronic renal failure reported a "bad" or "metallic" taste in their mouths. Furthermore, there is an increased desire to drink fluids, especially cold drinks or ice, which can exacerbate weight gain in dialysis patients. Concomitant nausea induces a preference for "hard, dry, and odorless" foods. The greater risk of dental caries prompts the need for dietary modifications, requiring a multidisciplinary approach with a nephrologist/dentist/dietician, giving preference to non-cariogenic foods [31]. It is crucial to intercept potential sources of oral infection, with consideration given to antibiotic prophylaxis for surgical procedures or interventions with bleeding or bacteremia risk [32]. Dental

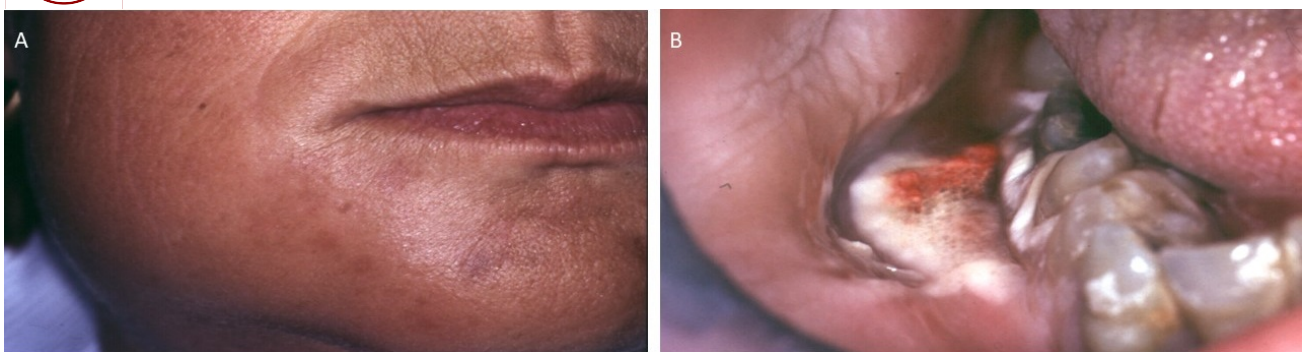

Fig. 4. Facial Abscess. (A) Dental Abscess with facial cellulitis and cheek swelling in the patient receiving dialysis for 10 years. (B) Incision and application of gauze for drainage. The pictures were obtained from the Department of Innovative Technologies in Medicine and Dentistry, and informed consent was obtained from the patient.

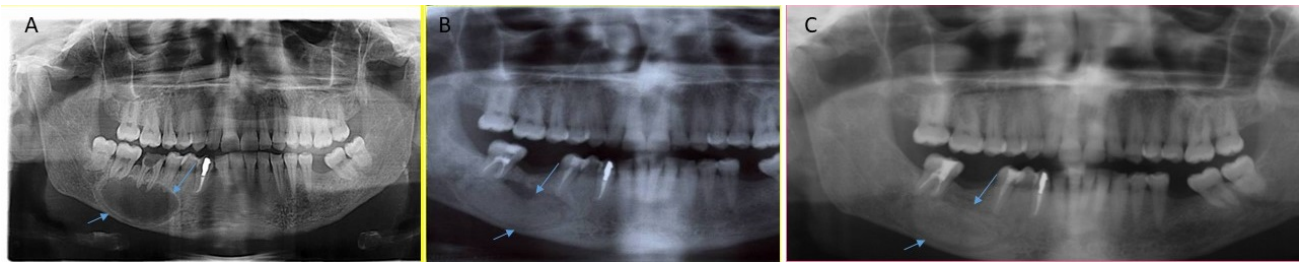

Fig. 5. The 15-year patient on dialysis. (A) Presence of a large cyst in the right mandible (blue arrows). (B) Follow-up after 1 year from cyst removal. (C) After 18 months. The cyst is completely filled with newly formed bone. The pictures were obtained from the Department of Innovative Technologies in Medicine and Dentistry, and informed consent was obtained from the patient.

Fig. 6. The patient on dialysis. (A) Patient with diffuse periodontal disease. (B) After periodontal treatment. (C) Extraction of incisors and insertion of two dental implants. The pictures were obtained from the Department of Innovative Technologies in Medicine and Dentistry, and informed consent was obtained from the patients.

Fig. 7. The patient on dialysis. (A) Dental calculus deposited on healing screws. (B) Application of dental crowns. (C) Panoramic X-ray after 1-year follow-up. The pictures were obtained from the Department of Innovative Technologies in Medicine and Dentistry, and informed consent was obtained from the patients.

treatment should be carried out during a non-dialysis period and should be preceded by a careful evaluation of the blood count and coagulation. Prophylactic antibiotic treatment with amoxicillin could be advantageous to avoid the risk of bacterial infection and endocarditis. The common hygiene procedure considers floss application at least once a day and teeth brushing after each meal. A brushing technique should be applied on all oral surfaces to reduce all

sources of bacteria-related bad breath. Mouthwashes and rinsing with antiseptics can be administered two to three times a day. Research has demonstrated the beneficial impact of probiotics on the oral microbiological environment, resulting in reduced plaque, gingival inflammation, tooth decay, and halitosis [20,33]. An increased risk of infections, chronic inflammation, and malnutrition represent the main clinical complications in chronic renal patients. Implementing education, screening, prevention, and treatment programs for oral diseases can significantly increase the quality of care and therefore the quality of life of chronic renal patients [33–35]. Patients with compromised periodontal status should be encouraged to avoid smoking. In cases of severe xerostomia [3], it is necessary to teach the patient to avoid mouth breathing, tobacco, caffeine, alcohol, and alcohol-containing mouthwashes, alongside the recommended use of a humidifier. In contrast, these patients can utilize sugar-free chewing gum, saliva substitutes, and optimal dosages of xerostomic drugs to stimulate salivary flow. In cases of surgery, patients may need antibiotic prophylaxis and local anesthetics with reduced vasoconstrictors, especially in patients with hypertension [30]. Temporary suspension of anticoagulants/antiplatelet therapy could also be necessary [35,36]. Patients treated according to the pharmacological protocols described above demonstrated favorable bone healing (Fig. 5).

Implant Therapy in CKD Patients

Patients with kidney disease present a diverse spectrum of disease severity and resulting systemic complications. Therefore, it is essential to take countermeasures for surgical management, specifically regarding dental implants, as these patients are considered high-risk.

A defined surgical risk assessment must be conducted, starting with an accurate diagnosis considering eventual bone alterations and implant risks. Additionally, the patient's renal function and bone condition should be evaluated through radiographic examinations.

During the surgical phase there are special precautions to be considered, such as the possibility that, for implant positioning, there could be low bone density associated with alterations in bone mineralization. A low-speed drilling protocol and manual osteotomy can be successfully applied (Figs. 6,7).

Considering the altered bone physiology, another critical phase is determined by the implant healing stage. Extending the healing duration to 9–12 months, coupled with a maintenance protocol that ensures adherence to pharmacological protocols, is crucial to prevent potential negative side effects such as hypermobility and implant failure [11].

Conclusions

Chronic kidney disease (CKD), depending on its severity grade, can produce a wide range of relevant clinical alterations that can influence oral health and potentially affect surgical outcomes in dental practice. Moreover, secondary electrolyte imbalances associated with CKD can produce a significant increase in the incidence risk of soft and hard oral tissues. Patients with ESRD have complicated general health conditions, necessitating comprehensive measures and tailored treatments in dental care to mitigate potential complications. Adopting a personalized medicine approach is essential in forming a therapeutic alliance that addresses individual patient needs effectively.

Availability of Data and Materials

All experimental data to support the findings of this study are available by contacting the corresponding author upon request.

Author Contributions

Conceptualization, AS, SRT; methodology, AS, IA, FL; validation, AS, CM, IA, FL, SAG, FI, AGL; formal analysis, AS; investigation, AS; writing—original draft preparation, AS, IA, FL, SRT; writing—review and editing, AS, CM, IA, FL, SAG, FI, AGL. All authors have given final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

All the clinical pictures (Fig. 1B, Figs. 4,5,6,7) in this study were obtained from the Department of Innovative Technologies in Medicine and Dentistry, and informed consent was obtained from the patients.

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Conflict of Interest

The authors declare no conflict of interest.

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