

## REVIEW ARTICLE

# Chronic kidney disease and periodontitis

Grethell Bertrán Herrero<sup>1\*</sup> , Amparo Pérez Borrego<sup>2</sup> 

<sup>1</sup>“Dr. Felipe Soto” Stomatology Clinic, Havana, Cuba

<sup>2</sup>“Dr. Enrique Cabrera” Faculty of Medical Sciences, Havana, Cuba

\*Grethell Bertrán Herrero. [grethell@infomed.sld.cu](mailto:grethell@infomed.sld.cu)

Received: 25/05/2022 - Approved: 11/08/2022

## ABSTRACT

**Introduction:** chronic kidney disease is defined by the presence of kidney damage and has a negative impact on the health and quality of life of patients. Periodontitis is the chronic inflammation of the supporting tissues of the tooth.

**Objective:** to describe the association that has been established between these two diseases.

**Methods:** a documentary type study was carried out, with an updated review of scientific articles from databases such as Pubmed, Scielo and Google Scholar in the period from October 2021 to February 2022. Twenty-five scientific texts written in Spanish and English published between 2017 and 2021 were selected.

**Results:** most of the literature consulted describes that there is a direct relationship between both diseases, the constant presence of uremia, as well as poor oral hygiene in these patients, is related to immune dysfunction that decreases the host response to bacteria.

**Conclusions:** in periodontal disease there is a permanent inflammatory state that aggravates the prognosis of chronic renal failure, so it is necessary to maintain an adequate oral health to avoid systemic complications in vulnerable patients such as those with chronic renal disease.

**Key words:** renal insufficiency, chronic; periodontitis

## RESUMEN

**Introducción:** la enfermedad renal crónica se define por la presencia de daño renal y tiene un impacto negativo sobre la salud y la calidad de vida de los pacientes. La periodontitis es la inflamación crónica de los tejidos de sostén del diente.

**Objetivo:** describir la asociación que se ha establecido entre estas dos enfermedades.

**Métodos:** se realizó un estudio de tipo documental, con una revisión actualizada, de artículos científicos de bases de datos como Pubmed, Scielo y Google académico en el período de octubre de 2021 a febrero de 2022. Fueron seleccionados 25 textos científicos escritos en español y en inglés publicados entre los años 2017 y 2021.

**Resultados:** la mayoría de la bibliografía consultada describe que existe una relación directa entre ambas enfermedades, la constante presencia de uremia, así como una higiene bucal deficiente en estos pacientes, se relaciona con la disfunción inmunológica que disminuye la respuesta del huésped ante las bacterias.

**Conclusiones:** en la enfermedad periodontal existe un estado inflamatorio permanente que agrava el pronóstico de la insuficiencia renal crónica, por lo que es

necesario mantener una adecuada salud bucal para evitar complicaciones sistémicas en pacientes vulnerables como los que presentan enfermedad renal crónica.

**Palabras clave:** insuficiencia renal crónica; periodontitis

## INTRODUCTION

Chronic kidney disease (CKD) is defined by the presence of renal damage (proteinuria and hematuria) and decreased renal function (reduction of the estimated glomerular filtration rate below 60ml/min/1.73m<sup>2</sup> for more than three months) -or both-. This disease has a great negative impact on the health and quality of life of patients. Despite advances in its treatment, the prevalence of CKD continues to increase.<sup>(1,2)</sup>

Ten percent of the world population lives with this condition, which represents about 850 million people, and 3.9 million live thanks to dialysis methods and renal transplantation, making it one of the most common diseases.<sup>(3)</sup>

In Cuba, it is estimated that there are around 600 thousand people with kidney disease and, despite the fact that most of the population is aware of dialysis or transplantation as the final cause of kidney damage, it is alarming that only one in five people is concerned about kidney problems caused by their diabetes or hypertension, while only one in 10 people know they have it and seven out of 10 start hemodialysis.<sup>(2)</sup>

Among the risk factors for CKD, hypertension, diabetes, age and smoking have been identified.<sup>(1)</sup> Regarding periodontal disease there is also growing evidence of its importance as a modifiable risk factor for CKD;<sup>(1,4)</sup> furthermore, it appears that periodontitis contributes to the deterioration of renal function over time.<sup>(2)</sup> In periodontitis, the ulcerated epithelium of the pocket allows, through different mechanisms, the passage of bacteria and their products into the body and influences general health and susceptibility to certain diseases.<sup>(5)</sup>

A review on the subject was carried out with the aim of describing the association between chronic kidney disease and periodontitis.

## METHODS

A documentary type study was conducted, with an updated review, of scientific articles from databases such as Pubmed, Scielo and Google Scholar in the period from October 2021 to February 2022. Twenty-five scientific texts written in Spanish and English and published between 2017 and 2021 were selected.

## DEVELOPMENT

Periodontitis is a chronic disease that affects the supporting tissues of the tooth and is characterized by loss of alveolar bone attachment and periodontal pocket formation and gingival inflammation, in addition to recession, gingival bleeding, and tooth mobility.<sup>(6)</sup>

In the 2017, the American Academy and European Federation of Periodontology,<sup>(7)</sup> presented at the 2018 workshop, four major groups were included:

- Group 1: Periodontal health, gingival diseases and conditions

- Group 2: Periodontitis
- Group 3: Systemic diseases and conditions affecting periodontal supporting tissue
- Group 4: Peri-implant diseases and conditions.

Five well-established risk factors for chronic immune-inflammatory periodontopathies have now been documented: sulcus microbiota, smoking, diabetes mellitus, stress and genetic factors.<sup>(8)</sup> The authors point out that chronic kidney disease shares important risk factors with this condition, such as diabetes and smoking; at the same time, both increase in prevalence with age.

There are several mechanisms that would explain this link between the two diseases. On the one hand, the arrival of periodontopathogenic bacteria and inflammatory cytokines from the periodontium to the bloodstream favors systemic inflammation and alterations in different organs, including the kidney. There, cytokines and other inflammatory factors can cause endothelial dysfunction and the appearance of proteinuria, thrombosis and fibrosis, alterations that can cause deterioration of renal function.<sup>(1,4)</sup> On the other hand, bacteremia, as well as cytokines and other inflammatory substances derived from periodontal disease, can also favor the appearance of diseases that worsen renal function and increase the risk of CKD.<sup>(1)</sup> Some examples are:

- **Type 2 diabetes mellitus:** is a risk factor for periodontal disease and an important risk factor for CKD.<sup>(1,9)</sup> It has also been observed that periodontitis can predict the development of diabetic nephropathy and end-stage renal disease in patients with type 2 diabetes mellitus
- **Arterial hypertension:** periodontal disease is associated with an increased predisposition to arterial hypertension which, in turn, is a known risk factor for CKD. It appears that periodontal disease promotes hypertension through inflammation and pro-inflammatory mediators and consequent endothelial damage to blood vessels<sup>(1)</sup>
- **Non-alcoholic fatty liver disease (NAFLD):** its occurrence has also been linked to periodontal bacteria and associated cytokines. This liver disease also poses an increased risk of CKD.<sup>(1)</sup>

Periodontal lesions contain a dysbiotic bacterial composition in the subgingival region, with growth of pathogenic species such as *Porphyromonas gingivalis*. Periodontitis may trigger a chronic infection and bacteria may enter the circulatory system.<sup>(6)</sup>

Subgingival biofilms contain a large and continuous bacterial load, which is a constant source of lipopolysaccharide (LPS) and gram-negative bacteria to the bloodstream. Proinflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , IFN- $\gamma$  and PGE can reach high concentrations in periodontal tissues and function as a reservoir (always renewed) for the dissemination of these mediators into the circulation. Therefore, periodontal pockets with gram-negative biofilm and tissues affected by periodontitis would have the potential to flood the circulation with bacteria, bacterial by-products such as LPS and inflammatory cytokines that can reach anywhere in the body and affect distant sites and organs such as the kidney.<sup>(8)</sup> The authors of this research assume that if one also suffers from CKD this situation complicates the underlying disease and helps its progression. A similar situation is expressed in a study that demonstrates that periodontitis intervenes in the progression of CKD.<sup>(10)</sup>

For these reasons, the authors of this research propose that in periodontal disease there is a permanent inflammatory state that aggravates the prognosis of chronic renal failure.

Several studies show the strong association between renal disease and periodontitis;<sup>(11,12,13,14)</sup> however, it does not behave in the same way in the study carried out by Wangerin.<sup>(15)</sup>

Periodontal inflammation represents a source of oxidative stress in patients with CKD, as a consequence of this process free radicals are formed with unpredictable damage at the cellular level, which is why they are involved in multiple diseases such as this.<sup>(16,17)</sup>

In a study carried out in 62 patients with chronic kidney disease, 49 presented severe periodontitis, five moderate and one mild, which represents that 98% were affected, and the greater number represents the severity of the disease.<sup>(18)</sup>

An investigation carried out in patients with chronic kidney disease showed that 82% had periodontitis: 13% were mild, 39% were moderate and 30% had severe periodontitis.<sup>(19)</sup>

In another, 94% of the patients had periodontitis: 74% had mild periodontitis, 20% had moderate periodontitis and only 6% had no periodontitis;<sup>(20)</sup> similarly, another study<sup>(21)</sup> showed 74.4% of the patients with periodontitis. These results show that a significant number of patients with CKD present periodontitis, which proves that this association is real and that both diseases aggravate each other, that is, that a bidirectional action is established.

Under normal conditions the salivary pH is slightly acidic (6 to 7) and is composed of a variety of electrolytes (sodium, potassium, calcium, magnesium, bicarbonate and phosphates), immunoglobulins (proteins, enzymes and mucins) and nitrogenous products (urea and ammonium); the former are involved in bone mineralization functions, antibacterial activity and regulation of the metabolism of dental plaque, while the modulation of pH and salivary buffering capacity is related to bicarbonate, phosphate and urea. An increase in salivary pH has been detected in these patients with elevated plasma urea concentrations and leakage of ammonium derivatives through saliva, implying that changes occur in the oral cavity as a result of renal disease.<sup>(22,23)</sup>

The constant presence of uremia, as well as poor oral hygiene in these patients, is related to immune dysfunction that includes defects in lymphocyte, monocyte and macrophage function, thereby decreasing host response to bacteria.<sup>(24)</sup>

The stomatologic changes observable in patients with renal dysfunction affect the teeth, bone, mucosa, salivary secretory function, neuromotor, tactile and nociceptive neurologic functions and the sense of taste.<sup>(24)</sup> Therefore, the Dental Specialist should identify these oral symptoms and signs as part of the patient's systemic disease and not as an isolated occurrence. Since 90% of oral manifestations have been reported in patients suffering from this disease, a more integral vision of the health/disease process by the Specialist is necessary; however, many professionals refuse to treat these patients due to the lack of knowledge of the high relationship that exists between these systemic diseases and their repercussion in the oral cavity.<sup>(24)</sup>

Finally, the impact of periodontal disease treatment in patients with CKD has also been evaluated. It has been observed that periodontal treatment attenuates systemic inflammation, improves levels of endothelial function markers and improves renal function. It is considered important for patients with CKD and periodontal disease to visit the dental specialist regularly and receive adequate periodontal treatment to maintain quality of life, prevent possible complications and improve survival.<sup>(1)</sup>

For the moment, research on the presence of periodontitis in CKD patients has been limited to the effectiveness of scaling and root planing therapy, while the use of adjuvant alternatives such as the implementation of probiotic strains has not been explored, although the latter is an area of opportunity in the management of this oral disease that could prevent, or at least delay, other complications that at first sight are not related to oral health such as attenuation in the concentrations of proinflammatory markers, possible increase in albumin concentrations and improvement in nutritional status.<sup>(24)</sup>

In a study by Buelvas<sup>(25)</sup> periodontal treatment in these patients improved clinical parameters such as gingival sulcus depth, clinical level of attachment, bleeding rate and biofilm index. The success of periodontal therapy reduces the inflammatory burden and decreases serum prohepcidin levels, indicating that it may be an important therapeutic intervention during the course of CKD.<sup>(24)</sup>

Interdisciplinary management gives support to the Dental Specialist on the drugs that affect oral health to implement or create new management protocols for each disease that patients present and that is directly related to these conditions. The use of different drugs to treat different diseases affects, directly and indirectly, the oral cavity, that is why the constant vigilance and follow-up that the Specialist in Stomatology should have with the Specialist in Internal Medicine to verify if it is possible to improve the pharmacological therapy with one that does not have a negative impact on the oral cavity.<sup>(24)</sup>

Maintaining adequate dental and periodontal health is essential for proper oral health, in order to avoid localized infectious processes at the oral level that can be triggers of future systemic complications in vulnerable patients such as those with chronic renal failure.

## CONCLUSIONS

In periodontal disease there is a permanent inflammatory state that aggravates the prognosis of chronic renal failure, so it is necessary to maintain adequate periodontal health to avoid systemic complications in vulnerable patients such as those with CKD.

## BIBLIOGRAPHIC REFERENCES

1. Kitamura M, Mochizuki Y, Miyata Y, Obata Y, Mitsunari K, Matsuo T, et al. Pathological Characteristics of Periodontal Disease in Patients with Chronic Kidney Disease and Kidney Transplantation. *Int J Mol Sci* [Internet]. 2019 [cited 04/20/2022];20(14):3413. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6678374/>. <https://doi.org/10.3390/ijms20143413>
2. Ministerio de Salud Pública [Internet]. La Habana: MINSAP; 2022 [updated 11/03/2021; cited 04/20/2022]. Día del riñón: Vivir bien con la enfermedad renal

- [about. 4 screens]. Available at: <https://salud.msp.gob.cu/dia-del-rinon-vivir-bien-con-la-enfermedad-renal/>
3. Candelaria-Brito JC, Gutiérrez-Gutiérrez C, Bayarre-Vea HD, Acosta-Cruz C, Montes de Oca DM, Labrador-Mazón O. Characterization of chronic renal disease in elderly adults. *Rev Colomb Nefrol* [Internet]. 2018 [cited 04/20/2022];5(2):166-178. Available at: <https://revistanefrologia.org/index.php/rcn/article/view/308/html>. <https://doi.org/10.22265/acnef.0.0.308>
  4. Lertpimonchai A, Rattanasiri S, Tamsailom S, Champaiboon C, Ingsathit A, Kitiyakara C, et al. Periodontitis as the risk factor of chronic kidney disease: Mediation analysis. *J Clin Periodontol* [Internet]. 2019 [cited 02/07/2022];46(6):631-639. Available at: <https://pubmed.ncbi.nlm.nih.gov/30993705/>. <https://doi.org/10.1111/jcpe.13114>
  5. Peña Sisto M, Calzado da Silva M, González Peña M, Cordero García S, Azahares Argüello H. Patógenos periodontales y sus relaciones con enfermedades sistémicas. *Medisan* [Internet]. 2012 [cited 02/07/2022];16(7):1137-1148. Available at: [https://scielo.sld.cu/scielo.php?script=sci\\_arttext&pid=S1029-30192012000700014](https://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192012000700014)
  6. de Armas Cándano A, Pérez Hernández LY, Lemus Martínez Y, Collazo Martínez Y, Labrador Falero DM. Probabilidad de enfermedad periodontal en función de los factores de riesgo empleando modelo matemático. *Rev Ciencias Médicas* [Internet]. 2017 [cited 04/20/2022];21(2):171-177. Available at: [https://scielo.sld.cu/scielo.php?script=sci\\_arttext&pid=S1561-31942017000200004](https://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1561-31942017000200004)
  7. Zerón A. La nueva clasificación de enfermedades periodontales. *Rev ADM* [Internet]. 2018 [cited 02/07/2022];75(3):122-124. Available at: <https://www.medigraphic.com/pdfs/adm/od-2018/od183a.pdf>
  8. Sarduy Bermúdez L, González Díaz ME, De la Rosa Samper H, Morales Aguiar DR. Etiología y patogenia de la enfermedad periodontal inmunoinflamatoria crónica. En: González Díaz ME, Toledo Pimentel B, Sarduy Bermúdez L, Morales Aguiar DR, De la Rosa Samper H, Veitia Cabarrocas F, et al. *Compendio de Periodoncia*. 2da ed. La Habana: Editorial Ciencias Médicas; 2017 [cited 02/07/2022]. p.73-148. Available at: [http://bvs.sld.cu/libros\\_texto/compendio\\_periodoncia/compendio\\_periodoncia\\_completo.pdf](http://bvs.sld.cu/libros_texto/compendio_periodoncia/compendio_periodoncia_completo.pdf)
  9. Shen Y, Cai R, Sun J, Dong X, Huang R, Tian S, et al. Diabetes mellitus as a risk factor for incident chronic kidney disease and end-stage renal disease in women compared with men: a systematic review and meta-analysis. *Endocrine* [Internet]. 2017 [cited 02/07/2022];55(1):66-76. Available at: <https://pubmed.ncbi.nlm.nih.gov/27477292/>. <https://doi.org/10.1007/s12020-016-1014-6>
  10. Valenzuela-Narváez RV, Valenzuela Narváez DR, Valenzuela Narváez DAO, Córdova Noel ME, Mejía Ruiz CL, Salcedo Rodríguez MN. Periodontal disease as a predictor of chronic kidney disease (CKD) stage in older adults. *J Int Med Res* [Internet]. 2021 [cited 02/07/2022];49(7):3000605211033266. Available at: <https://pubmed.ncbi.nlm.nih.gov/34311597/>. <https://doi.org/10.1177/03000605211033266>
  11. da Silva Schütz J, Barrera de Azambuja C, Reolon Cunha G, Cavagni J, Kuchenbecker Rösing C, Nogueira Haas A, et al. Association between severe periodontitis and chronic kidney disease severity in predialytic patients: A cross-sectional study. *Oral Dis* [Internet]. 2020 [cited 02/07/2022];26(2):447-456. Available at: <https://pubmed.ncbi.nlm.nih.gov/31742816/>. <https://doi.org/10.1111/odi.13236>

12. Salimi S, Ng N, Seliger SL, Parsa A. Periodontal disease, renal dysfunction and heightened leukocytosis. *Nephron Clin Pract* [Internet]. 2014 [cited 02/07/2022];128(1-2):107-14. Available at: <https://pubmed.ncbi.nlm.nih.gov/25402594/>. <https://doi.org/10.1159/000366445>
13. Toth-Manikowski SM, Ricardo AC, Salazar CR, Chen J, Khambaty T, Liu J, et al. Periodontal Disease and Incident CKD in US Hispanics/Latinos: The Hispanic Community Health Study/Study of Latinos. *Kidney Med* [Internet]. 2021 [cited 02/07/2022];3;3(4):528-535.e1. Available at: <https://pubmed.ncbi.nlm.nih.gov/34401720/>. <https://doi.org/10.1016/j.xkme.2021.02.015>
14. Li L, Zhang YL, Liu XY, Meng X, Zhao RQ, Ou LL, et al. Periodontitis Exacerbates and Promotes the Progression of Chronic Kidney Disease Through Oral Flora, Cytokines, and Oxidative Stress. *Front Microbiol* [Internet]. 2021 [cited 02/07/2022];12:656372. Available at: <https://pubmed.ncbi.nlm.nih.gov/34211440/>. <https://doi.org/10.3389/fmicb.2021.656372>
15. Wangerin C, Pink C, Endlich K, Rettig R, Stracke S, Nauck M, et al. Long-term Association of Periodontitis With Decreased Kidney Function. *Am J Kidney Dis* [Internet]. 2019 [cited 02/07/2022];73(4):513-524. Available at: <https://pubmed.ncbi.nlm.nih.gov/30704881/>. <https://doi.org/10.1053/j.ajkd.2018.10.013>
16. Sharma P, Fenton A, Dias IHK, Heaton B, Brown CLR, Sidhu A, et al. Oxidative stress links periodontal inflammation and renal function. *J Clin Periodontol* [Internet]. 2021 [cited 02/07/2022];48(3):357-367. Available at: <https://pubmed.ncbi.nlm.nih.gov/33368493/>. <https://doi.org/10.1111/jcpe.13414>
17. Viada Pupo E, Gómez Robles L, Campaña Marrero IR. Estrés oxidativo. *CCM* [Internet]. 2017 [cited 02/07/2022];21(1):171-186. Available at: [http://scielo.sld.cu/scielo.php?script=sci\\_arttext&pid=S1560-43812017000100014](http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1560-43812017000100014)
18. Vizuite Bolaños MX, Dona Vidale MA, Gordon Navarrete DP, Sempertegui Jácome DA, Sosa Carrero MA, Singo Salazar CA. Estado de salud bucal en pacientes con insuficiencia renal crónica bajo tratamiento con hemodiálisis. *Rev Odont Mex* [Internet]. 2018 [cited 02/07/2022];22(4):206-213. Available at: [https://www.scielo.org.mx/scielo.php?script=sci\\_arttext&pid=S1870-199X2018000400206](https://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S1870-199X2018000400206)
19. Herrera Alvarado KM. Estado dental y periodontal en pacientes con insuficiencia renal crónica. Serdidyv S.A, 2018 [thesis]. Guayaquil: Universidad Católica de Santiago de Guayaquil; 2019 [cited 02/07/2022]. Available at: <http://repositorio.ucsg.edu.ec/bitstream/3317/12262/1/T-UCSG-PRE-MED-ODON-431.pdf>
20. Seng Montes de Oca L. La enfermedad periodontal y su relación con la insuficiencia renal crónica. *Invest Medicoquir* [Internet]. 2018 [cited 02/07/2022];10(2):[about. 7 p.]. Available at: <https://revcimeq.sld.cu/index.php/imq/article/view/440/515>
21. Rodríguez Condezo JM. Relación entre enfermedad periodontal y la enfermedad renal crónica en pacientes del Hospital Nacional Alberto Sabogal Sologuren, Lima, Perú, 2017 [thesis]. Lima: Universidad Privada Norbert Wiener; 2019 [cited 02/07/2022]. Available at: [https://repositorio.uwiener.edu.pe/bitstream/handle/20.500.13053/3386/TESIS\\_Rodriguez\\_Joan.pdf](https://repositorio.uwiener.edu.pe/bitstream/handle/20.500.13053/3386/TESIS_Rodriguez_Joan.pdf)
22. López Cisneros S, Espinosa Cuevas MA, Reyes Guerrero R. La periodontitis en el paciente con enfermedad renal crónica. *Rev Mex Nutr Ren* [Internet]. 2019 [cited 02/07/2022];2(2):40-48. Available at: <https://www.imbiomed.com.mx/articulo.php?id=113920>

23. Ordóñez Pesántez MG, Piedra Idrovo MP. Lesiones de la mucosa oral en pacientes con enfermedad renal crónica en diálisis [thesis]. Cuenca: Universidad de Cuenca; 2018 [cited 02/07/2022]. Available at: <http://dspace.ucuenca.edu.ec/handle/123456789/30370>
24. Rebolledo-Cobos M, De la Cruz-Villa A, Ibarra-Kammerer R, Hernández-Miranda K. Hipertensión arterial e insuficiencia renal crónica: repercusiones estomatológicas, una revisión. Av Odontoestomatol [Internet]. 2018 [cited 02/07/2022];34(4):175-182. Available at: [https://scielo.isciii.es/scielo.php?script=sci\\_arttext&pid=S0213-12852018000400002](https://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0213-12852018000400002)
25. Buelvas Montes LA. Efectividad del tratamiento periodontal en la enfermedad renal: revisión sistemática [thesis]. Cartagena de Indias: Universidad de Cartagena; 2021 [cited 02/07/2022]. Available at: <https://repositorio.unicartagena.edu.co/bitstream/handle/11227/12460/Informe%20final.pdf>

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest in relation to this article.