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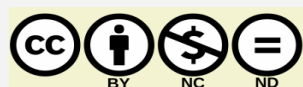
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The Interplay Between Chronic Kidney Disease and Periodontal Health: A Comprehensive

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Abstract:

Chronic kidney disease (CKD) and periodontal disease are both chronic conditions with systemic implications, yet their potential interplay remains underexplored. This comprehensive review aims to elucidate the association between CKD and periodontal health status. Several mechanisms underlie the association between CKD and periodontal health. Shared risk factors such as diabetes, hypertension, and inflammation contribute to the development and progression of both conditions. Additionally, CKD-related immune dysfunction and impaired wound healing may exacerbate periodontal inflammation and tissue destruction, while periodontal pathogens and their byproducts may exacerbate systemic inflammation and renal injury in CKD patients.

Understanding the complex interplay between CKD and periodontal health status is crucial for comprehensive patient management. Multidisciplinary approaches integrating nephrology and periodontology are warranted to optimize the oral and systemic health outcomes of CKD patients. Future research should focus on elucidating the mechanistic pathways linking CKD and periodontal disease and evaluating the efficacy of periodontal interventions in improving renal outcomes in CKD populations.

Keywords: Chronic kidney disease (CKD), periodontitis (PD), periodontal health

Introduction:

In 2002, clinical practice guidelines developed by the US National Kidney Foundation Kidney Disease Outcomes Quality Initiative defined chronic kidney disease, as kidney damage with kidney function at <60 mL/min/1.73 m for at least three months or a GFR indicating the same. This framework provided an outline that was mainly built around a new framework of categorization—it was based on the glomerular filtration rate (K/DOQI, 2002).

The following evaluations also emphasized the importance of albuminuria in total clinical outcomes for the population (Matsushita et al.,

2010). Leading to the Kidney Disease: KDIGO 2012 Checklist of updates in the Chronic Kidney Disease: Evaluation and Management by the KDIGO 2012 Improving Global Outcomes (KDIGO) Work Group that included albuminuria (KDIGO 2013)

New scheme thus includes also the underlying causes of chronic kidney disease since they are crucial determinants of prognosis and therapeutic management. Early CKD diagnosis is essential in preventing CKD disease progression and reducing the occurrence of cardiovascular events and death. Consequently, making the identification a public health priority and investing in proper techniques and personnel to achieve the goal is becoming increasingly important. By the given course of time, it has been expected that the population group that suffers from chronic kidney disease will increase dramatically, especially in the countries where the economic development is relatively low. But there is a very regrettable factor, the link between low economic development and poor access to renal replacement therapy. (Jha V. et al., 2013)

The prevalence of CKD is also inclined to low- and middle-economic countries more than high-economic ones (Mills et al., 2015). Diabetes and/or hypertension remains the main causal factors of CKD in the global community; however, other factors include glomerulonephritis, infections, and environmental factors such as air pollution, herbal remedies, and pesticides in regions such as Asia, sub-Saharan Africa, many developing nations, among others (Chen et al., 2019). Some current guidelines pointed to the more rational utilization of risk-based approach in managing CKD (KDIGO 2013, Inker et al., 2014).

Clinical Presentation:

CKD is often diagnosed when performing a routine check-up test including serum chemistry profile and urinalysis or when the disease is diagnosed accidentally. Patients may complain or have complaints that once and again they present with gross hematuria, “foamy urine”, nocturia, flank pain or oliguria, etc. Despite the fact that CKD is asymptomatic initially, the common problems in the late stage may include fatigue, anorexia, nausea, vomiting, changed sense of taste to metallic, weight loss, skin itching, confusion, shortness of breath, and peripheral edema. More specifically, when evaluating a new patient with known or suspected CKD s/p, the clinicians should inquire about thematically different symptoms that may suggest a non-renal systemic cause/etiology (e. g. hemoptysis, rash, lymphadenopathy, hearing loss, and neuropathy) or urinary obstruction (e. g. urinary hesitancy, urgency, frequency, or sensory urge or inability to complete the micturition (Skorecki et al., 2016).

Additionally, patients must be assessed the risk factors that are linked with patients and those are the history of exposure to possible nephrotoxic agents including NSAIDs, phosphate-sodium preparations for colon cleanse, and certain natural products containing such substances as alkaloids, steroids, and metabolism-modifying substances, such as aristolochic acid, some classes of antibiotics, for instance gentamicin, and some chemotherapy drugs. Further, calculus formation in the kidney or any past history of urinary tract infections, use of antihypertensive drugs, autoimmune diseases, or chronic infections, and a family history of kidney-related diseases this condition and other attention genetic predispositions like, the sickle cell trait ought to be contemplated (Skorecki et al., 2016, Naik et al., 2014)

Diabetic neuropathy could be initiated by diabetic condition or rarely from other health problems such disorders like vasculitis, amyloidosis, gout, or lupus, or other types of glomerulonephritis. Skin changes may be rash and this is usually a sign of systemic lupus erythematosus, acute interstitial nephritis. Some of the symptoms that one is likely to experience in the later stages of CKD are; pallor, skin lesions, muscular atrophy, asterixis among others. Myoclonic jerks, altered mental status, and pericardial rub can also be commonly found in patients with Reye syndrome (Skorecki et al., 2016).

Definition and Staging of CKD:

This is the abnormality in the organs' structure and function that has lasted for over 3 months and can be referred to as chronic kidney disease (KDIGO 2013, Levey et al., 2015). This encompasses one or more of the following criteria: (1) GFR is below 60 mL/min/1.73m² (2) albuminuria, including: (history of proteinuria [defined as urine albumin ≥ 30 mg per 24 hours or urine albumin-to-creatinine ratio ACR ≥ 30 mg/g, dysmorphic red blood cells; white blood cells: 5 or more white blood cells per high-power field in any specimen or any report of pyuria and, casts: coarsely granular, or finding compatible with kidney injury] (3) 'abnormal' histology; urine sediment, or imaging suggestive of kidney damage: (4) renal tubulopathy; or (5) having received a kidney transplant (Jha V. et al., 2013).

However, these values are valid only in cases when the duration of kidney disease is under question, and repeated measurements are necessary to distinguish between CKD and AKI.

It may also include acute kidney injury AKI (determined as change in kidney function within 2-7 days) and acute kidney disease (which involves kidney injury or reduced kidney that has lasted for at least 3 months) (Levey et al., 2015). In making the decision for further evaluation of the cause of CKD, consideration should be given to the clinical history, physical inspection, abdominal and respiratory sounds, results of fundoscopy, electrocardiography, dermatologic examination, pulmonary auscultation, stethoscopes findings, and urinary lab reports (KDIGO 2013, Skorecki et al., 2016) (Figure 1) after identifying the chronic kidney disease (CKD) the next step involves staging CKD; this largely depends on certain as [3]. GFR staging consist of G1 (eGFR greater than 90 mL/min/1.73m²), G2 (eGFR from 60-89 mL/min/1.73 m²), G3a (moderate CKD with a GFR of 45-59 mL/min/1.73 m²), G3b (30-44 mL/min/1.73 m²), G4 (15-29 mL/min/1.73 m²) and G5 (<15 mL/min/1.73 m²) [3].

Currently, clinical labs commonly provide eGFR values calculated using various filtration markers, with creatinine, a 113 dalton byproduct of creatine metabolism being the most frequently used marker (Levey et al., 2015), subject to laboratory tests of uniform standards since 2003 (Myers et al., 2006). The most recommended method for measuring albuminuria is the urine Albumin-to-Creatinine Ratio (ACR). Albuminuria staging is categorized as A1 (urine ACR <30 mg/g), A2 (urine ACR 30-300 mg/g), and A3 (urine ACR >300mg/g). Recommendations support the preference of urine ACR over urine protein to-creatinine ratio because of superior results, consistency and accuracy, especially when it comes to lower levels of albuminuria. For maximum accuracy, it is preferable to collect measurements from either a first morning sample or a 24-hour collection, taking into account the significant variations in urine albumin excretion at different times of the day (KDIGO 2013, Lieske et al., 2013).

Screening for CKD:

Because symptoms are rarely present initially in patients with CKD, testing is essential for early identification (Inker et al., 2014). Recently, National Kidney Foundation has come up with what is referred to as a kidney profile test, which involves assessment of serum creatinine level together with the estimation of the GFR and urine ACR (NKF/ASCP. 2019). Clinical practice guidelines, proposed a risk-based screening policy whereby screening should be offered to patients aged 60 years or older or those with hypertension or diabetes (Inker et al., 2014). The creatinine test diagnoses impaired kidney functions and measures the amount of creatinine phosphate in the blood (NKF/ASCP. 2019, Hassoon et al., 2013). However, in clinical risk factors encompassed autoimmune diseases, obesity, renal stones, recurrent UTI, reduce renal mass, NSAIDs or lithium use, previous AKI, and other comorbid diseases, the screening should be hold (Inker et al., 2014, Naik et al. 2014, Chang et al. 2019). (Table 1)

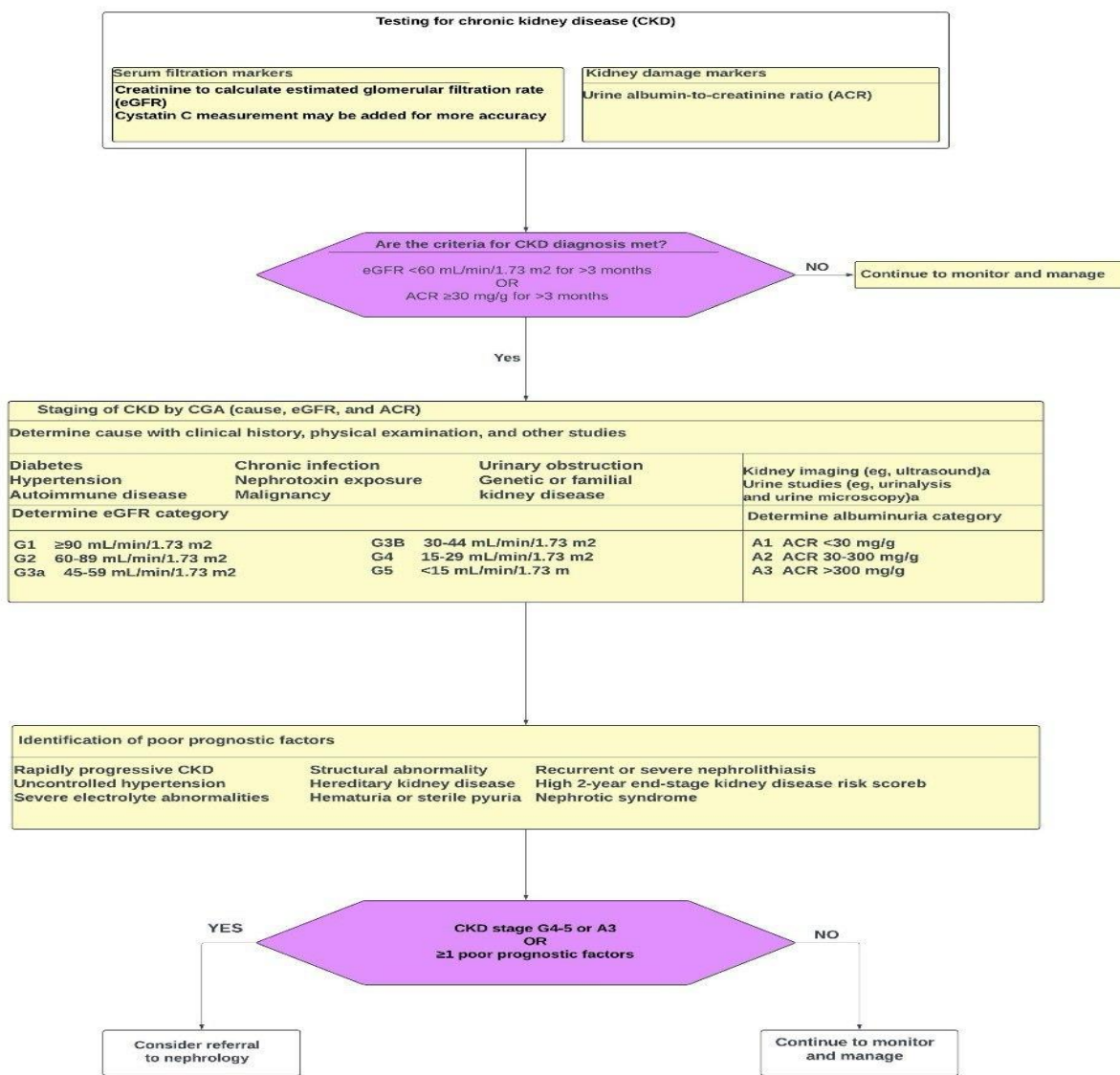


Figure 1 Diagnosis, Staging, and Referral of Patients with Chronic Kidney Disease (Chen et al., 2019)

Table 1 presents the clinical, sociodemographic, and genetic risk factors associated with chronic kidney disease (Myers et al., 2006, Yesubabu et al., 2020).

Clinical	Sociodemographic	Genetic
Diabetes	Age >60 years	<i>APOL1</i> risk alleles
Hypertension	Nonwhite race	Sickle cell trait and disease
Autoimmune diseases	Low income	Polycystic kidney disease
Systemic infections (eg, HIV, hepatitis B virus, hepatitis C virus)	Low education	Alport syndrome
Nephrotoxic medications (eg, nonsteroidal anti-inflammatory drugs, herbal remedies, lithium)		Congenital anomalies of the kidney and urinary tract
Recurrent urinary tract infections		
Kidney stones		
Urinary tract obstruction		
Malignancy		
Obesity		
Reduced kidney mass (e.g., nephrectomy, low birth weight)		
History of acute kidney injury		
Smoking		
Intravenous drug use (eg, heroin, cocaine)		
Family history of kidney disease		

Risk Factors at Different Stages Leading to Chronic Kidney Disease:

The risk factors for CKD can be categorized into four main stages:

1. Susceptibility factors: They include inherited predisposing factors such as CKD in the family; neonatal factors such as low birth weight, kidney weight, and age; race, color and ethnic background (blacks, whites and coloreds); and economic factors; low income, illiteracy.

2. Initiation factors: At this stage, the initiation of factors of CKD includes; hypertension, diabetes, systemic infection, toxic drugs, autoimmune disease, urinary tract infection, Urinary stones, Lower urinary tract obstruction.
3. Progression factors: After CKD has started; some elements can tilt the degree of deterioration either in a positive or negative manner. These are smoking, proteinuria of $>1\text{g}/24\text{hours}$, hypertension and poor glycemic control in the diabetic population.
4. End-stage factors: Some of these factors can lead to the progression of CKD in its-terminal stage. This include: delayed presentation to medical care services, insufficient dialysis dose, temporary dialysis vascular access, anemia, and low serum albumin level. (Yesubabu et al., 2020).

Signs and Complications of Chronic Kidney Disease (CKD):

Webster et al., have defined several symptoms of CKD which include the development of anemia, altered cerebral function, high blood pressure, gastrointestinal problems, breathlessness, changes in the color, amount and composition of urine, itching, muscle cramps as well as the damage to the arteriovenous walls of the glomerulus and tubule. Also, there will be sodium retention that may lead to such a symptom as peripheral edema. The following comorbidity areas are considered the most critical for CKD patients: anemia, bone-related disorders, CVD, and some types of cancer. (Webster et al., 2017)

Treatment and Prophylaxis:

For persons with an estimated glomerular filtration rate (eGFR) higher than $60\text{ mL}/\text{min}/1.73\text{ m}^2$, where cardiovascular disease (CVD) is usually caused by atherosclerosis, statin medication seems to have a consistent effect on vascular events, regardless of kidney function. (Yu et al., 2018) When the estimated glomerular filtration rate (eGFR) falls below about $30\text{ mL}/\text{min}/1.73\text{ m}^2$, a specific cardiovascular condition arises. Significantly, atherosclerotic statin medication has been found to be more effective in individuals undergoing dialysis than in those who are not on dialysis (Baigent et al., 2011). In persons with renal failure and low vitamin K levels, certain cephalosporins can cause hypoprothrombinemia; this is especially true in cases of malnutrition or parenteral feeding, if appropriate dosage changes are not done. These cephalosporins interfere with vitamin K metabolism (Andrassy et al., 2013). Quality care should include four basic areas: (1) monitoring the progression the stage of chronic kidney disease (CKD), (2) reducing the risk of cardiovascular disease, (3) monitoring metabolic bone disease and anemia, and (4) assuring the safety of medications. It is recommended to assess the clinical performance of these markers at least one year after the first diagnosis of CKD (Allen et al., 2011).

Four interventions have been demonstrated to slow the progression of CKD: maintaining blood pressure below $140/90\text{ mm Hg}$, effectively managing diabetes, utilizing angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers to address albuminuria and hypertension, and rectifying metabolic acidosis. In order to reduce medication-related risks, it is important to customize prescriptions based on the patient's estimated glomerular filtration rate (eGFR) and to refrain from using nephrotoxic substances, such as NSAIDs. Significant acute kidney injury (AKI) and extensive albuminuria are indicative of a low eGFR ($<30\text{ mL}/\text{min}/1.73\text{ m}^2$). The primary goal is to slow the progression of CKD, reduce complications, and improve the quality of life (Vassalotti et al., 2016). Murshid et al., conducted a study in which they implemented innovative technical tools,

including decision trees, logistic regression, naive Bayes, artificial neural networks, and data mining techniques, to create an automated diagnostic system. This system streamlines the intricate healthcare process by analyzing data from the database and delivering early predictive results with a higher degree of accuracy than conventional diagnostic methods. It is anticipated that these technical instruments will be instrumental in the prevention of CKD. (Murshid et al., 2019)

Periodontal Health, Gingivitis, and Gingival Conditions:

A new classification of Periodontal and Peri-implant Diseases and Conditions, was co-sponsored by the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) in early 2015. By delineating between the presence of gingival inflammation at one or more sites and the definition of a gingivitis case, the workshop sought to resolve unresolved issues with the previous classification system. The primary parameter for establishing gingivitis thresholds should be bleeding on probing, as consensus was reached (Trombelli et al., 2018). Based on the depth of the residual sulcus/pocket and bleeding on probing, specific definitions were established for instances of gingival health or inflammation following periodontitis treatment. This distinction emphasized the importance of comprehensive maintenance and surveillance for patients who have successfully undergone periodontitis treatment. The fact that a patient with gingivitis can regain their health was recognized; however, a periodontitis patient persists in this condition for life, even after successful therapy, necessitating lifelong supportive care to prevent disease recurrence (Chapple et al., 2018). Furthermore, the workshop reorganized the extensive range of non-plaque-induced gingival diseases and conditions according to their primary etiology (Holmstrup et al., 2018).

Periodontitis (PD):

A chronic inflammatory disease known as periodontitis (PD) causes periodontal attachment around teeth to gradually deteriorate over time. It is characterized by considerable local inflammation that originates from sub gingival infection (Sainz & Quirynen 2005). Periodontitis is a persistent inflammatory condition that causes periodontal tissues to deteriorate due to host cell secretion of inflammatory cytokines and reactive oxygen species (ROS) overproduction in vulnerable individuals (Abdulqader & Mahmood 2024). Roughly 11% of the population has been affected by severe symptoms of PD in the last 20 years, according to a new meta-regression study on the global prevalence of PD (Kassebaum et al., 2014). Progressive PD, if left untreated, causes significant systemic inflammation tooth loss (Linden et al., 2013, Cairo et al., 2018), and a worse quality of life overall. Multiple investigations have shown a link between PD and systemic diseases, including type 1 and type 2 diabetes mellitus (Dicembrini et al., 2021), cardiovascular disease (Hamad & Mahmood 2022), and chronic kidney disease (CKD) (Deschamps- Lenhardt et al., 2019, Kapellas et al., 2019). Intriguingly found that age, smoking, and poorly controlled diabetes are common risk factors for both PD and CKD (Fisher et al., 2008). Based on biological theories, numerous studies have proposed a bidirectional link between the two illnesses.

The possibility for periodontal bacteria to move from lesions into the bloodstream and create bacteremia is one concern with PD. This could have an impact on the kidneys. Within this framework, research has shown that decreased kidney function is associated with higher levels of IgG antibodies directed against Gram-negative bacteria, *Aggregatibacter actinomycetemcomitans*, *Treponema denticola*, and *Porphyromonas gingivalis* (Kshirsagar et al., 2007). By elevating levels of

pro-inflammatory cytokines such IL-6, IL-8, TNF- α , and IL-1 β , PD can exacerbate the systemic inflammatory response, improved vascular permeability, increased production of adhesion molecules, and overexpression of TGF- β can result from this increase in inflammation in addition to increase reactive oxygen species (ROS) which strongly correlated to periodontal tissue destruction (Mousa et al., 2024, Maher & H.F., 2023). In the long run, these conditions can lead to impaired kidney function, proteinuria; via glomerular permeability, renal thrombosis and fibrosis (Kitamura et al., 2019).

The flip side is that uremic-induced variables might cause dysregulation of innate and adaptive immunity in CKD patients (Kato et al., 2008). Patients may be more vulnerable to infections as a result of this dysregulation, which may hinder the maturation of T h cells (Ando et al., 2005). Opportunistic infections, such as PD, may be more common in patients with uremic-induced immunological dysregulation, according to some researchers. Nevertheless, the exact link between PD and CKD is still not well understood (Borgnakke, 2013). Researchers have found that periodontopathogenic bacteria are involved in the development of periodontal disease. These bacteria produce substances that might trigger an inflammatory immune response, including lipopolysaccharide and endotoxin. The secretion of inflammatory mediators is a hallmark of this reaction and one of the main causes of periodontal tissue degradation. Patients receiving hemodialysis may be at increased risk for death due to periodontal disease (Sedý et al., 2010).

Revised Classification of Periodontal Disease:

In accordance with the most recent understanding of pathophysiology, three distinct forms of periodontitis can be identified: necrotizing periodontitis, periodontitis as a manifestation of systemic disease, and periodontitis (Needleman et al., 2018).

The workshop refined the classification and established a framework for periodontitis classification that is further characterized by a multidimensional staging and grading system. The severity of the disease at the time of its presentation and the complication of its management are the primary factors in staging. Conversely, grading provides additional information regarding the biological aspects of the disease, including an evaluation of its progression rate, the likelihood of further progression, the potential impact of the disease or its management on the patient's overall health (Tonetti et al., 2018).

The staging process is a multifaceted process that assesses a variety of factors, including clinical attachment loss, extent of bone loss, probing depth, presence and severity of angular bony defects and furcation involvement, tooth mobility, and tooth loss attributable to periodontitis. Consequently, grading is essential for comprehensive case management, as it allows clinicians to take into account the unique characteristics of each patient in the diagnostic process (Tonetti et al., 2018).

Oral Bacteria and the Pathogenic Effects of Distal Bacteria:

Within the year 1891, W. Mill operator was the primary individual to offer the thought that oral bacteria might make a distal pathogen influence. He contended that oral microorganisms might move to distant areas of the body, which could be a concept that's nowadays known as the focal infection theory (Miller, 1891). On the other hand, this concept was brought back into the highlight within the 1990s, when the American Foundation of Periodontology and the World Workshop on Periodontitis put up the suggestion that oral infection are as often as possible connected to both local and systemic

disorders (Scannapieco, 1998). As a result of this, the focal infection hypothesis has created into the thought of periodontal medication, the concept places an accentuation on the linkage between periodontitis and systemic diseases, in this manner building up an association between oral status and common systemic health (Pizzo et al., 2010).

Transformation Oral Pathogens:

A healthy mouth has a mucous layer and naturally occurring antimicrobial molecules like defensins that protect against external pathogens. These molecules protect the host from harm caused by both commensalism and opportunistic microbes. But this block can be broken in a number of ways. For example, trauma, like the tiny scratches that come from brushing your teeth (Addy, Hunter 2003), or periodontal pathogens getting into the gingival margin (Bosshardt, 2017). Oral bacteria can cause other diseases in three ways: (1) Infection from metastatic short-term bacteremia; (2) Damage to the immune system that spreads through metastasis; and (3) Toxic injury that spreads through metastasis (Pizzo et al., 2010).

When microorganisms move through the body, they can causes damage called metastatic transient bacteremia. Metastatic immunological injury, on the other hand, is damage that is caused by an immune reaction, like the inflammatory process seen in periodontitis. Lastly, metastatic toxic injury happens when toxic compounds are released. These compounds can be made by microorganisms or by parts of the cell's structure, such as endotoxins or Lipopolysaccharide (LPS) which can stimulate an immune response through host toll like receptors (TLRs) (Gendron et al., 2000, Aderem& Ulevitch, 2000).

How periodontitis has systemic effect:

Recent research has shown that periodontitis is linked to diseases outside of the mouth, such as atherosclerosis, diabetes, stroke, and coronary heart disease. However, the exact ways these diseases start are still being studied (Gualtero et al., 2018, Beck et al., 2018). Many of the systemic effects of periodontitis are caused by an imbalance of the oral microbiota and the spreading of bacteria or their waste products to other parts of the body. In periodontitis, inflammatory cytokines like interleukin-6 and tumor necrosis factor- α can be produce locally. These can raise amounts of C-reactive protein in the body, and induce inflammation throughout the body (Mahmood & Abbas 2013). Damage to the oral cavity and periodontium, along with systemic inflammation, can make it harder for CKD patients to eat right and take their medications as prescribed. This can lower their quality of life and make them more likely to become malnourished and get other diseases (Anad & Alam 2013).

Systemic Consequences of Chronic Kidney Disease:

Uremic toxemia is when the levels of urea and uremic toxins stay high for a long time. This can affect the immune system and cause immune dysregulation and chronic inflammation (Cohen & Horl 2012). Toxins like these can affect the innate immune response by affecting function of polymorphonuclear leukocytes (PLs) like basophils, monocytes, and neutrophils (Vaziri et al., 2012). This kind of imbalance may make CKD patients more likely to get oral infections, which can lead to periodontitis. Also, medicines used to suppress the immune system after a transplant (like calcineurin inhibitors) and calcium channel blockers (used to control cytosolic calcium levels and hypertension in people with renal disease) have been linked to gingival enlargement in CKD patients. (Brown & Arany, 2015).

It's interesting that not taking care of oral hygiene properly, which is common in people with CKD, can make this gingival swelling worse. Some reports think that this kind of overgrowth leads to inflammation of the gingiva, which in turn raises the risk of getting periodontitis. In addition it has been found that both chronic kidney disease and periodontitis are associated with an increase in oxidative stress and inflammatory mediators and accelerated dental calculus formation (Real et al., 2009, Mohammed & Mahmood, 2019, Al-jubouri, & Hadi, 2011).

The suggested connection between PD and CKD:

Both periodontitis (PD) and chronic kidney disease (CKD) are widespread illnesses in the general population, and they share risk factors like inflammation and malnutrition, which are more apparent in developing nations (Van Dyke & Dave 2005, Luyckx et al., 2017). It is not surprising that there is some comorbidity between the two diseases given their high individual prevalence rates. PD may worsen the severity of CKD, nevertheless, as recent long-term survival evaluations of CKD patients have shown a marked increase in mortality rates (32%-41%) when periodontitis coexists. (Sharma et al., 2016). Cohort study meta-analyses have corroborated this, showing a higher death risk in patients with chronic kidney illness who also had periodontal disease (Zhang et al., 2017). The relationship between CKD and PD is reciprocal; through gingival overgrowth and pH changes, CKD affects the oral micro environment, which makes some periodontal bacteria more at oral environment (Listgarten, 1986). On the other hand, PD increases systemic inflammation, which is linked to CKD, as shown by higher C-reactive protein levels (Paraskevas et al., 2008). According to new research, systemic inflammation brought on by PD may contribute to the development of CKD or operate as a non-traditional risk factor (Wahid et al., 2013). Furthermore, there appears to be a bidirectional interaction between CKD and PD, wherein PD treatment may have a beneficial effect on glomerular filtration rate and gingival tissue acts as a source of chronic inflammation (Fisher et al., 2011). Even while the connection between the two illnesses is becoming stronger, not much is known about the underlying mechanisms. The majority of the evidence available now comes from correlations and observational cohort studies; causal processes are not directly investigated. Rather than a single causative element, it is more likely that the association includes a combination of many pathways.

Conclusion:

It could be concluded that although the connection between chronic kidney disease (CKD) and periodontitis (PD) is proven to be more likely, it is still unclear how the relation between these two diseases function. A greater clarification of the flow of causality and the bidirectional influence of these two variables is needed. Thus, even in large sized-cohort studies that look at CKD and PD, it remains difficult to exclude the different systemic diseases as well as other variables so as to arrive at a conclusive finding. However, several early research trials about treating CKD patients by using PDs has depicted an encouraging sign in further research for CKD's future management. More data from other both experimental and population-based studies involving interaction between CKD and PD, and type of therapies used are still awaited. In summary, we need to use the enhanced view of these diseases and how they are linked to address the potential of improving patients' health and developing more sophisticated treatment strategies.

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