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REVIEW ARTICLE

IMPACT OF CHRONIC KIDNEY DISEASE ON NUTRITION AND ORAL DISEASES

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ABSTRACT

Background and Aim: A healthy oral cavity is an integrated sign of a healthy systemic health. Oral cavity is also known to be a powerful tool in diagnosing overall systemic health. CKD like any other systemic disease is known to directly or indirectly affect the oral tissues. This condition can also affect the disease process and therapy in some patients. Nutrition plays a very important role in modifying the oral health in CKD patients. Therefore, it is important for the clinicians to recommend a regular dental checkup and also refer the patients to nutritionists for tailored diet plan in CKD and end stage renal disease patients who are under hemodialytic therapy. Here, in this review we will dive deep to explore how nutrition in chronic renal disease patients effects oral mucosa and tissues.
Materials and methods: PubMed, Scopus, Web of Science, Google scholar were searched using pre-specified search strategy. Narrative and systematic reviews were included for the data synthesis.The results of this review were reported following the PRISMA guidelines. A narrative synthesis of the findings was provided.
Results: Extensive literature search was carried out using pre-defined search strategy. A total of 125 titles were screened rigorously by two independent evaluators and after duplicate exclusion (58), removal of irrelevant titles (5) and other exclusions, 32 articles were included in total for review preparation.
Conclusion: Oral diseases have a very strong relation with chronic kidney disease. Most of research has found out to have a positive association between both of them. Having thorough knowledge on all systemic diseases is very important for budding clinicians since these diseases negatively impact the progression of oral diseases and vice versa. Positive association can be established with further research and larger sample size studies.

Keywords: Chronic Kidney Diseases, Oral diseases, Nutrition, Systemic health

INTRODUCTION

A healthy oral cavity is an integrated sign of a healthy systemic health. Oral cavity is also known to be a powerful tool in diagnosing overall systemic health. As oral cavity is a point of exit and entry for external sources, it has an importance in depicting one's own systemic health.[1]

As we all know that few oral conditions and systemic health are interrelated, there is a high chance of changes in the oral cavity such as inflammation, bone loss, lesions on buccal mucosa and cheeks, ulcers, when a person is affected with a systemic condition.[2] Oral diseases are also known to be vital diseases which can affect the mechanical and functional aspect of oral cavity, quality of life and overall health. Though there are several systemic conditions which are related to oral diseases, chronic kidney disease (CKD) is one of the conditions which is directly related to major signs and symptoms in oral cavity.[3]

CKD or chronic renal disease (CRD), according to the National Kidney Foundation (NKF), is kidney impairment that lasts for three months or more and is accompanied by structural or functional abnormalities of the kidney, either with or without a decline in glomerular filtration rate (GFR).[4]

CKD like any other systemic disease is known to directly or indirectly affect the oral tissues. This condition can also affect the disease process and renal therapy in some patients. Few of the oral conditions which are frequently affected in chronic kidney disease patients include white and red patches, periodontitis, mucositis, oral candidiasis, pale mucosa or pigmented mucosa, burning sensations on cheeks and lips as well as changes in salivary composition. [5]

Clinical and radiological alterations in the oral cavity are linked to chronic kidney disease. Loss of lamina dura and radiolucent lesions in the maxilla and mandible are among the radiographic alterations. Clinical results in individuals with chronic kidney disease are similar to those reported for oral lesions in systemic illness.[6] Untreated oral lesions in CKD can lead to a high graft rejection rate (in kidney transplant patients) and an increase in systemic inflammatory load, which exacerbates the underlying systemic illness.[7] Nutrition or diet also play a major role in maintaining overall systemic health and oral health in CKD patients. CKD patients cannot maintain salts and minerals in the body properly and therefore need a proper diet to balance these salts and minerals. Calcium and vitamin D deficiency is most common in CKD patients and may lead to TMJ dysfunctions and renal osteodystrophy's.[8] There is a need for dentists to know in and out about CKD, its complications, diet modifications and how does diet improve overall health and oral health in CKD patients. Therefore, this review focuses on the nutritional therapy in CKD patients and its effect on oral cavity.

MATERIALS AND METHODS

PubMed, Scopus, Web of Science, Google scholar were searched using pre-specified search strategy. Narrative and systematic reviews were included for the data synthesis. The results of this review were reported following the PRISMA guidelines (figure 1). A narrative synthesis of the findings was provided.

RESULTS

Extensive literature search was carried out using pre-defined search strategy. A total of 125 titles were screened rigorously by two independent evaluators and after duplicate exclusion (58), removal of irrelevant titles (5) and other exclusions, 32 articles were included in total for review preparation.

Effect of Nutrition in CKD patients and their associated Oral diseases

Oral diseases are most common in CKD patients with abnormal blood urea levels. Let us discuss nutrition in CKD patients and its effect on oral cavity.

Medical nutrition therapy in CKD patients can help in delaying progression of the disease thereby improving the quality of life as well as oral health. Through elevated insulin resistance, chronic inflammation in CKD patients can cause protein catabolism, which can seriously harm a person's nutritional condition. Hyperkalemia, hyperphosphatemia, anorexia, and muscle and fat wasting are all possible symptoms of chronic kidney disease (CKD).[9,10] Hemodialysis patients are more prone to malnutrition and can be due to inadequate caloric and protein intake which is protein energy wasting and typical CKD related comorbidities such as uremic gastritis, depression, metabolic acidosis and uremic gastritis.[11] This can lead to hypo vitaminosis C, D and B. Vitamin C deficiency can also due to non-consumption of fresh fruits and vegetables. Vitamin C can help in maintaining oral and gingival health by regulating physiological blood vessel activity. It also favors animal and vegetable iron absorption. It interferes with the healing processes of wounds and aids in the development and maintenance of bone and connective tissues.[12]

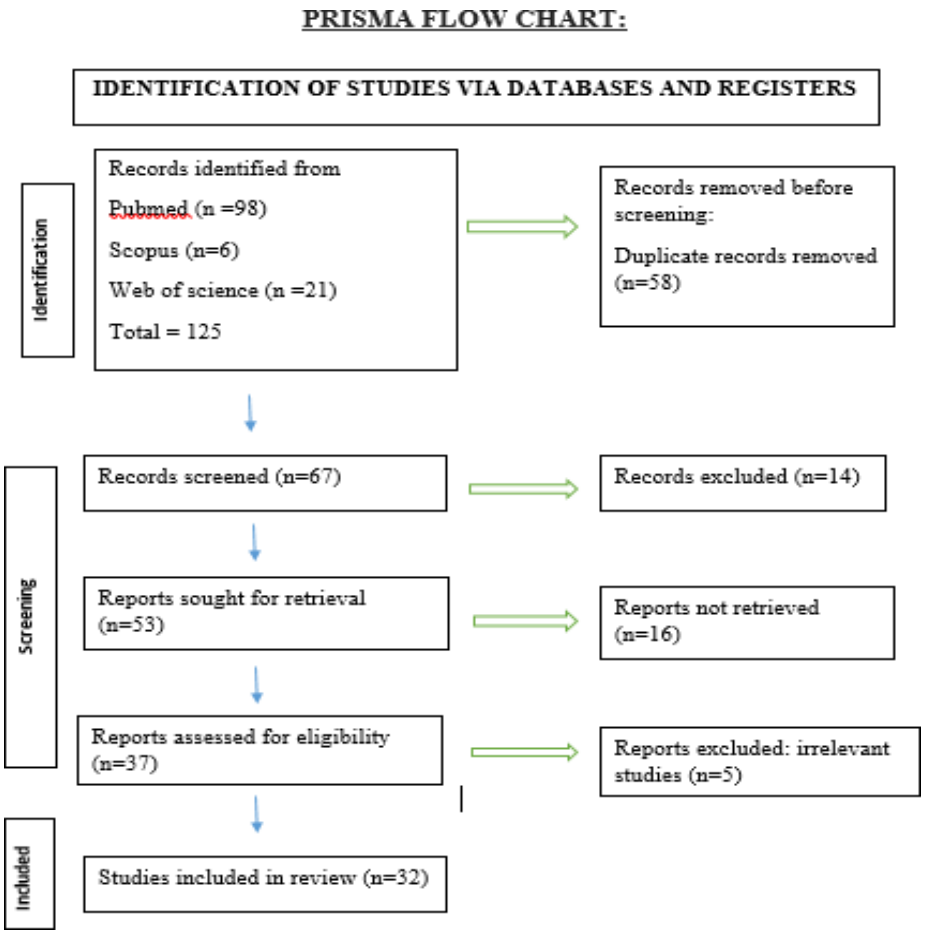

Figure 1. Diagram study flow method used the PRISMA

Etiology for vitamin deficiency in CKD patients under hemodialysis:[13]

VITAMIN C	B GROUP VITAMINS	VITAMIN D
• Dietary restrictions • Removal during Hemodialysis treatment • Gastro intestinal symptoms	• Poly pharmacy • Dietary restrictions • Removal during HD treatment • Uremic gastropathy	• Decrease activity of 1 α hydroxylase • Increased vitamin D inactivation • Decreased sun exposure • Unbalanced diet

Uremic Stomatitis

Uremic stomatitis is one of the most common condition in CKD patients due to vitamin deficiency. Here, the patient may have erythema-pultaceous, ulcerative, hemorrhagic, and hyperkeratotic forms. Untreated uremic patients also have a condition called "uremic frost" where urea crystals appear on epithelial surfaces of oral cavity after evaporation of saliva.[14]

Uremia can also cause oral ulcers/ stomatitis, bad odor, metallic taste leading to high salivary phosphate, high salivary urea, xerostomia and renal osteodystrophy.[15] These in turn cause dental caries, masticatory problems,[16] ill-fitting dentures and temporo-mandibular joint problems. The process of CKD leading to oral diseases in explained in the figure 2 below. Please have a look.

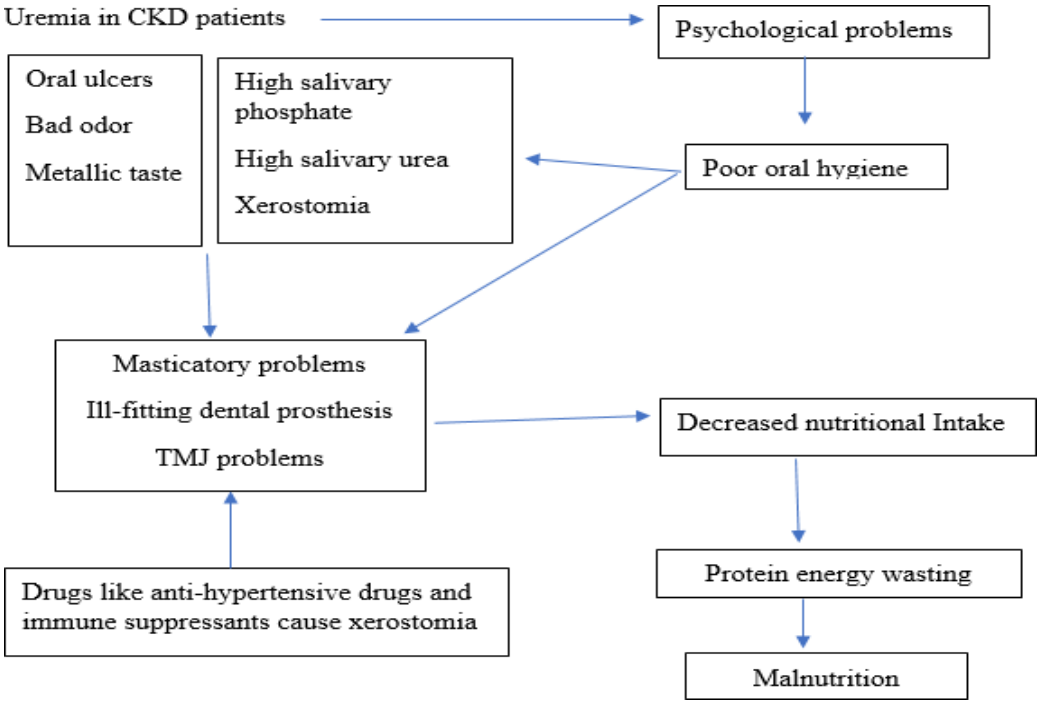

Figure 2. Flow chart **.** CKD and Oral diseases

A study from the Netherlands reported similar values for the majority of dental features, whereas a study from Spain revealed that HD patients had significantly greater plaque and calculus indices and decreased salivary secretions when compared to healthy controls.[17]

End Stage Renal Disease (ESRD)

CKD patients are more prone to ESRD. End stage renal disease patient who is under hemodialysis treatment can have malnutrition, hypovitaminosis C, B, D; low grade inflammation, metabolic acidosis, oxidative stress (figure 3). These can consequently lead to decreased bone turn over, periodontal disease, decreased salivary secretion, decreased healing process and oral microbiota alteration.[18] Proctor et al in 2005 found out that most of the CKD patients had metallic taste due to excessive usage of medication.[19]

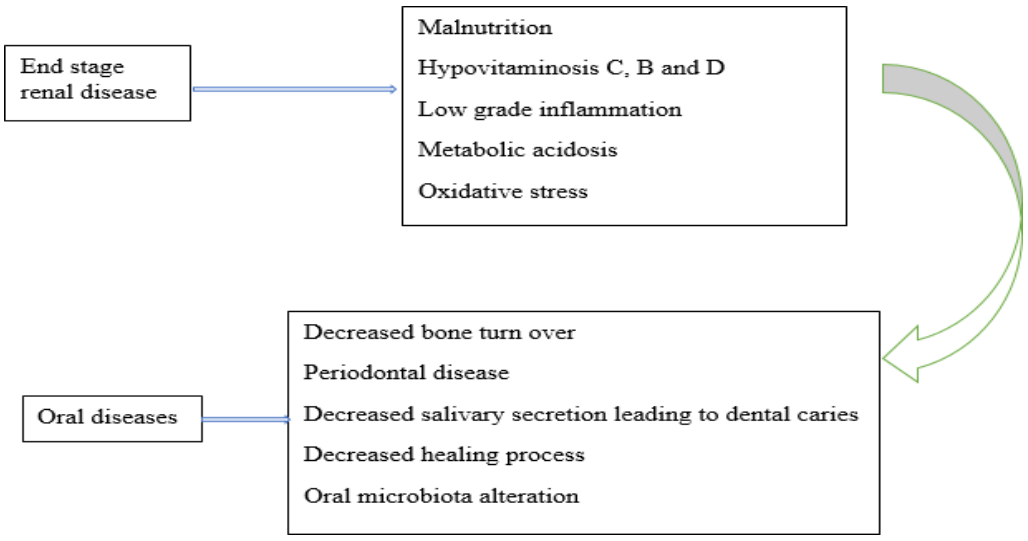

Figure 3. Link between ESRD and Oral diseases in Adults

Let us see nutritional deficiencies in CKD patients and their effects:[20]

Deficient nutrition	Effect on oral structures
Protein malnutrition	Salivary gland dysfunction
Vitamin B1	Angular cheilitis Cracked red lips
Vitamin B2	Glossitis
Vitamin B3	Uremic stomatitis or gingival ulcerations
Vitamin B6	Periodontitis Anemia, sore tongue Burning sensation in the oral cavity
Vitamin B12	Angular cheilitis Bad breath or Halitosis Alveolar bone loss Erythematous and bleeding gingivitis Oral ulceration Periodontal fiber detachment
Vitamin C	Impaired wound healing Incomplete collagen formation Periodontal disease
Vitamin D and calcium	Alveolar bone loss and gingival inflammation Renal osteo dystrophy TMJ dysfunction
Iron	Angular cheilitis Burning mouth syndrome Angular cheilitis Uremic stomatitis and ulcerations

Micronutrient deficiency in CKD and Oral diseases

Deficiencies in iron, folic acid are associated with oral candida infections. Chronic atrophic candidiasis, chronic mucocutaneous candidiasis, angular stomatitis and atrophic glossitis are seen in iron deficiency patients. CKD patients are more prone to iron deficiency.[21] This iron deficiency leads to depletion of enzyme levels, impaired host deficiencies, reduction in epithelial thickness, decreased hemoglobin levels leading to insufficient oxygen to oral mucosa. This insufficient oxygen supply causes epithelial atrophy leading to overgrowth of candida in CKD patients.[22]

Calcium and Vitamin D

CKD patients are more to renal osteo dystrophy and temporomandibular joint dysfunctions due to calcium deficiency. Numerous body processes depend on calcium, an electrolyte and multivalent cation. It is vital for bone development, blood cell production, and the proper operation of the digestive, circulatory, and muscular systems.[23] Calcium exchange in the bones, reabsorption in the kidney, and absorption in the gut all tightly control calcium equilibrium.

As chronic kidney disease (CKD) worsens, the serum calcium level falls because the kidneys play a crucial role in maintaining calcium homeostasis. Reduced calcium levels can result in secondary hyperparathyroidism, which causes metabolic bone disorders, whereas excess calcium can produce extraosseous calcification, which increases mortality and causes cardiovascular disease.[24]

A number of parameters, such as mineral controlling hormones, renal function, bone turnover, the use of vitamin D analogs, and calcium consumption via supplements, must be considered in order to maintain a balanced blood calcium level in patients with chronic kidney disease (CKD). The dialysate's calcium content and the dialysis mode are two further variables that need to be considered for patients who need maintenance dialysis. Because each patient's calcium balance is affected by different circumstances, it might be difficult to provide appropriate dietary calcium.[23]

The deficiency of calcium can be managed by

incorporating a daily intake of dietary calcium of 800 to 1,000 mg/day. Similarly, vitamin D can be taken in the form of supplements and can also be achieved by increasing the degree of sunlight exposure. There are no safe guidelines recommended for vitamin D supplements in CKD patients. Dental practitioners should refer the patient to a nephrologist for consent before commencement of any dental procedure.[25]

Phosphorous, CKD and Oral diseases

Phosphorus is an essential nutrient which helps in maintaining homeostasis in body. It also helps in acid-base balance, bone growth, mineralization and regulation of energy. Resistance to parathyroid hormone and fibroblast growth factor may result in hyperphosphatemia, or high blood phosphate levels, as chronic kidney disease (CKD) worsens. Here, phosphorus excretion is halted causing increase in phosphate levels in blood.[26]

This hyperphosphatemia can lead to inflammation of tissues eventually leading to gingivitis and periodontitis. Dietary phosphorous has an inverse relationship with salivary IL-4 concentration and a direct relationship with salivary IL-1β concentration. Dentists can recommend low phosphate diet by consulting the concerned nephrologist to decrease the level of inflammation in gingival tissues. They can also educate patient to consume low phosphate diet.[27]

CKD and Periodontal disease

It has been discovered that CKD patients had higher prevalence's of oral keystone bacteria linked to periodontitis, such as Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola, Aggregatibacter actinomycetemcomitans, and Actinomyces dentalis, than the general population.[28] Another mechanism is that changes in the microenvironment brought on by CKD also have a permissive effect, impairing both innate and adaptive immunity. In CKD, the diminished antigen presentation skills of dendritic cells and macrophages lead to decreased cytokine production, impaired neutrophil phagocytic capabilities, and decreased monocyte stimulation effectiveness (figure 4).
This can lead to periodontal disease in CKD patients.[29]

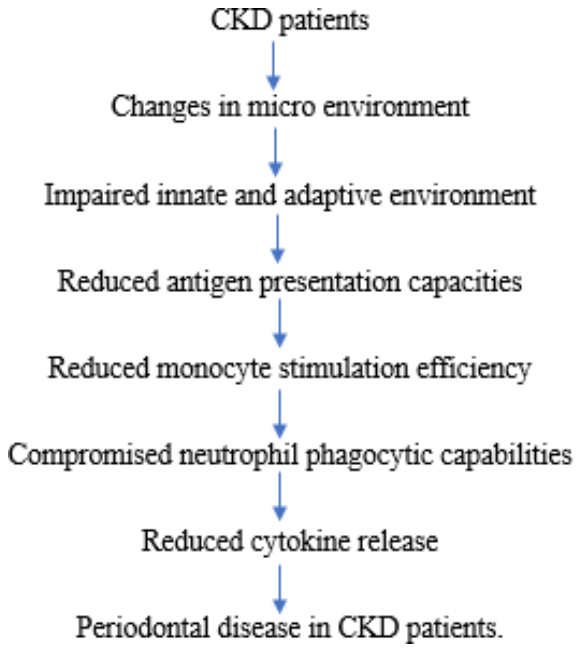

Figure 4. Flow chart CKD and Periodontal Disease

Antigen-presenting cell malfunction and decreased toll like receptors expression or activity can also lead to decreased immune function causing periodontal infections. Basic scaling and root planning can help in reducing micro-organisms and inflammation to some extent in CKD patients.[30]

Oral and Cutaneous hyper pigmentation

The inability of the kidney to eliminate excess beta melanocyte stimulating hormone (b-MSH), which builds up and stimulates melanocytes in the basal layer of the oral epithelium, causes oral and cutaneous hyperpigmentation in renal patients. Orthodox drugs prescribed for CKD patients such as antimalarials (quinacrine, chloroquine, hydroxychloroquine) can cause oral hyperpigmentation.[22]

Psychological issues in CKD patients

Uremia is most common in CKD patients which can lead to psychological problems. These psychological issues can consequently can decreased nutrition intake leading to abnormal oral conditions. Similarly, due to the usage of anti-hypertensive drugs and immune suppressants, patients with CKD have xerostomia and taste disturbances. Psychological problems can also lead to poor oral hygiene leading to increased dental caries.[18,21,22]

Poor Oral hygiene

Poor oral hygiene is the major cause of periodontal diseases which can increase gingival inflammation, bone loss and eventually tooth loss. This tooth loss in turn effects the masticatory function and digestion in CKD patients leading to poor nutritional intake and protein energy wasting.[29]

Recommendations for Clinicians, Practitioners and Hygienists

Since we know oral illness is gateway for many systemic illnesses such as CKD, dentists should recommend kidney profile has a regular investigation to rule out any renal abnormalities. These investigations include serum creatinine, glomerular filtration rate and other blood investigations. Dentists can conduct a regular checkup for risk of oral diseases and can educate the patients for blood investigations.

Thorough history of nutrition intake in CKD patients is also essential to rule out any deficiencies or protein energy wasting. Nutritional deficiencies are the major etiologies for oral diseases in CKD patients.[31,32] Patients should be referred to nutritionists for tailored diet plan so that oral diseases can be controlled to a certain extent.

CONCLUSION

A healthy oral cavity is an integrated sign of a healthy systemic health. Oral cavity is also known to be a powerful tool in diagnosing overall systemic health. Systemic diseases are always in close relationship with oral diseases. There is an overwhelming

CKD is one of them where nutrition in these patients effect the oral tissues and epithelium. Having thorough knowledge on CKD and ESRD patients as well as their diet can help the clinicians to diagnose the oral condition precisely and manage accordingly. This knowledge can also help in diagnostic and therapeutic procedures even in hemodialytic and end stage renal patients.

Since CKD is a common global condition, its association with oral diseases should be studied in detail to aid for betterment in management. Further studies to identify the association of CKD and oral conditions should be done to provide awareness in budding practitioners and patients.

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The authors declare no conflict of interest

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