REVIEW ARTICLE

Oral conditions in renal disorders and treatment considerations – A review for pediatric dentist

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Abstract This article reviews the current understanding of the oral and dental aspects of chronic renal disease (CRD). A PubMed literature search was performed and all relevant studies were assessed. As the number of people suffering from CRD increases worldwide, dentists are expected to encounter more patients with CRD who need oral care. In children, CRD can elicit a wide spectrum of oral manifestations in the hard and soft tissues. Bleeding, altered drug metabolism, impaired immune function, and an increased risk of dentally induced bacterial endocarditis are some important features that require attention. Dental management of patients with CRD requires that clinicians appreciate that multiple systems can be affected by the disease. Dentists should consult with nephrologists regarding the specific precautions required for each patient. Medical treatments in these patients may need to be postponed due to an unfavorable oral health status or potential risk of life-threatening infection after surgery. Improving oral hygiene and performing necessary dental and oral treatment before hemodialysis or transplantation may prevent endocarditis and septicemia in these patients. Hence, treatment plans should be formulated to restore the patient’s dentition and protect them from potentially severe infections of dental origin.

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1. Introduction

Various medical conditions can affect the oral health of patients. With advances in medical treatment and improved survival rates for many disorders, dentists can be expected to treat an increasing number of patients with complex medical conditions. In particular, the prevalence of chronic renal disease (CRD) is increasing worldwide (Olivas-Escárcega et al., 2008). Common renal disorders seen in children include congenital nephropathies, nephrotic syndrome, chronic renal failure (CRF), glomerulonephritis, hydronephrosis, and multicystic renal dysplasia, which ultimately lead to end-stage renal disease (ESRD) (Bagga et al., 2009; Warady and Chadha, 2007).

CRF is a progressive and irreversible decline in the total number of functioning nephrons, which causes a decline in the glomerular filtration rate. CRF is accompanied by clinical and laboratory changes that are related to the inability of the kidney to excrete metabolites and perform endocrine functions, including secretion of active vitamin D and erythropoietin (Fogo and Kon, 2004). Nephrotic syndrome is a common chronic disorder that is characterized by alterations of permselectivity at the glomerular capillary wall, resulting in protein loss through the urine. Nephrotic range proteinuria is defined as proteinuria exceeding 1000 mg/m²/d or a spot urinary protein-to-creatinine ratio exceeding 2 mg/mg (Bagga and Mantan, 2005). ESRD is the stage when renal replacement therapy by dialysis or transplantation is required (Greenberg and Glick, 2003).

In children, renal disease can give rise to a wide spectrum of oral manifestations in the hard and soft tissues. Renal disease may lead to the development of pale oral mucosa (Al Nowaiser et al., 2003), dental calculus (Davidovich et al., 2009; Martins et al., 2008), enamel hypoplasia (Al Nowaiser et al., 2003; Martins et al., 2008), dry mouth (Martins et al., 2008), low carries rate (Al Nowaiser et al., 2003; Nakhjavani and Bayramy, 2007; Nunn et al., 2000), poor oral hygiene, and uremic stomatitis, and may cause changes in the salivary composition (Guzeldemir et al., 2009) and flow rate (Al Nowaiser et al., 2003; Guzeldemir et al., 2009; Martins et al., 2008). These complications can lead to excessive bleeding, anemia, increased susceptibility to infection, drug intolerance, renal osteodystrophy, adrenal crisis, and enamel defects in children. This manuscript provides an up-to-date review of the clinical and oral manifestations of CRD and the role of pediatric dentists in the treatment of patients with CRD.

2. Epidemiology

There is limited information on the epidemiology of CRD in the pediatric population. Because this disease is often asymptomatic in its early stages, it is both underdiagnosed and underreported (Warady and Chadha, 2007). The estimated incidence of ESRF in childhood, either due to a congenital or acquired condition, is 10–12 cases per 1 million children, with a prevalence varying from 39 to 56 million children (Trivedi and Pang, 2003). In North America, up to 11% of the population (19 million) may have chronic kidney disease (Coresh et al., 2003). Surveys in Australia, Europe, and Japan describe the prevalence of chronic kidney disease to be 6–16% of their respective populations (El Nahas and Bello, 2005; Hallan et al., 2006). The overall prevalence of genetic kidney disease in children in Australia and New Zealand is 70.6 children per million in the age-representative population. Congenital anomalies of the kidney and urinary tract (16.3 cases per million children) and steroid-resistant nephrotic syndrome (10.7 cases per million children) are the most frequent anomalies (Fletcher et al., 2013).

Fifty-seven percent of the world’s population resides in Asia, which is a geographic region characterized by a very high proportion of children. In spite of this, epidemiological information from Asia is scant and primarily based on patients referred to tertiary medical centers (Hari et al., 2003). Estimates of the annual incidence of nephrotic syndrome range from 2 to 7 cases per 100,000 children and prevalence from 12 to 16 cases per 100,000 (Eddy and Symons, 2003). There is epidemiological evidence of a higher incidence of nephrotic syndrome in children from South Asia (Mc Kinney et al., 2001). Prevalence rates of genetic renal diseases, like congenital and infantile nephrotic syndrome, are high in Kingdom of Saudi Arabia. Postinfection glomerular pathologies are also common (Kari, 2012).
3. Etiopathogenesis

The kidney performs four essential functions: (1) excretion of metabolites, particularly urea, (2) regulation of blood volume and electrolyte concentration, (3) regulation of erythrocyte production in the bone marrow by secreting erythropoietin, and (4) participation in calcium homeostasis through hydroxylation of vitamin D₃ into active or inactive metabolites (Fogo and Kon, 2004). Any pathology involving renal function would be expected to have serious pleiotropic effects.

ESRD is a chronic and progressive disease characterized by the destruction of nephrons (Greenberg and Glick, 2003). Diabetes, pyelonephritis, glomerulonephritis, nephrosclerosis, polycystic kidney disease, and collagen vascular disease are among the leading causes of this destruction (De Rossi and Glick, 1996). Congenital causes are responsible for the greatest percentage of all cases of CRD seen in children. However, infectious or acquired causes predominate in developing countries, where patients are referred in the later stages (Warady and Chadha, 2007).

When injury to the renal tissue occurs (e.g., due to congenital or acquired disease), the normally functioning nephrons adapt to the tissue insult and continue functioning. However, beyond a certain limit, renal hypertrophy leads to glomerular hyperfiltration (increased workload) of the remaining nephrons, which ultimately causes the nephrons to fail (Fogo and Kon, 2004). Moreover, the original renal lesion can initiate progression of immunological damage. A hallmark of renal disease, proteinuria causes and exacerbates tubular and interstitial damage, leading to complete (end stage) renal failure. Resulting complications include anemia, electrolyte and acid–base disturbances, renal osteodystrophy, growth delays, and hypertension (Davidovich et al., 2005).

4. Clinical manifestations

Clinical signs and symptoms of renal failure are collectively termed as uremia (Proctor et al., 2005). Uremia is a state of intoxication that involves multiple extrarenal systems, such as the bone, heart, vasculature, and lungs (Fogo and Kon, 2004). Uremia causes suppression of lymphocytic responses, dysfunction of granulocytes, and suppression of cell-mediated immunity. In consequence of these changes, uremic patients are more susceptible to infection (De Rossi and Glick, 1996; Naylor and Fredericks, 1996).

CRF affects most parts of the body, and the clinical features depend on the stage of renal failure and the systems involved. Pallor due to anemia, platelet dysfunction, impaired cell-mediated immunity, signs of fluid overload, hypertension, flow murmurs, pruritis, pulmonary edema, and renal osteodystrophy are common signs of CRD (Proctor et al., 2006). The most severe growth delay is found in children with early-onset CRF. Other factors that contribute to growth delay are reduced food intake, low-protein diets, and chronic metabolic acidosis (Naylor and Fredericks, 1996).

5. Oral manifestations

5.1. Soft tissue

Oral symptoms are observed in 90% of patients with renal disease, as the disease itself and treatments have systemic and oro-dental manifestations (De Rossi and Glick, 1996; Saini et al., 2010). Reduced erythropoietin and the resultant anemia lead to pallor of the oral mucosa. Platelet aggregation is altered during uremia (Skorecki et al., 2005). This situation, combined with the use of heparin and other anticoagulants in hemodialysis, leads patients to become predisposed to ecchymosis, petechiae, and hemorrhages in the oral cavity (Seraj et al., 2011). Stomatitis, mucositis, and glossitis can cause pain and inflammation of the tongue and oral mucosa. Altered taste sensations, dysgeusia, as well as bacterial and candidiasis infections can develop due to the underlying renal disease (Thomas, 2008).

A common oral symptom of CRF is the sensation of a dry mouth, which may be caused by restricted fluid intake (necessary to accommodate the reduced excretory capacity of the kidney), adverse effects of drug therapy, and the low salivary flow rate (Klassen and Krasko, 2002; Proctor et al., 2005). Patients also suffer from odorous breath (uremic breath) and sensations of metallic tastes in the mouth (uremic fetor). Uremic fetor occurs as a result of a high salivary concentration of urea, which is converted to ammonia (De la Rosa-Garcia et al., 2006). Additional possible causes are increased phosphate and protein concentrations, as well as changes in salivary pH (Skorecki et al., 2005). Gingival inflammation has been reported to be due to plaque accumulation and poor oral hygiene (Olivas-Escarcega et al., 2008). Attention has been given to general medical care, prolonged hospitalization, and hypoplastic teeth as causes of high plaque scores in these patients (Martins et al., 2008). However, the frequency of gingival inflammation is low (Al Nowaiser et al., 2003; Lucas and Roberts, 2005) because the immunosuppression and uremia associated with renal disease alter the inflammatory response to bacterial plaques in gingival tissue (Nunn et al., 2000). Pallor caused by anemia can also mask inflammatory signs in the gingiva (Lucas and Roberts, 2005).

Another manifestation of CRD is gingival enlargement secondary to drug therapy or transplantation. Gingival enlargement chiefly affects the labial interdental papillae. The unpleasant appearance of gingival enlargement has adverse psychological impacts on the patient, interferes with the normal oral function, speech, and oral hygiene, as well as results in delayed or ectopic eruption. Meticulous oral hygiene is essential to reduce the inflammation associated with gingival overgrowth (Al Nowaiser et al., 2003; Chabria et al., 2003; Lucas and Roberts, 2005).

Calculus has an important effect on gingival and periodontal disease incidence. Children with CRD demonstrate an elevated level of calculus (Martins et al., 2008). Elevated salivary pH, decreased salivary magnesium, and high levels of salivary urea and phosphorus lead to precipitation of calcium-phosphate and calcium oxalate, and, thus, dental calculus formation. Calculus is more prevalent on the lingual surface of the lower incisors due to their proximity to the submandibular gland orifices (Davidovich et al., 2009).

Uremic stomatitis is a complication associated with uremia and occurs in advanced renal failure with blood urea nitrogen (BUN) levels above 300 mg/mL (De Rossi and Cohen, 2008). Uremic stomatitis has two forms: the erythe-mopultaceous form, characterized by red burning mucosa covered with a gray exudate and pseudomembrane; and the ulcerative form, characterized by frank ulceration with redness and a pultaceous
covering. Stomatitis occurs due to a loss of tissue resistance, which can be the result of trauma or pathology. These lesions are commonly painful and most often appear on the ventral tongue and anterior mucosal surfaces. They heal spontaneously once the underlying uremia and elevated BUN levels are resolved (DeRossi and Cohen, 2008).

White patches of the skin, called “uremic frost,” can occasionally be seen intraorally. Uremic frost results from the formation of urea crystal on the epithelial surfaces after perspiration and saliva evaporation (Hovinga et al., 1975). Candidiasis is seen as patients lose the ability to fight infections. Candidiasis is more frequent in transplant patients because of generalized immunosuppression (Olivas-Escárcega et al., 2008; Klassen and Krasko, 2002).

5.2. Hard tissue

Disruptions during the histodifferentiation, apposition, and mineralization stages of tooth development result in tooth structure abnormalities (Mc Donald et al., 2011). In children with renal disease, incidence rates of enamel hypoplasia range from 31% to 83%, depending on the racial, ethnic, nutritional, and socio-economic statuses of the child’s family/parent and the type of examination or classification system (Ibarra-Santana et al., 2007; Koch et al., 1999; Lucas and Roberts, 2005; Nakhljavani and Bayramy, 2007; Nunn et al., 2000; Olivas-Escárcega et al., 2008). Enamel hypoplasia of the primary and permanent dentition has been observed (Koch et al., 1999).

The age at which metabolic disturbances occur correlates with the abnormalities of dental developmental (Nunn et al., 2001). Enamel hypoplasia in the form of white or brown discoloration of primary teeth is commonly seen in young children with early-onset renal disease (Al Nowaiser et al., 2003; Koch et al., 1999). In the primary teeth, enamel formation starts around the 14th week of gestation and is complete by the end of the first year of life (Lunt and Law, 1974). Therefore, enamel defects in deciduous teeth indicate prenatal or early postnatal damage affecting ameloblast or enamel maturation. Calcium, phosphorus, or vitamin D metabolism can be disturbed in children with CRF during the first months of infancy. Koch et al. reported enamel defects of the primary dentition, particularly canine hypoplasia, in 22% of studied children (Koch et al., 1999). Narrowing or calcification of the tooth pulp chamber (Galili et al., 1991) and delayed eruption of the permanent teeth (Jaffe et al., 1990; Martins et al., 2008) have been reported in children with renal disease.

In patients with renal disease, the risk of caries formation is increased by poor oral hygiene and a carbohydrate-rich diet (necessary to reduce the renal workload), in addition to disease-related debilitation, hypoplastic enamel, low salivary flow rate, and long-term medication use (Al Nowaiser et al., 2003; Martins et al., 2008). Nevertheless, the incidence of dental caries appears to be low in these patients, owing to the presence of highly buffered and alkaline saliva due to elevated urea and phosphate concentrations (Al Nowaiser et al., 2003; Lucas and Roberts, 2005; Martins et al., 2008; Nakhljavani and Bayramy, 2007; Nunn et al., 2000). The salivary pH remains above the critical level for demineralization of the dental enamel.

Renal osteodystrophy results from disorders in calcium, phosphorus, or vitamin D metabolism and increased parathyroid activity. Calcium absorption by the intestine is reduced early in CRF because the kidneys cannot convert vitamin D to its active form (1,25 dihydroxycholecalciferol). There is a corresponding retention of phosphate, which ultimately leads to decreased serum calcium levels, as calcium phosphate is maintained within normal levels in healthy subjects. This situation is associated with compensatory hyperactivity of the parathyroid gland, leading to increased urinary excretion of phosphates, decreased urine calcium excretion, and increased calcium release from bone (De Rossi and Glick, 1996).

Manifestations of metabolic renal osteodystrophy and compensatory hyperparathyroidism include demineralization, decreased trabeculation, and a “ground-glass” appearance of the bone, decreased cortical bone thickness, loss of lamina dura, radiolucent giant cell lesions, maxillary brown tumors, enlargement of the skeletal base, and metastatic soft-tissue calcification. Patients have an increased risk of jaw fracture due to trauma or oral surgery (Proctor et al., 2005). Other dental findings include tooth mobility, malocclusion, enamel hypoplasia, pulp stones, and abnormal bone healing after dental extraction. Radiographically, osteodystrophy manifests as a failure of the lamina dura to resorb and the deposition of sclerotic bone around the socket (Klassen and Krasko, 2002; Proctor et al., 2005). Children may demonstrate brown discoloration of the teeth due to the underlying uremia and oral iron supplements (Martins et al., 2008).

6. Medical management

Medical management of renal disease depends on the stage of disease and clinical status of the patient. Management may include dietary changes, administration of sodium bicarbonate to reduce acidosis, and correction of systemic complications (Proctor et al., 2005; De Rossi and Glick, 1996). In early renal disease, dietary modifications can minimize the effects of kidney failure and perhaps slow disease progression. Patients are administered vitamin D supplements to treat hypocalcemia. Adherence to a high-carbohydrate, low-protein diet can minimize production of toxic nitrogen-containing metabolites. Elevated potassium levels can be treated by reducing the dietary intake of potassium-rich fruits like bananas. Restriction of sodium helps to control blood pressure (Proctor et al., 2005).

Vitamin D compounds combined with phosphorus-binding agents can treat renal osteodystrophy (Davidovich et al., 2005). In CRF, dialysis is performed to remove nitrogenous and other toxic metabolites from the blood. Dialysis is a life-saving intervention that has significantly reduced mortality rates of CRF. Arteriovenous fistulae in the arm are required for regular vascular access by wide-bore needles. Transplantation with renal allografts from cadavers or living donors may be attempted, but is limited by the availability of organs (Proctor et al., 2005).

7. Role of the pediatric dentist

Close collaboration between the dentist and pediatric nephrologist is required in the treatment of children with CRD. Early evaluation of the oral health status of renal patients is essential...
to eliminate potential infection foci from the oral cavity (Naugle et al., 1998). Before any surgery, renal patients should undergo a detailed oral assessment, and any necessary dental treatment should be carefully planned and performed (Klassen and Krasko, 2002).

7.1. Drug therapy

Dental treatment, especially in children, is often a source of anxiety and fear. Dentists should avoid excessive stress that could elevate the systolic blood pressure. Antianxiety medication should be given to fearful patients, and blood pressure monitoring before, during, and after the procedure is recommended.

Many drugs are excreted via the kidney; therefore, diminished renal function changes the volume of distribution, metabolism, rate of elimination, and bioavailability of many drugs. Plasma half-lives of agents eliminated in the urine are often greatly prolonged in patients with renal failure and effectively reduced by dialysis. A 50% decrease in creatinine clearance theoretically represents a twofold increase in the elimination half-life of a drug cleared exclusively by renal excretion. Even for drugs metabolized by the liver, renal failure can lead to increased risk of toxicity. Therefore, dentists should avoid excessive accumulation of drugs in patients by lengthening the interval between doses according to the degree of elimination impairment. Nephrotoxic drugs should be avoided entirely. Drugs that depress respiration, such as narcotics, should be used with caution in patients with anemia (De Rossi and Glick, 1996). For patients who are undergoing invasive dental procedures and are on corticosteroids (e.g., patients with nephrotic syndrome), appropriate corticosteroid cover should be administered to minimize the risk of adrenal crisis (Bagga and Mantan, 2005; Proctor et al., 2005).

7.2. Treatment considerations

In patients with chronic systemic uremia or nephrotic syndrome, alterations of the cellular immunity and malnutrition due to adherence to a protein-restricted diet lead to immunodeficiency. These patients are susceptible to bacterial infection and have a diminished ability to produce antibodies (Bagga and Mantan, 2005; Davidovich et al., 2005; De Rossi and Glick, 1996). Oral diseases and dental procedures create bacteremia, which may lead to morbidity and potential mortality in patients with renal failure or on dialysis. Carious teeth, oral ulcers, plaque, and calculus can be points of entry for microorganisms into the bloodstream. Antibiotic prophylaxis, typically with vancomycin, has been recommended before invasive dental procedures (Gudapati et al., 2002; Naylor and Fredericks, 1996; Nunn et al., 2000), although this recommendation is contrary to guidelines of the British Society for Antimicrobial Chemotherapy (Proctor et al., 2005). Klassen and Krasko (2002) have stated that good oral health lowers the risk of oral infection and, subsequently, the risk of sepsis, endocarditis, or enteritis at the site of vascular dialysis access.

Currently, there are no clear guidelines for the appropriateness of antibiotic prophylaxis for bacteremia-producing dental procedures in patients with CRD. The mildest form of dental infection should be treated with caution. Good home oral care supplemented with aggressive in-office oral health maintenance should be employed to reduce the risk of dental infections. Patients undergoing dialysis are exposed to numerous transfusions and renal failure-related immunosuppression; thus, they are at greater risks of infection by human immunodeficiency virus (HIV) and hepatitis types B and C (Gudapati et al., 2002). In these patients, dentists should perform liver function tests before extractions and minor oral surgical procedures.

Patients with renal disease undergoing hemodialysis require special consideration with regard to the risk of excessive bleeding or infection and medications (Proctor et al., 2005). The bleeding tendency in these patients is attributed to the use of anticoagulants and maintenance of vascular access. Patients on hemodialysis often have reduced platelet counts, platelet adhesiveness, and availability of platelet factor 3, as well as increased prostacyclin activity and capillary fragility, all of which lead to greater blood loss. Patients with significantly increased bleeding/clotting times or receiving therapies involving antifibrinolytics, fresh-frozen plasma, vitamin K, or platelet replacement may be prescribed drugs or undergo electrocautery to control hemorrhage during invasive dental procedures (Lockhart et al., 2003).

Elective dental procedures should be performed on the day after dialysis, when circulating toxins have been eliminated, the intravascular volume is high, and the products of heparin metabolism are at an ideal state (Proctor et al., 2005). At this time, the patient is best able to tolerate dental treatment. The anticoagulant effects of heparin used during dialysis do not produce residual bleeding abnormalities because they last only 3–4 h postinfusion (Lockhart et al., 2003). Arteriovenous shunts should not be jeopardized, and the affected arm should never be used for intravenous or intramuscular injection. Patients should not be kept in cramped positions in the dental chair and should be allowed to stand or walk occasionally to minimize the risk of access obstruction (De Rossi and Glick, 1996).

Long-term effective plaque control measures should be employed. Treatment of enamel hypoplasia depends on the severity of the defects. Conservative treatment may consist of a bonded composite restoration or full-coverage restoration. Prescription of additional fluorides (other than fluoridated water and toothpastes) is contraindicated because even moderate renal impairment is likely to lead to fluoride retention. Additionally, as these patients have a low incidence of dental caries, fluoride supplementation is not required.

8. Conclusion

A better understanding of the systemic and oral abnormalities in individuals with renal disease will help dentists and oral healthcare workers to render efficient oral care and plan preventive regimens tailored to individual needs. With the increased availability and use of dialysis, renal transplantation, and other advancements, many oral manifestations of renal failure and uremia are observed less frequently. However, as the signs and symptoms of renal disease can be observed in the oral cavity, the dentist can play an important role in the diagnosis and treatment of these patients. Early diagnosis and prompt treatment of oral disease are mandatory and will minimize the need for extensive dental care. Patients and
guardians should be informed about the role of oral hygiene in reducing the risks of oral infections, septicemia, and endocarditis.

**Ethical statement**

This review article does not require ethical approval.

**Conflict of interest**

The authors have no conflicts of interest to declare.

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