

Review Article

Oral Manifestations of Chronic Renal Disease

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Chronic Renal Disease is a Global Health Problem which has multiple clinical features which are problematic to the patient, reduces their life expectancy and changes their way of living. It is mainly comprised of hematuria, proteinuria and progressive loss of kidney function. If it reaches end-stage that means there is 90% loss of the kidney function. At times, it also gives rise to oral manifestations which are misdiagnosed and as a result go untreated. This review article deals with the oral manifestations of Chronic Renal Disease so that proper awareness of this problem can be met among Dentists as well.

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Key words : Chronic, Renal, Oral manifestations, Hematuria, Proteinuria.

Chronic Kidney Disease (CKD) is a major health issue in today's time around the Globe. It is the 12th leading cause of death Globally and 17th leading cause of disability¹. It is defined as "structural or functional abnormalities of the kidney, with or without decreased GFR, manifested by pathological abnormalities or markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests²." As it progresses it can lead to gradual loss of kidney function which further gives rise to different conditions such as bony changes, altered immune status which can be of significance to every diagnostician.

Floege J, *et al* (2010) classified CKD (Table 1) on the basis of Glomerular Filtration Rate (GFR)³:

The end stage of CKD is End-Stage Renal Disease (ESRD). The main causes of ESRD are Diabetes Mellitus and Hypertension which themselves can cause problems of their own. The commonest cause of death in patients with ESRD is Cardiac failure, followed by infection and malignancy⁴. The analysis in 2017, suggests that prevalence of CKD globally was 9.1% (697.5 million cases). Nearly 1/3rd of all cases were in China (132.3 million) or India (115.1 million)⁵.

The oral manifestations primarily include generalized pallor of oral mucosa, platelet alteration in such patients can lead to renal anaemia⁶. Due to platelet defects there may be formation of ecchymosis and petechiae. Xerostomia is also reported in such

Editor's Comment :

- A health practitioner should have a understanding of the renal diseases and their manifestations to have an updated approach and dental treatment protocol against patients with CKD and put them into practice for the betterment of society.

Table 1 — Classification of CKD on basis of GFR

CKD Stage	Definition
1	Normal or Increased GFR, some evidence of kidney damage reflected by microalbuminuria, proteinuria and hematuria as well as radiologic or histologic changes
2	Mild decrease in GFR (89-60ml/min per 1.73m ²) with some evidence of kidney damage reflected by microalbuminuria, proteinuria and hematuria as well as radiologic or histologic changes
3	GFR 59-30 ml/min per 1.73m ²
3A	GFR 59 to 45 ml/min per 1.73m ²
3B	GFR 44 to 30 ml/min per 1.73m ²
4	GFR 29- 15 ml/min per 1.73m ²
5	GFR < 15 ml/min per 1.73m ² , when renal replacement therapy in the form of dialysis or transplantation has to be considered to sustain life
The suffix p has to be added to the stage in proteinuric patients (proteinuria > 0.6g/24h)	

patients⁷.

These patients also have a characteristic smell in oral cavity known as "Uremic Feter". There is also altered taste sensation due to high content of urea in the saliva⁸.

DISCUSSION

As far as oral cavity is concerned the renal diseases affect both the soft and hard tissues.

Soft Tissue :

One of the first symptoms that can be seen in the soft tissue is a generalized pallor of the oral mucosa.

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Advanced Renal Diseases can lead to anemia because of reduced erythropoietin, that's why the generalized pallor⁷. Chronic Renal Failure (CRF) can cause dry mouth as there is limited fluid intake in CRF, the adverse effect of the associated drugs and low salivary flow rate⁸. Another symptom which we see is 'uremic fetor' in the oral cavity which occurs due to conversion of urea (high concentration in the saliva) into Ammonia. Patients with CKD are hospitalized for a longer period of time which may result in more plaque accumulation in the patient and that lead to Gingiva inflammation. However, the signs of inflammation can be masked by the generalized mucosal pallor⁹.

One of the most important manifestation of CKD is Uremic Stomatitis (Fig 1). This condition occurs secondary to uremia and is seen in patients with Advanced Renal Failure and Blood Urea Nitrogen (BUN) levels above 300 mg/ml¹⁰.

It is of two types:

- Erythemo-pultaceous form
- Ulcerative form

The erythemo-pultaceous form is characterised by erythematous mucosa which is covered with a grayish pseudo membrane. The ulcerative form shows marked ulceration along with erythema. Painful lesions are also seen on the ventral surface of tongue. Uremic Stomatitis heals spontaneously once the causative uremia and elevated BUN levels are normalized¹⁰.

Uremic Frost (Fig 2) are the white patches seen on skin and is caused due to formation of crystals of urea on the epithelial surface after sweating and evaporation of sweating. These patches can also be seen intra orally and that occurs after evaporation of saliva¹¹.

In patients who have undergone Renal Transplant are generally immuno- compromised. This condition can give rise to Oral Candidiasis. It may present as angular Cheilitis, erythematous, atrophic or pseudomembranous type. Even Herpes Simplex infection are also prevalent in patients with CKD¹².

In patients with CKD, gingival hyperplasia is also evident. This enlargement occurs secondary to usage of anti-hypertensive medications such as calcium-channel blockers (amlodipine, verapamil) and also due



Fig 1 — Uremic Stomatitis



Fig 2 — Uremic Frost

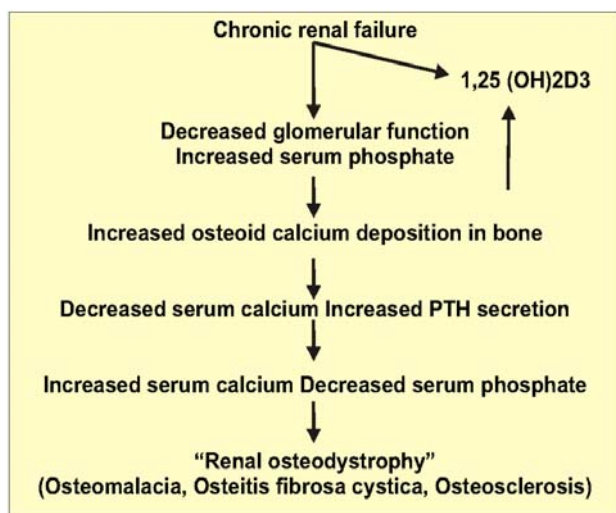
to immune- suppressive agents such as tacrolimus, which is given in patients with renal transplant¹³.

Alteration in platelet function can lead to gingival bleeding, ecchymosis and petechiae.

Hard Tissue :

Chronic Renal Diseases (CRD) patients, both deciduous and permanent dentitions are affected. In deciduous dentition, it can cause problems in mineralization, histodifferentiation, etc. leading to enamel hypoplasia¹⁴. According to different studies, the range of enamel hypoplasia in children with CKD ranges from 31-83% depending upon nutritional, socio economic status and ethnicity of child's parents¹⁵. In deciduous teeth, the formation of enamel starts around 14th week of Intra-Uterine Life (IUL) and is completed by the end of 1st year of life. As a result, any kind of enamel defects in deciduous dentition indicates a pre or early post-natal damage affecting ameloblasts. In children with CRF during first month of infancy leads to defects in Vitamin D metabolism, Calcium and Phosphorus metabolism; which may result in enamel defects. Jaffe, *et al* (1990) and Martins, *et al* (2008) in their respective studies have reported delayed eruption of permanent teeth in children with CKD^{9,16}.

In cases of CRF, kidneys cannot convert Vitamin D to 1,25 dihydroxy cholecalciferol which is the active form. CRF also results in retention of Phosphate and all these things leads to decreased Serum Calcium level. The systemic manifestations of this whole process leads to Renal Osteodystrophy. Levels of fibroblast growth factor 23 (FGF-23), a key regulator of Phosphorus and Vitamin D metabolism, also increase and result in inhibition of osteoblast maturation and matrix mineralization. The progression of osseous changes is as follows: osteomalacia (increased unmineralized Osteoid Bone Matrix)



(Flowchart Showing Pathophysiology of Renal Osteodystrophy)¹⁷

followed by Osteitis Fibrosa (bone resorption with lytic lesions and marrow fibrosis) and finally, Osteosclerosis of variable degree (enhanced bone density)¹⁷.

The Parathyroid Gland undergoes a compensatory hyperactivity leading to reduction in excretion of Calcium in urine, increased excretion of Phosphates and increased Calcium released from bone. Renal osteodystrophy leads to bone pain, fatigue, Osteomalacia. In the jaw region, the demineralization of the bone leads to reduction in trabeculation which ultimately leads to a radiographic "ground glass appearance" (Fig 3), a generalized loss of lamina dura, radiolucent Giant Cell lesions, enlargement of skull base¹⁸. It also leads to malocclusion, pulp stones, problem in healing after extraction, tooth mobility. Deciduous dentition may demonstrate brown discoloration due to underlying uremia¹⁹.

Secondary to Renal Osteodystrophy, symmetrical non-painful enlargement of both the maxilla and mandible occurs. This distortion of the facial structure in human beings is secondary to renal secondary Hyperparathyroidism. This typical facial feature is called as uremic leontiasis ossea. This facial feature can be seen in patients of any age²⁰. Patients with CKD also have an increased risk of caries formation which may be due to poor oral hygiene, xerostomia, carbohydrate rich diet (this diet is necessary to reduce the renal work load)¹⁹.

Since gingival enlargement is a common finding in patients with CKD, it leads to more accumulation of plaque and calculus which ultimately leads to periodontal destruction.

Considerations in Dental Treatment :

Proper considerations has to be followed in the



Fig 3 — Ground Glass Appearance Seen In Patients With CKD

dental clinics while dealing with patients of CKD as in all those systemic diseases which has oral manifestations, the main goal should be to treat the primary disease and then the symptomatic treatment. Proper evaluation and risk assessment of the patient has to be done and always a medical opinion is must. Blood Pressure monitoring should also be done as hypertension is commonly present in patients with CKD, also before any invasive procedure screening for Bleeding Disorders should be done in patients with CKD as excessive bleeding is reported in patients with poorly controlled CKD. If the GFR rate is <50ml/min then dose adjustments of Analgesics and antibiotics has to be done. Analgesics like morphine and pethidine are dependent on renal function; while their alternatives like fentanyl, levomethadone are independent of renal function. Adjustments in the drug doses are considered in antimicrobials (eg. ampicillin, cefazoline), antivirals (eg. Acyclovir), chemotherapeutic and cytotoxic drugs. Patients with CRF are immunodeficient because of altered B-cell and T-cell activity. They present with several bacterial and fungal infection secondary to inability to produce sufficient antibodies and hence antibiotic prophylaxis before any dental treatment should be considered. If the patient is on hemodialysis; it's best to avoid giving appointment to the patient on the day of dialysis and it's better to treat the patient the day after the dialysis¹⁷.

CONCLUSION

CKD being one of the prime diseases in World today is a problematic venture for the patient. Through this review and different literature which is available, we have seen that it has numerous oral manifestations. As per oral diagnosticians, it is our prime duty that these manifestations don't get misdiagnosed. A proper diagnosis is the only way for a proper treatment plan.

Conflict of Interest :

There is no conflict of interest among the authors and this review has been written by the contributions of all of them.

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