

# Connection between periodontal disease and chronic kidney disease: A literature review

**Abstract / Introduction:** *The association between periodontal disease (PD) and chronic kidney disease (CKD) is bidirectional, as individuals with CKD may have oral manifestations, and PD may develop as a complicating factor of CKD. The systemic inflammatory response found in periodontal patients may have a synergistic effect on the chronic inflammation found in CKD.*

**Objective:** *To review the literature to find evidence of the importance of the association between these two conditions.*

**Methods:** *A PubMed search of studies published between 2003 and 2013 was conducted to retrieve clinical trials and systematic reviews.*

**Results:** *Six clinical trials and one systematic review met the established criteria. Clinical trials used different approaches for the association between PD and CKD. Studies investigating the association between PD and CKD used a crossover design, evaluation of the oral manifestations in patients with CKD, and analysis of the effect of periodontal treatment on markers of renal disease.*

**Conclusion:** *In addition to systemic functions, CKD also affects oral health, particularly causing periodontal tissues. Moreover, PD may affect kidney functions and lead to complications in individuals with CKD.*

**Keywords:** *Chronic renal insufficiency. Periodontitis. Renal dialysis.*

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## INTRODUCTION

Chronic kidney disease (CKD) is a progressive condition characterized by renal failure.<sup>1</sup>

Structural changes result from certain diseases, usually underlying pathologies, such as diabetes, hypertension and glomerulonephritis, that lead to loss of renal function.<sup>1</sup> As kidneys adapt to loss of function, important signs of failure are only detected at advanced stages of the disease.<sup>2</sup>

Patients with CKD may present several oral manifestations, such as dry mouth, uremic stomatitis, X-ray detected maxillary and mandibular abnormalities secondary to calcium loss due to the increase of parathyroid hormone, dental calculus due to higher serum calcium and phosphorus concentrations, high concentration of urea in saliva, abnormal bone remodeling after extraction, delayed tooth eruption, tooth mobility, malocclusion, and sensitivity to percussion and mastication, as well as a high prevalence of periodontal disease (PD).<sup>3</sup>

The association between PD and CKD is bidirectional, as individuals with CKD may have oral manifestations due to CKD, and PD may become a complicating factor of CKD. The systemic inflammatory response in patients with PD may have a synergistic effect on the chronic inflammation found in CKD.

Therefore, considering the severity of CKD, the high prevalence of PD and the importance of PD for the health of individuals with CKD, this study reviewed the literature to find evidence that may demonstrate the relevance of the association between CKD and PD.

## MATERIAL AND METHODS

A literature review was conducted using PubMed to retrieve studies published

between 2003 and 2013. Clinical studies and systematic literature reviews were selected. The keywords used were renal disease, kidney disease and periodontitis. The title and abstract of the studies retrieved were evaluated to define whether they met the following inclusion criteria:

- » Evaluation of PD and CKD according to their incidence, prevalence and bidirectional association;
- » Patients undergoing renal dialysis;
- » Controlled clinical trials and systematic reviews;
- » Publication between 2003 and 2013;
- » Texts in English or Portuguese.

## RESULTS

Twenty studies were retrieved; 11 were excluded after their title and abstract were read because they did not deal with the topic of this study or were not systematic reviews. Of the nine studies included in this review, three are systematic reviews and six are controlled clinical trials.

The clinical trials used different approaches to analyze the association between PD and CKD, such as the use of a crossover design to search for an association between PD and CKD, the investigation of oral manifestations in patients with CKD, and the evaluation of the effect of periodontal treatment on CKD.<sup>4-9</sup>

Kshirsagar et al<sup>4</sup> investigated the association between PD and CKD by using a sample of 5537 individuals that underwent examination of their periodontal health and renal function. Initial (odds ratio = 2.00) and severe (odds ratio = 2.14) PD were associated with low glomerular filtration rates and elevated serum creatinine levels.

Dias et al<sup>6</sup> evaluated the oral health of patients with CKD who underwent

hemodialysis. One hundred and seven patients were divided into three groups according to the time that they had been on hemodialysis (3 months to 1 year; 1 to 3 years; more than 3 years) and evaluated according to their plaque and caries index. The authors found that the time of disease treatment did not affect or change bacterial film accumulation or the prevalence of caries.

Bayraktar et al<sup>5</sup> studied the oral health and presence of inflammation in patients with end-stage renal failure and found that the patients with CKD had worse periodontal and dental health than the controls. This finding may play an important role in systemic inflammation among these patients.

Graziani et al<sup>9</sup> assessed the effect of periodontal treatment on glomerular filtration rate of 20 systemically healthy patients. Their results revealed that periodontal treatment improves the concentration of cystatin C, a glomerular filtration marker. They found that periodontal treatment may affect glomerular filtration, and suggested that further studies be conducted to confirm their findings.

Vilela et al<sup>8</sup> studied the impact of periodontal treatment on serum prohepcidin levels and systemic inflammatory markers in patients with CKD not undergoing dialysis. Thirty-six patients with CKD and 20 systemically healthy controls received periodontal treatment. The levels of C-reactive protein, IL-6 and prohepcidin were lower in both groups, which confirmed that periodontal treatment is an important intervention to reduce inflammation in patients with CKD.

Wehmeyer et al<sup>7</sup> assessed the result of intensive periodontal treatment on metabolic and inflammatory markers of 53 patients with CKD undergoing dialysis. Their results did not show any

improvements in serum albumin and IL-6 concentrations after 6 months of treatment. However, the authors suggested that studies with a larger number of patients might validate their findings.

The systematic reviews included in this study found that there is consistent evidence to support the existence of a positive association between periodontitis and CKD, as well as of a positive effect of periodontal treatment on glomerular filtration rates.<sup>10</sup>

## DISCUSSION

PD may interact with other conditions that affect the human body. Several risk factors that make individuals susceptible to PD and accelerate its progression may also be found in patients with CKD, such as immunodeficiency, diabetes, smoking, deficient oral hygiene, dry mouth and poor nutrition. Several study findings support the hypothesis that individuals with PD also have a high risk of CKD, even after statistical adjustment to other independent risk factors.<sup>10</sup>

Some studies demonstrate that the incidence and severity of periodontitis are greater in patients with CKD than in the population in general.<sup>3, 11-15</sup> Evidence also suggests that the type of renal disease treatment may affect PD severity and extension. This disease is usually more advanced in patients undergoing hemodialysis, and is less severe in patients undergoing continuous ambulatory peritoneal dialysis or predialysis.<sup>13,14</sup>

The association between PD and CKD is bidirectional, in other words, uremia contributes to the increase of gingival inflammation in patients undergoing dialysis, and the systemic inflammatory response in patients with PD may have a synergistic effect on the chronic inflammation found in CKD.<sup>11</sup>

Individuals with initial or severe PD are more likely to have loss of renal function than individuals with a healthy periodontium or with gingivitis.<sup>v</sup> Additionally, these patients may have a low glomerular filtration rate and a high serum creatinine concentration.<sup>4,16</sup> Some studies found an association between subgingival infection by *Porphyromonas gingivalis* and systemic inflammation indicated by elevated C-reactive protein levels in patients with PD undergoing dialysis.<sup>17,18,19</sup>

In addition to PD, individuals with CKD also have a low salivary flow rate<sup>5</sup> and a high index of missing or filled teeth.<sup>6</sup>

CKD affects the human body because it changes its systemic functions. One third of the population of patients with CKD have suppressed cell and humoral immune responses, as well as serum IgA, IgM and IgG concentrations below normal levels. Studies of salivary IgA in patients with PD and healthy individuals showed that there are differences that may be used to detect groups with a high risk of PD.<sup>20,21</sup>

The acute phase response is triggered after infection, and the purpose of this reaction is to remove the aggressive agent and

promote cure. Effects of the acute phase response are mostly unspecific, in contrast with cell or humoral immunity.<sup>17</sup>

If PD increases systemic inflammation and the risks for patients with CKD, periodontal treatment should be able to reduce systemic levels of inflammation.<sup>7,8,10</sup> D'Aiuto et al<sup>22</sup> suggested that periodontal treatment may lead to a decrease in inflammatory markers, a consequent reduction in the levels of C-reactive protein, IL-6 and TNF- $\alpha$  and a partial restoration of endothelial functions. Moreover, Graziani et al<sup>9</sup> found that periodontal treatment may reduce cystatin C, an important marker of glomerular filtration levels.

## CONCLUSION

CKD affects the systemic functions as well as the oral health of patients with this disease, particularly their periodontal tissues. Moreover, PD may also affect patients' renal function and lead to further complications. Therefore, it seems to be plausible that these two diseases have a bidirectional association, but further studies should be conducted to confirm such association.

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