Oral Health in Children with Chronic Kidney Disease, Hemodialysis, and Renal Transplantation: A Comprehensive Narrative Review of the Oral Manifestations and Dental Implications

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ABSTRACT: Chronic kidney disease (CKD) in children presents multifaceted challenges, impacting various aspects of health, including oral health. This narrative review provides a comprehensive synthesis of literature focusing on the oral health status of pediatric CKD patients, encompassing oral manifestations, dental considerations, and management challenges associated with hemodialysis and kidney transplantation. A comprehensive search strategy was employed, utilizing databases such as PubMed, Scopus, Web of Science, and Google Scholar, to identify relevant literature on oral manifestations in children with CKD, including those undergoing hemodialysis or renal transplantation. Search terms were carefully selected to capture studies examining enamel hypoplasia, dental caries, delayed tooth eruption, gingival diseases, periodontal diseases, radiographic alterations, craniofacial development, dry mouth, and changes in the oral mucosa. Our narrative review meticulously selected articles through a systematic process. Ultimately, 12 studies meeting the inclusion criteria were included in the review. Relevant data from each included study were independently extracted and synthesized, focusing on oral manifestations and their implications in pediatric CKD patients. The synthesized findings were organized and presented in a structured manner within the review article, considering their clinical implications and informing recommendations for dental management of children with CKD. This article highlights the importance of a coordinated effort between nephrologists, dentists, and other healthcare professionals in providing holistic care for pediatric CKD patients. A comprehensive understanding of the oral health status of these children, along with proactive dental management strategies, contributes to improved overall health outcomes and a better quality of life. This review aims to serve as a valuable resource for the oral healthcare providers involved in the care of pediatric CKD patients.

KEYWORDS: Chronic kidney disease, kidney transplantation, hemodialysis, pediatrics, oral health

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Background

The kidney is a principal organ that plays pivotal roles in the homeostasis of blood and blood pressure regulation, acid–base balance, and bone integrity. The diseased kidney was shown to disturb the integration between energy balance, neuroendocrine signaling, and innate immunity, which results in a high-risk clinical profile including protein–energy wasting, inflammation, altered function of the autonomic and central nervous systems in addition to vascular, cardiopulmonary, and bone diseases.[1-3]

Chronic kidney disease (CKD), a condition characterized by a gradual loss of kidney function, affects millions of children worldwide. While the primary focus in the management of CKD is often centered around renal function, the implications of this disease on oral health are frequently overlooked. However, the interconnected nature of the human body means that oral health is intimately linked with systemic health, and children with CKD face a myriad of oral health challenges, which are often exacerbated by their underlying medical conditions and the treatments they receive.[1,4]

The prevalence of oral diseases in children with CKD is a significant concern within the pediatric healthcare landscape. Numerous studies have demonstrated a notably higher incidence of oral health issues in this population compared to their healthy counterparts.[5-9] One of the key factors contributing to this increased prevalence is the systemic nature of CKD and its various complications, which can impact the oral cavity. Dry mouth, a side effect of CKD and certain medications, predisposes these children to dental caries and gingival diseases.[6,8,10]

This review addresses the relationship between CKD and oral health in children, serving as a comprehensive guide for pediatric oral health providers. It covers the impact of CKD and its treatments on oral health, specific oral manifestations of CKD, and tailored guidelines for dental management in children undergoing hemodialysis and renal transplantation. The aim is to equip healthcare professionals with the necessary knowledge and tools for effective care delivery and emphasize the importance of integrating oral health into the holistic management of children with CKD.

Methods

Identification of databases and search strategy

A comprehensive search strategy was employed by 2 independent reviewers, GAE and WS. The search aimed to identify relevant literature on oral manifestations in children with CKD, including those undergoing hemodialysis or renal transplantation. The databases searched included PubMed, Scopus, Web

of Science, and Google Scholar. The search terms were carefully chosen to capture all relevant studies and included combinations of key terms such as "oral manifestations," "oral health," "children," "pediatric," "chronic kidney disease," "CKD," "renal disease," "hemodialysis," "renal transplantation," "enamel hypoplasia," "dental caries," "delayed tooth eruption," "gingival diseases," "periodontal diseases," "radiographic alterations," "craniofacial development," "dry mouth," and "oral mucosa."

The following inclusion and exclusion criteria we applied in this review

Inclusion criteria:

- Studies focused on oral manifestations and dental implications in children with CKDs, including those undergoing hemodialysis or renal transplantation.
- Studies examining enamel hypoplasia, dental caries, delayed tooth eruption, gingival diseases, periodontal diseases, radiographic alterations, craniofacial development, dry mouth, and changes in the oral mucosa.
- Articles and clinical guidelines published in peer-reviewed journals.
- Studies published in English language.
- Studies up to the current year.

Exclusion criteria:

- Studies focused solely on adult populations.
- Studies not relevant to oral health or dental implications in children with CKD.
- Studies lacked sufficient detail on the oral manifestations or dental management strategies in children with CKD.
- Studies with insufficient data or lack of relevance to the topic of interest.
- Studies focused primarily on interventions or treatments unrelated to oral health in children with CKD.
- Case reports and case series.

Articles selection

Our narrative review meticulously selected articles through a systematic process, as demonstrated by the data from the PRISMA flow chart. Initially, we identified 54 records from various databases including PubMed, Scopus, Web of Science, and Google Scholar. Following the removal of 18 duplicate records, 36 unique records underwent screening. During the screening phase, 22 reports were assessed for eligibility, with 10 being excluded either for not meeting the inclusion criteria or being published in languages other than English. Ultimately, 12 studies were included in our review (Figure 1).

Data extraction

- Relevant data from each included study were extracted independently by 2 reviewers (GAE, WS). The data extracted included information on study characteristics (author, year of publication, country where the studies were performed, studied parameters, demographics of the participants and the main outcomes of each study.
- Oral manifestations such as enamel hypoplasia, dental caries, delayed tooth eruption, gingival diseases, periodontal diseases, radiographic alterations, dry mouth, and changes in the oral mucosa were categorized and analyzed. Then, the synthesized findings were organized and presented in a clear and structured manner within the review article.

The synthesized data were interpreted and discussed in the context of existing knowledge and clinical implications. The implications of the findings for clinical practice, research, and policy were considered, and recommendations for dental management of children with CKD were formulated based on the synthesized evidence.

Oral manifestations of children with CKD

Enamel hypoplasia. Patients with CKD are known to exhibit enamel hypoplasia, which manifests as white or brown discoloration of the teeth. Enamel hypoplasia was noticeably more widespread in CKD patients than in healthy individuals.[9,11-13] Developmental abnormalities in enamel can arise from calcium insufficiency in CKD during the mineralization of teeth.[12,14]

Enamel hypoplasia affects children with renal disease with incidence rates ranging from 31% to 83%, depending on the family's history, the parent's race, ethnicity, nutritional status, socioeconomic position, and the kind of examination or categorization system.[9,11-13] Developmental defects of enamel (DDE) have been defined as alterations in dental enamel quality and quantity caused by disruption and/or damage to the enamel organ.[15] Several cross-sectional studies prove that there is a greater prevalence of DDE in children with CKD than in their healthy peers (Table 1).[9,11-13]

The quality of enamel is affected by the bioavailability of calcium and phosphate ions during the mineralization stage. Preeruptive DDE is typically present in children with CKD and is only produced during enamel development and mineralization.[15] The incidence of DDE depends on both the age of the patient and early management of the renal disease, which minimizes metabolic disturbances and dental decalcification. It has been proposed that DDE defects in CKD children are caused by hypocalcemia causing disruption of mineralization, decreased serum levels of 1,25-dihydroxycholecalciferol, and elevated serum phosphate, parathyroid, and fluoride levels.[6]

Dental caries. Dental caries can be caused by the cavitated or rough surface of the tooth and the increased bacterial

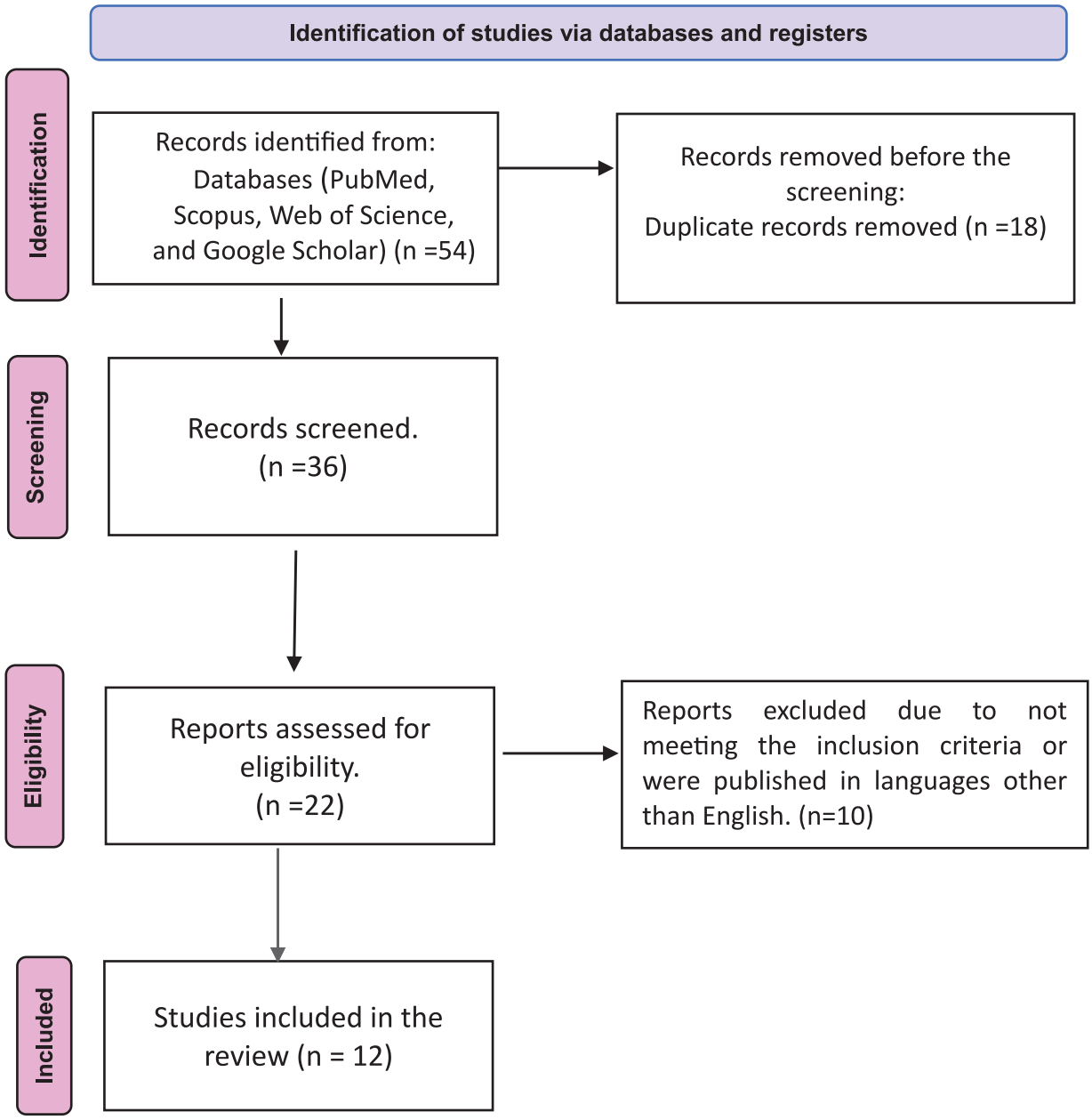

Figure 1. PRISMA flow chart of article selection.

accumulation interfering with removal of plaque, providing an area for carious lesions to occur.[16] Children with CKD have exhibited a notably low occurrence of dental caries even though they require a high carbohydrate diet to compensate for the protein-sparing diet intended to decrease nitrogenous waste products.[17] Furthermore, CKD children presented lower caries experience in addition to fewer decayed and missing teeth than healthy individuals.[9,11,12,18-22] The reason for this may be the high salivary buffering capacity and the elevated salivary urea concentration in patients with CKD.[12,18] In addition, the lower caries prevalence in CKD children may be due to splitting salivary urea into ammonia and carbon dioxide, raising the pH over the critical level for demineralization of dental enamel.[17,21] In addition, a lower risk of caries in renal patients may also be due to the antibacterial effects of urea.[21]

Delayed tooth eruption. Multiple cross-sectional studies have identified that CKD may cause delayed eruption of permanent teeth.[17,23,24] Its etiology is not clear, but it may be caused by overall decreased somatic growth.[25] Furthermore, anemia, a typical systemic symptom of CRF, is treated with oral iron supplements, which results in delayed tooth eruption and dental discoloration in patients with renal disease. Although delayed tooth eruption generally does not adversely affect oral health, periodic clinical and radiographic dental surveillance is recommended.[20,26]

Gingival and periodontal diseases. CKD is associated with impaired immune function, making children more susceptible to infections, including oral infections. Periodontal disease, characterized by inflammation and infection of the gingiva and

surrounding tissues, is more prevalent in CKD patients. The presence of periodontal disease can exacerbate systemic inflammation and potentially worsen the kidney condition. In comparison to a healthy population, studies have found that children with kidney failure had higher levels of plaque and gingival inflammation, as well as a faster rate of dental calculus accumulation.[9,21,22,27-29] Therefore, poor oral hygiene, may account for the high occurrence of gingival bleeding in children with kidney diseases.[12,30,31]

In addition, calculus buildup is frequently observed in children with CKD, while it is typically negligible or absent in healthy children. The reason for this rise in calculus is high amounts of salivary urea and pH, as well as phosphorus causing calcium phosphorus and calcium oxalate to precipitate.[9,17,32]

A possible explanation for the finding of poor dental health is the reduced rate of induced salivary production in CKD patients compared to normal controls. This confirms earlier research showing that a drop in salivary flow is a significant risk factor for people with CKD who have poor tooth health.[8,33] In addition, the higher prevalence of gingival and periodontal diseases among CKD patients may be attributed to weakened resistance to infection, slow wound healing, damage to the alveolar bone caused by renal osteodystrophy, diabetes mellitus, bleeding diathesis, malnutrition, and a general condition that compromises oral hygiene.[33,34]

Radiographic alterations in teeth and jaw. Many unusual radiographic findings have been identified in CKD children, including loss of lamina dura, narrowing of the dental pulp chamber, DDE, hypercementosis, and poorly calcified bone with ground glass appearance. These findings are caused mainly by increased osteoclastic activity affecting all bones, including alveolar bone supporting teeth and jaw. Additionally, hyperparathyroidism associated with CKD and renal osteodystrophy causes notable radiographic dental findings. Children with CKD had a lower production of the metabolite of vitamin D, which is necessary for the absorption of calcium. Among the sequelae are demineralization in the maxilla and mandible, loss of bone trabeculation, and giant cell lesions.[35,36] By comparing children with kidney failure to age- and gender-matched controls in cephalometric assessment of craniofacial growth, decreased cranial base length, shorter length of mandible and more obtuse mandibular angle have been detected in kidney failure children.[37]

Craniofacial development. Impaired growth was detected in children with CKD, and this was caused by protein malnutrition, growth hormone deficiency, renal osteodystrophy, anemia, metabolic acidosis, and combinations of the above. Growth of the face is also affected by these endocrine and metabolic alterations.[38] Three-dimensional facial photographs of patients with autosomal dominant polycystic kidney disease have been analyzed, showing vertical lengthening of the face, mild midface hypoplasia, and moderate lengthening of the nose.[39] Children with somatic growth retardation caused by growth hormone deficiency, chromosomal abnormalities, endocrine diseases, or idiopathic short stature showed similar craniofacial features despite the cause of growth retardation. A short length of the cranial base, increased lower facial height, short mandibular length, obtuse mandibular angle, and retrusive mandible position are common variants of craniofacial features compared to standard values.[40]

Dry mouth. Many children with CKD experience dry mouth, a condition known as xerostomia. This dryness results from several factors, including a restriction in fluid intake, which is necessary to account for the kidney's diminished excretory function, electrolyte imbalances, and the use of medications such as diuretics.[33,34,41] Dry mouth has been detected in children with CKD.[12,17,42] Several drugs may have adverse effects on xerostomia. Anticholinergic, cytotoxic, sympathomimetic drugs as well as disruption of ion transport pathways in acinar cells can cause salivary dysfunction, although the exact mechanism of action of these drugs is yet unknown.[43] Reduced saliva production, a hallmark of dry mouth, creates an oral environment conducive to dental caries, gingival disease, and oral fungal infection. Saliva plays a vital role in neutralizing acids, cleaning the mouth, and protecting tooth enamel, and its deficiency increases the risk of these oral health issues.[33]

Changes in the oral mucosa. As a result of the CKDs and their treatments, systemic and oro-dental manifestations were reported, while 90% of patients with kidney disease experienced oral symptoms.[44] In trials involving children and adolescents with CKD, oral stomatitis, oral ulcerations, and oral leukoplakia were uncommon; however, uremic odor, metallic taste, and dry mouth were common. The breakdown of urea to ammonia in the oral cavity is the cause of atypical breath odor in patients with CKD.[9] Xerostomia is linked to a higher chance of mouth ulcers, a rise in Candida infections, and loss of taste.[8,10,45] Metallic taste sensation and uremic breath occur due to the saliva's high quantity of urea, which is then transformed to ammonia[46] also elevated levels of protein and phosphate in saliva and changes in Ph.[47]

Reduced erythropoietin causes anemia, resulting in a pallor color of the oral mucosa.[21,47] In addition, the use of anticoagulants in hemodialysis leads to alterations in platelet aggregation, which in turn causes hemorrhage, petechiae, and ecchymosis in the oral cavity.[48] In addition, renal diseases are associated with bacterial and candida infections leading to glossitis, mucositis, stomatitis, altered taste sensation, dysgeusia, pain, and inflammation of the oral mucosa and tongue.[49]

Dental management of CKD children

Currently, it is common for pediatric dentists to see an increasing number of children with renal diseases. Thus, it is essential for them to know and understand the general health parameters of these children. The dental management of children with CKD is a complex and multifaceted challenge that requires a

deep understanding of both the disease and its implications for oral health. Children with CKD often experience oral health issues that can be attributed to the disease itself, as well as the medications and treatments associated with CKD.[8,45]

Pretreatment considerations

Multidisciplinary collaboration. A thorough review of the child's medical history is paramount. Dentists should inquire about the stage and severity of CKD, the underlying cause, and any complications. Information about recent or planned kidney transplants, hemodialysis, or peritoneal dialysis is crucial, as it affects the timing and nature of dental procedures. Thus, the collaboration between pediatric nephrologists, pediatric dentists, and other healthcare professionals is essential in delivering comprehensive care to children with CKD. Effective communication and coordination between these healthcare professionals ensure that the oral health needs of the child are addressed while considering the implications for their systemic health.[50]

Bleeding risk assessment. Consultation with the physician is necessary regarding the best timing and any potential medical complications. Additionally, prior to initiating any dental procedures that could result in bleeding, coagulation parameters should be assessed. The amount of medication given to the child must be modified to account for the kidney's diminished capacity for secretion and metabolism. CKD can lead to bleeding abnormalities, primarily due to platelet dysfunction or clotting factor deficiencies. Before performing any dental procedures, dentists should assess the child's bleeding risk. This may involve monitoring platelet counts and coagulation profiles if necessary. Hemostatic measures, such as the use of local hemostatic agents or sutures, may be employed to minimize bleeding during dental work.[42,51]

Medication awareness. Children with CKD often take multiple medications, including immunosuppressants, antihypertensive drugs, and phosphate binders. These medications can have implications for dental management. Dentists must be well informed about the specific drugs the child is taking, their potential side effects, and any contraindications with dental treatments or anesthesia. This awareness is essential to avoid interactions and complications.[52] Renal dysfunction affects how certain medications are metabolized and eliminated. In these situations, changing the dosage or the dosing schedule is necessary. The prescription of aminoglycosides and tetracyclines is to be avoided because of their nephrotoxicity.[44]

Antibiotic prophylaxis, before invasive dental procedures, has been recommended,[11,50,53,54] as patients with nephrotic syndrome or chronic systemic uremia have immunodeficiency caused by alterations in cellular immunity and malnutrition, making them more prone to bacterial infection and reduced capability of producing antibodies.[44,55,56]

Orofacial infections should be treated aggressively, keeping in mind the needed antibiotic dosage adjustment. Patients on antihypertensive medications should be regularly monitored for early identification of hypertension during dental treatment brought by the usage of adrenaline in local anesthetics in addition to stress from dental treatment. Most significant is to keep in mind that because of the increased bleeding tendency due to the uremic state, the preparation of local coagulation medications such as topical thrombin is mandatory.[12]

In regard to nonnarcotic analgesics, paracetamol is the preferred choice when treating episodic pain. Because aspirin has antiplatelet properties, it should be avoided by uremic patients. Since the other nonsteroidal anti-inflammatory medications (ibuprofen, sodium diclofenac, naproxen, and indomethacin) suppress prostaglandins and cause hypertension, it is recommended to reduce or avoid taking them altogether in the more severe stages of renal failure. It is possible to prescribe benzodiazepines without having to change the dosage, but severe sedation could still occur. Since the liver metabolizes narcotic analgesics such as codeine, morphine, and fentanyl, dosage adjustments are typically not necessary.[50]

Anesthesia considerations. The choice and administration of anesthesia require careful consideration. Kidney function plays a pivotal role in metabolizing anesthetic agents. In children with CKD, dentists must select appropriate anesthetic options while accounting for the child's renal status. Minimal sedation, local anesthesia, or general anesthesia may be indicated depending on the complexity of the procedure and the child's overall health. Local anesthesia used should be of amide type, such as lidocaine or xylocaine, because of their resorption potential in the liver.[57,58]

Infection control measures. Children with CKD often have compromised immune systems, making them more susceptible to infections. In the dental office, strict infection control measures are of utmost importance. This includes proper sterilization of instruments, adherence to standard precautions, and the use of personal protective equipment to prevent any potential infections.[59] To eliminate any septic foci, early evaluation of the oral health status of renal patients is mandatory.[5]

Fluid and electrolyte balance. CKD can disrupt the body's fluid and electrolyte balance. Dentists must be cautious when managing dehydration or overhydration in these patients, as both can have adverse effects on kidney function. Careful monitoring and adjusting dental treatment plans accordingly is essential.[60] To minimize the risk of adrenal crisis during invasive dental procedures, patients on corticosteroids (eg, patients with nephrotic syndrome) who are undergoing invasive dental procedures should have corticosteroid cover[33,55] (Figure 2).

Treatment considerations

Patients with CKD may experience morbidity and even death because of bacteremia caused by dental procedures and oral infections. Carious teeth, oral ulcers, plaque, and calculus can

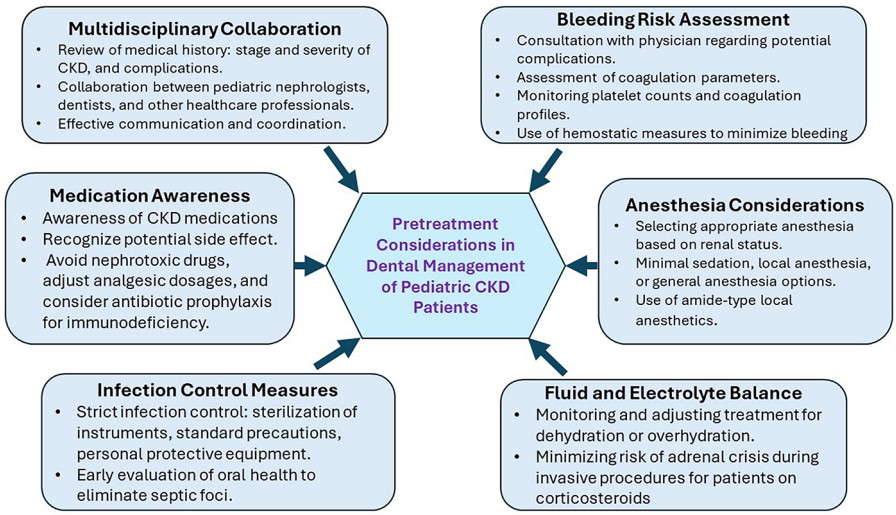

Figure 2. Pretreatment considerations in dental management of pediatric CKD patients.

be points of entry for microorganisms into the bloodstream.[11] In addition, during dental treatment, excessive stress should be avoided that may increase blood pressure. Fearful patients should take antianxiety medications, and blood pressure should be monitored before, during, and after any dental procedure.[52] It is important to record the allergies' history, such as penicillin. Oral healthcare providers should avoid nephrotoxic medications such as doxycycline. Since GI resorption is poor, antibiotics should be used via intramuscular injection.[8,54]

A dental health practitioner should monitor the symptoms of oral diseases in CKD children and adolescents. Following professional cleaning, enhanced oral home care and oral mouth rinses may help to reduce common problems such as bad breath. Eating sugar-free gum or topical oral treatments can help with xerostomia. Pilocarpine daily as initial therapy or cevimeline are 2 options for sialagogue therapy.[61] Conservative treatment of enamel hypoplasia consists of bonded composite restorations or full-coverage restorations to improve esthetics. However, fluoride supplementation is contraindicated, as it may be retained due to renal impairment.[52]

Not all DDE-affected teeth require dental filling; posterior teeth that are only obvious when smiling or speaking can be watched and, if stable, kept in place without care. Dietary components and/or drugs may be the cause of post eruptive extrinsic enamel discoloration. During dental prophylaxis, abrasive paste can be used to remove extrinsic stains from enamel surfaces.[8]

Patients on hemodialysis

Hemodialysis is an artificial system that removes harmful byproducts of metabolism, such as nitrogen waste, from the blood. The majority of patients receive hemodialysis 3 times a week. The hemodialysis process itself often results in dehydration and a persistent sensation of dry mouth. This dryness contributes to an increased susceptibility to dental caries and periodontal diseases. Furthermore, the medications prescribed to manage CKD and support hemodialysis, such as immunosuppressants, may lead to side effects such as gingival overgrowth, exacerbating difficulties in maintaining proper oral hygiene.[34,62]

Patients with renal failure who are undergoing hemodialysis are at greater risk of excessive bleeding or infection.[33] These individuals' tendency for bleeding is linked to their usage of anticoagulants and maintenance of vascular access. Hemodialysis patients frequently have lower platelet counts, platelet adhesiveness, and platelet factor 3 availability in addition to higher prostacyclin activity and capillary fragility, all of which contribute to increased bleeding tendency. To control bleeding during invasive dental procedures, patients who have significantly increased bleeding/clotting times or are undergoing therapies involving anticoagulant medications, fresh-frozen plasma, vitamin K, or platelet replacement may be prescribed to control hemorrhage.[51]

To control bleeding after dental procedures, topical thrombin, mechanical compression, sutures, microfibrillar collagen, and oxidized regenerated cellulose should be utilized as local hemostatic measures. In patients with renal insufficiency, desmopressin has been suggested as a treatment for severe bleeding, and conjugated estrogens can be administered to achieve longer-term hemostasis. Tranexamic acid may also be helpful if used as a rinse or taken orally at a rate of 10 to 15 mg/kg body weight each day, divided into 2 to 3 doses.[44,63]

On the day following dialysis, dental procedures should be performed while the intravascular volume is large, and the byproducts of heparin metabolism are in their optimal state. The patient can handle dental treatment the best at this point because the anticoagulant effects of heparin used in dialysis only continue for 3 to 5 hours post infusion, while they do not cause residual bleeding anomalies.[51]

Individuals receiving dialysis are susceptible to infection by human immunodeficiency virus (HIV), hepatitis B virus

(HBV) and hepatitis C virus (HCV) because they receive several transfusions and immunosuppression linked to renal failure. Before extracting teeth or performing minor oral surgery on these patients, liver function tests should be performed.[50] It is necessary to conduct routine monitoring and implement preventative measures to prevent cross-contamination within the dental clinic as well as personal contagion on the part of dental professionals.[44,63] To reduce the danger of access obstruction, patients should not be maintained in tight postures in the dental chair and should occasionally be allowed to stand or move. Preventive dental care is paramount in managing the oral health of children on renal dialysis. Regular dental check-ups, typically recommended every 3 to 6 months, enable early detection of oral issues and provide an opportunity for intervention before problems escalate.[5,34,64]

Dental management of children with kidney transplantation

General considerations before kidney transplant in children. Renal transplantation is the treatment of choice in patients with permanent kidney failure. Before and after the surgical procedure for kidney transplantation, immunosuppressive treatment needs to be administered to prevent severe rejection. This generally includes a combination therapy of corticosteroids, calcineurin inhibitors (cyclosporine, tacrolimus), and lymphocyte proliferation inhibitors (azathioprine, mycophenolate mofetil). All transplant recipients need to take immunosuppressive medication for the rest of their lives unless they are getting an organ from an identical twin.[65,66]

It is advised that during the peak of immune suppression just after transplantation, dentists only treat oral infections as an emergency. Therefore, prior to kidney transplantation, a comprehensive clinical and radiographic dental examination should be accomplished to identify dental and oral diseases. Dental procedures, including dental restorations, root canals, extensive calculus removal, or extractions, should be performed to eliminate all potential sources of acute or chronic mouth infections. Regular dental treatment can start again after a patient enters the posttransplant maintenance phase. Preventive services and elective procedures (such as orthodontics and esthetic restorations) to improve appearance, boost self-confidence, and increase oral health wellbeing may fall under this category.[67]

Antibiotic prophylaxis may be considered when bleeding and/or a risk of septicemia is anticipated. Treatment options that may require antibiotic prophylaxis include extractions, periodontal therapy, endodontics, periapical surgery when bleeding is anticipated, implant surgery, and the reimplantation of avulsed teeth.[68] Children with CKD who are on prolonged corticosteroid therapy may require the administration of an additional dose to prevent an adrenal crisis.[50]

Emphasizing good oral hygiene practices is essential to minimize the risk of infections and maintain overall oral health. Children and their caregivers should be educated about the importance of regular brushing, flossing, and routine dental care to prevent oral health issues.[6]

Dental considerations during post kidney transplantation periods. Children who have undergone kidney transplantation face unique challenges in maintaining oral health due to the use of immunosuppressive medications. These drugs, which are vital for preventing organ rejection, place these patients at an increased risk of systemic infections from dental sources, such as dental or periodontal abscesses.[69,70]

Elective dental care is a critical aspect of maintaining oral health, but in the context of pediatric kidney transplantation, caution must be exercised within the first 6 months post-transplantation. Elective dental procedures should be avoided during this initial recovery phase to minimize the risk of infection. Instead, focus should be on preventive measures, such as maintaining good oral hygiene through regular brushing and flossing, as well as using mouth rinses recommended by the healthcare team. Once the immune system stabilizes and the medical team gives the green light, elective dental care can be resumed to maintain the child's overall health.[9,50]

The administration of immunosuppressive medications can lead to a range of oral conditions. Patients must be informed about the caries risk that comes after a successful transplant; the pH of the oral cavity will drop to normal levels, changing to the biofilm that promotes caries. Patients who did not develop caries prior to transplantation despite poor dental hygiene practices and diets heavy in carbohydrates may have an increased risk for caries after transplantation. Periodic dental examinations that evaluate the condition of the enamel, dietary habits, and oral hygiene practices are beneficial for all patients in identifying their caries risk and creating preventative measures.[6]

Gingival overgrowth (GO) is another concern linked to immunosuppressive and antihypertensive medications. This condition can lead to delayed tooth eruption, speech difficulties, and esthetic concerns.[9] Cyclosporine A and nifedipine are often associated with GO, which can be particularly problematic in adolescents and females. The ideal management of drug-induced GO is to substitute another drug, but this may not always be possible. Surgery may be considered for severe cases, but it typically recurs if the causative medications are not adjusted.[8,10] Several studies indicate that replacement of cyclosporine therapy with tacrolimus therapy may reduce the severity of GO, with minimal risk of graft dysfunction.[71,72] It may be possible to lessen the harmful effects of medications such as calcium channel blockers and cyclosporine on the gingiva by implementing an oral hygiene program early in childhood and adolescence.

Cyclosporin-induced gingival overgrowth largely depends on the patient providing very high-quality home care.[73] At least 2 visits to the dental hygienist should be made. Once a good standard of oral hygiene has been obtained, gingival reduction can be carried out by conventional cutting and electrosurgery, and it can be completed under local anesthesia.

Table 1. Overview of studies on oral manifestations in children with CKD.

STUDY ID	COUNTRY	DENTAL FINDING STUDIED	NUMBER OF PATIENTS	AGE IN YEARS(Y)	GENDER MALES(M) FEMALES(F)	MAIN OUTCOMES
Nakhjavani and Bayramy[21]	Iran	1-Gingival inflammation. 2-Decayed, missing or filled teeth (DMF)	53	5-18y	20 M 33 F	1. CKD children: 33% caries-free. 2. Mean DMF score: 2.25 (SD=2). 3. No absence of gingival inflammation observed. 4. Gingivitis is related to anemia ($P=.0002$) and dialysis duration ($P=.007$). 5. Moderate/severe gingivitis five times more prevalent than mild after 1 y of dialysis. 6. Anemic patients show higher rates of moderate/severe gingivitis than mild.
Silva et al[29]	Brazil	1-Decayed, missing, and Filled Teeth Index (DMFT) 2- Plaque Index 3- Gingival Index System 4- Developmental Enamel Defect	100 CKD patients 100 Healthy controls	13.04 ± 2.75 y	66 F 134 M	1. CKD patients: lower caries prevalence, poorer oral hygiene, more gingival inflammation, severe enamel defects compared to non-CKD. 2. Significant differences in caries, plaque index, gingival inflammation, and enamel defects between CKD and non-CKD groups ($P<.001$). 3. CKD associated with caries ($P=.001/<0.001$), moderate/severe gingival inflammation ($P<.001$), and enamel defects ($P=.015$).
Martins et al[17]	Brazil	1-Dry mouth 2-Salivary flow rate 3- Delayed tooth eruption 4-Presence plaque, and dental calculus	30 Renal group (RG) and 30 healthy group (HG)	7-19	NA	1. Positive correlation between saliva flow rates in RG ($r=.75$, $P<.05$). No significant difference found in dry mouth sensation with xerostomia drugs or saliva flow rates. 2. Similar DMFT values between RG and HG 3. No significant difference in caries-free subjects between RG and HG. 4. RG subjects had significantly higher dental calculus than HG. 5. Significant difference in calculus formation between RG and HG subjects.
Tuma et al[9]	Brazil	1-Caries experience: DMFT/DMFT index 2-Enamel defects: Modified Developmental Defects of Enamel Index (DDEI) 3-Periodontal condition: Modified Community Periodontal Index (Modified CPI) 4-Soft tissue lesions: Drug-induced gingival overgrowth	120	Mean age of 12.78 ± 3.9 y	63 M & 57 F	1. Gingival bleeding: 95.8%, Dental calculus: 57.5%, Enamel defects: 40.8%, Dental caries: 42.5%. 2. Caries experience: 42.5%, DMFT mean 0.85 ± 1.42, dmft mean 1.64 ± 2.85. 3. Drug-induced gingival overgrowth: 16.7%, mostly degree 1. 4. Soft tissue lesions post-kidney transplant: 4.2%. Lesions: Oral wart, oral ulcers, geographic tongue.

(Continued)

Table 1. (Continued)

STUDY ID	COUNTRY	DENTAL FINDING STUDIED	NUMBER OF PATIENTS	AGE IN YEARS(Y)	GENDER MALES(M) FEMALES(F)	MAIN OUTCOMES
Subramaniam et al[86]	India	1-Dental caries 2- DMFT scores 3-Enamel defects 4-Oral hygiene was assessed using the Oral Hygiene Index Simplified (OHI-S) 5-Salivary pH and buffering capacity	36 Patients with CKD	4-15y	28 M 8 F	1. Normal soft tissue observed in all children. 2. Mean OHI-S score: 1.56. 3. DMFT: 0.5. 4. Salivary pH: 6.92, buffering capacity: 9.86. 5. Enamel defects in 58.3% of children. 6. Hypoplasia of primary maxillary anterior teeth, enamel missing in gingival half. White/cream opacities on permanent molars.
Tadakamadla et al[22]	India	1. Caries: DMFT index 2. Oral hygiene: OHI-S 3. Gingival status: Loe and Silness gingival index 4. Periodontal status: Community Periodontal Index.	74 CKD patients 150 Healthy controls	Study group (16-70) y Control gp (18-67) y	NA	1. Subjects with CKD had significantly lower caries experience compared to controls. 2. The study group had a mean gingival index score (1.88) more than twice that of controls (0.92). 3. Oral hygiene and gingival status worsened with advancing stages of kidney disease. 4. Diseased subjects showed a higher prevalence of periodontal pockets (70.3%) compared to controls
Wondimu et al[87]	Sweden	1. Gingival condition: Gingival inflammation 2. Gingival overgrowth 3. Periodontal attachment level	32	2.5-18y	19 M & 13 F	1. Thirteen percent of children had gingival overgrowth and inflammation. 2. No loss of periodontal attachment. 3. Children with gingival overgrowth received significantly higher tota cyclosporine A(CsA) doses in the first 6 post-transplant months compared to those without. 4. Development of CsA-induced gingival overgrowth is positively associated with total drug dose in the first 6 post-transplant months.
Ertuğrul et al[42]	Turkey	1-Determining causes of low caries prevalence. 2-Use of CRT bacteria and buffer tests. 3-Investigation into oral health factors.	Study group: 38 Control group: 38	4-17y	Study group:16 F & 22 M Control group: 21 F& 17 M	1. In the study group, 89.5% of patients had high salivary buffer capacity. 2. Salivary levels of cariogenic Streptococcus mutans and lactobacilli were significantly lower in the study group compared to the control group.

(Continued)

Table 1. (Continued)

STUDY ID	COUNTRY	DENTAL FINDING STUDIED	NUMBER OF PATIENTS	AGE IN YEARS(Y)	GENDER MALES(M) FEMALES(F)	MAIN OUTCOMES
Al-Nowaiser et al[12]	England	1-Assessment of dental caries. 2-Evaluation of dental plaque. 3-Observation of gingival enlargement. 4-Determination of salivary urea levels. 5-Measurement of salivary buffering capacity. 6-Analysis of oral streptococcal flora	70 Children with CRF& 70 controls	4-13.6 y	43 M & 27 F	1. CRF children had significantly higher caries-free rates (40%) compared to controls (8.5%). 2. Mean plaque scores were significantly higher in CRF group for primary (12.7) and permanent dentition (22.0) compared to controls. 3. Eight CRF children had gingival enlargement. 4. Enamel defects affected permanent teeth in 57% of CRF children compared to 33% of controls. 5. CRF group had significantly higher buffering capacity (pH 6.4) compared to controls (pH 5.6). 6. Mean salivary urea level was significantly higher in CRF children (11.6 mmol/l) compared to controls (3.6 mmol/l). 7. Streptococcus mutans isolation frequency was significantly higher in controls compared to CRF children ($P = .002$).
Nunn et al[11]	England	1-Periodontal disease 2-Gingival hyperplasia 3-Dental caries 4-Enamel defects	38 CKD children	2-16 y	NA	1. Periodontal disease was rare. 2. Gingival hyperplasia was observed in 22 children, unrelated to immunosuppressant therapy. 3. Two patients required surgical removal due to excessive gingival overgrowth. 4. Dental caries prevalence was low. 5. Enamel defects were common, with a higher prevalence of diffuse opacities (83%) and enamel hypoplasia (22%), likely due to disordered calcium and phosphate metabolism.
Koch et al[13]	Germany	1-Enamel defects 2-Enamel hypoplasia	62 CKD children & 86 healthy controls	1.1-13.9 y	NA	1. Enamel defects were found in 12 children (31%) of CKD, either clinically or under the microscope. 2. Among clinically affected CKD children, 6 (19% of all examined) had localized hypoplasia of primary canines, rare in healthy controls (3%).
Peterson et al[88]	United States	1-Salivary composition 2-Salivary pH 3-Plaque pH	21 CKD children & 15 healthy controls	5-18 y	NA	1. Chronic renal failure subjects had higher salivary urea nitrogen than transplanted subjects. 2. Plaque pH correlated directly with salivary urea nitrogen and was more alkaline in chronic renal failure than comparison groups. 3. Salivary urea nitrogen mainly influenced plaque pH, while salivary pH and phosphorous had minimal impact. 4. Transplanted patients with normal renal function, especially those with enamel hypoplasia and poor oral hygiene, may be at increased caries risk.

Reducing the dose of cyclosporin appears to facilitate the resolution of gingival enlargement.[74]

Patients on immunosuppressant drugs, such as sirolimus and everolimus, may exhibit oral stomatitis. Due to the inhibition of the mammalian target of rapamycin by these medications, there is a transient ulceration of the oral mucous membranes. Usually, the ulcerations are temporary and go away in 10 to 15 days. Topical steroids may be used to treat ulcerations to reduce discomfort. If the ulcerations are severe and recurring, it might be necessary to discontinue the drug for a few weeks to give the body time to recover before starting it again at a reduced dosage.[75] Pain management, nutritional assistance, oral decontamination, dry mouth relief, and topical anesthetic mouthwash (2% viscous lidocaine with diphenhydramine) are also used as treatments for oral stomatitis.[76,77]

Immunosuppressed patients are also more susceptible to various fungal and viral infections with oral manifestations, including herpes simplex virus (HSV).[8,9] The most frequent virus responsible for oral infections in transplant recipients is HSV, which typically manifests 2 to 6 weeks after transplantation. HSV-caused oral mucosa ulcerations that are severe and/or recurring might make it uncomfortable for a child to eat or undertake oral self-care. Oral HSV lesions occur in 0% to 11.3% of kidney transplant recipients. If these patients have recurrent HSV infections, 400 mg of acyclovir can be taken orally 3 times a day for 10 days or more (typically longer than 2 weeks).[33,56] Transplant patients with mucocutaneous HSV infection (including orolabial, anogenital, or any other areas of skin) may be treated with IV acyclovir (5 mg/kg/dose given every 8 hours), oral acyclovir, or one of the other oral antiviral agents with better bioavailability (valacyclovir or famciclovir), depending on the severity of the disease, the proximity to the transplant, and the level of immunosuppression.[78,79]

The primary cause of oral candidiasis development and progression is immunosuppression. There is a reported range of 4% to 43% for the occurrence of oral candidiasis among kidney transplant patients.[80,81] Any oral mucosal surface can become infected; however, the palate, tongue, and buccal mucosa are the most frequently affected. The disease can appear in several ways, but the most prevalent forms are erythematous, pseudomembranous, and hyperplastic candidiasis. Maintaining proper dental hygiene is essential for both disease prevention and treatment. It is recommended to rinse the oral cavity with a solution of chlorhexidine or 0.1% hypochlorite. Antifungal medications such as nystatin can be used topically, while fluconazole or itraconazole can also be used in systemic therapy.[82,83]

Kidney transplant recipients are at an increased risk of developing oral cancers, including Kaposi's sarcoma and squamous cell carcinoma, possibly due to a compromised immune system's inability to control malignant cells and viral oncogenes. These cancers may develop in areas affected by GO. Therefore, regular oral health monitoring and tailored care plans are crucial for pediatric kidney transplant recipients to address the unique challenges posed by their immunosuppressive regimens and reduce the risk of oral health complications and associated systemic infections.[33]

Children with CKD face a complex interplay between systemic health and oral health, which can significantly impact their overall well-being. Nutritional status plays a crucial role in CKD, as these children often experience dietary restrictions and may have difficulty maintaining adequate nutrition. These restrictions can lead to deficiencies in essential vitamins and minerals, which in turn can affect oral health by weakening the tooth structure and increasing susceptibility to decay. Additionally, medications commonly used to manage CKD, such as phosphate binders and calcimimetics, can have side effects such as xerostomia and altered taste sensation, further compromising oral health. Moreover, the chronic nature of the illness and the demanding treatment regimens may affect access to dental care and compliance with oral hygiene practices. Children with CKD may have limited access to dental services due to financial constraints, transportation issues, or the prioritization of medical appointments. Furthermore, the physical and emotional toll of managing a chronic illness may lead to decreased motivation or ability to adhere to recommended oral hygiene routines. This combination of factors places children with CKD at a higher risk for dental caries, periodontal disease, and other oral health problems.[6,44,84,85]

Barriers to effective dental care for children with CKD include limited integration of oral health into healthcare policies, inadequate insurance coverage, challenges in interdisciplinary collaboration, limited access to specialized care, and lack of parental education and awareness. Strategies to overcome these barriers include advocating for the integration of oral health into healthcare policies, expanding insurance coverage for dental care, promoting interdisciplinary education and training, increasing access to specialized pediatric dental care, improving referral systems, and providing comprehensive parental education and awareness programs.

Conclusion

Oral health in children with CKD is an aspect of their care that cannot be overlooked. Therefore, the dentist and medical team must work together to collaborate to alleviate oral health issues, prevent systemic infections that originate in the mouth, and keep an eye out for the development of oral diseases in patients. The intricate relationship between CKD and oral health underscores the need for a holistic approach to healthcare, where both conditions are considered together.

Pediatric oral health providers play a crucial role in addressing the unique oral health needs of children with CKD. Preventive measures such as regular dental check-ups, oral hygiene education, and dietary counseling can significantly reduce the incidence of dental caries and periodontal disease. Collaboration between pediatric nephrologists and pediatric dentists is essential in delivering comprehensive care to children with CKD.

Implementing these recommendations to address the oral health needs of children with CKD faces several barriers in

clinical practice. These include limited integration of oral health into healthcare policies, resulting in a lack of prioritization and specific guidelines for collaboration between nephrologists and dentists. Additionally, inadequate insurance coverage for dental care, challenges in interdisciplinary collaboration, limited access to specialized pediatric dental care, and insufficient parental education contribute to the barriers.

One limitation of our review is the limited number of studies meeting our inclusion criteria, particularly in pediatric populations with CKD, hemodialysis, or renal transplantation, which may restrict the breadth of our findings and the generalizability of our conclusions. Another limitation of our review is the potential for selection bias in the included studies. Despite our rigorous selection criteria, the studies ultimately included may not fully represent the diversity of populations and settings affected by CKD and its oral manifestations in children.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable.

Author contributions

GAE and WS contributed to the study's conception and design. Material preparation and data collection by GAE and WS. The first draft of the manuscript was written by GAE and WS. All authors reviewed the final manuscript.

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Data availability statement

The data that support the findings of this review are available from the corresponding author upon reasonable request.

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