

Effect of periodontitis treatment on renal function in chronic kidney disease patients: a systematic review and meta-analysis

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To evaluate the effect of non-surgical periodontal therapy (NSPT) on renal function and systemic inflammatory markers in patients with chronic kidney disease (CKD). A systematic literature search was conducted in PubMed, SCOPUS, EMBASE, and the Cochrane Library for articles published up to October 2025, strictly following PRISMA guidelines. The protocol was registered in PROSPERO (CRD42021232030). Eligible studies included clinical trials and before-after studies evaluating the effect of NSPT on renal parameters (eGFR, serum creatinine, BUN, UACR) in patients with CKD. Meta-analyses were performed using random-effects models and stratified by CKD stage (pre-dialysis vs. dialysis). Ten studies (seven before-after studies and three randomized controlled trials) met the inclusion criteria. The overall pooled meta-analysis indicated that NSPT did not significantly improve traditional renal filtration parameters. In subgroup analyses, pre-dialysis patients demonstrated a modest, but non-significant trend toward improved eGFR. Among dialysis patients, serum creatinine and eGFR showed no significant improvement and occasionally increased, which may paradoxically reflect altered nutritional status rather than a deterioration in renal filtration. Although NSPT does not result in statistically significant improvements in traditional renal filtration markers, it effectively reduces systemic inflammatory burden in both pre-dialysis and dialysis patients. Integrating periodontal care into multidisciplinary CKD management remains crucial for minimizing inflammation-driven cardiovascular risks. Future robust, long-term trials targeting pre-dialysis populations and utilizing highly sensitive novel biomarkers are warranted to evaluate potential slowing of CKD progression.

Keywords: chronic kidney disease, chronic, kidney diseases, periodontal debridement, periodontitis, renal insufficiency, root planing

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Introduction

Chronic kidney disease (CKD) is characterized by a progressive decline in renal function, typically indicated by a reduction in estimated glomerular filtration rate (eGFR) and elevations in serum creatinine and blood urea nitrogen (BUN) levels. Serum Creatinine (SCr) [1]

is a freely filtered biomarker commonly used in equations to estimate GFR (eGFR). However, its concentration may vary due to factors such as muscle mass and tubular secretion. Blood urea nitrogen (BUN) [1] is also used to assess kidney function, but it is considered less reliable than SCr because its production may vary independently of GFR due to dietary intake or tissue catabolism.

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The urine albumin-to-creatinine ratio (UACR) [2] is a key marker of kidney damage. UACR estimates 24-hour albumin excretion, with albuminuria defined as $\text{UACR} > 30 \text{ mg/g}$. Monitoring UACR is essential for diagnosing and tracking CKD progression, as albuminuria is a strong predictor of disease progression and adverse clinical outcomes and often precedes declines in eGFR.

The eGFR is a crucial measure used to determine the stage of kidney disease and is calculated using equations that incorporate a person's age, sex, race, and serum creatinine levels. CKD is classified into five stages based on eGFR values: stage 1 ($\text{eGFR} > 90 \text{ mL/min/1.73 m}^2$), stage 2 ($60\text{--}89 \text{ mL/min/1.73 m}^2$), stage 3A ($45\text{--}59 \text{ mL/min/1.73 m}^2$), stage 3B ($30\text{--}44 \text{ mL/min/1.73 m}^2$), stage 4 ($15\text{--}29 \text{ mL/min/1.73 m}^2$), and stage 5 ($\text{eGFR} < 15 \text{ mL/min/1.73 m}^2$). Stage 5 represents the final stage of kidney disease, in which the kidneys have permanently lost their ability to perform essential functions, requiring dialysis or kidney transplantation for survival. Patients with CKD stage 5 are diagnosed as End-Stage Renal Disease (ESRD). Additionally, the UACR is used to assess albuminuria and is categorized into A1 ($<30 \text{ mg/g}$, normal to mildly increased), A2 ($30\text{--}300 \text{ mg/g}$, moderately increased), and A3 ($>300 \text{ mg/g}$, severely increased) [3, 4].

CKD is a growing global health issue that contributes significantly to morbidity and mortality. Despite its substantial impact, awareness among both patients and healthcare providers remains relatively low. Several risk factors, including chronic inflammation, oxidative stress, and ectopic calcification, have been linked to poor outcomes in CKD and contribute to disease progression, ultimately affecting patients' quality of life [5].

Chronic periodontitis is a chronic inflammatory disease affecting the supporting structures of the teeth and is primarily driven by microbial plaque and calculus. It results in the destruction of

connective tissue and alveolar bone. Although the disease generally progresses slowly, episodes of rapid deterioration may occur and are associated with variations in microbial composition and host immune responses [6]. The onset of periodontitis involves an innate immune response triggered by microbial biofilms, which stimulate epithelial cells and neurons to release cytokines and neuropeptides, leading to local vasodilation. As the disease progresses, a transition to an adaptive immune response occurs, characterized by increased numbers of macrophages, plasma cells, and T and B lymphocytes (particularly IgG1 and IgG3). These immune responses contribute to periodontal tissue destruction and alveolar bone loss [7]. Systemically, periodontitis can elevate inflammatory markers such as C-reactive protein (CRP) and biomarkers of oxidative stress, including cystatin C [8].

An increasing number of studies have highlighted the association between CKD and periodontal disease. A systematic review by Chambrone *et al.* [9] provided substantial evidence supporting a positive link between the two conditions. Similarly, Zhao *et al.* [10] demonstrated a bidirectional relationship between CKD and periodontitis, even after adjusting for both traditional and non-traditional risk factors. Although the direction of causality remains underexplored, it is well documented that individuals with CKD are more prone to oral health problems [11], and clinical indicators of periodontal disease tend to be more severe in CKD patients both dialysis [12] and pre-dialysis groups [13]. Periodontal inflammation may act as a contributing factor to both localized and systemic inflammation in CKD patients, potentially exacerbating complications such as infections, protein-energy wasting, and cardiovascular events [14]. In a longitudinal observation study, Chen *et al.* [15] found a significantly greater decline in eGFR over 2–3 years in patients with periodontal disease compared with those without disease. Similarly, Lertpimonchai *et al.* [16]

observed that periodontitis contributed to CKD incidence both directly and indirectly through diabetes.

Several studies have also investigated the biochemical pathways linking periodontal disease and CKD. In hemodialysis patients, altered biochemical status, including elevated serum albumin and ferritin levels, has been associated with the progression of periodontal disease from gingivitis to periodontitis [17]. Disturbances in calcium metabolism are also observed in CKD due to reduced calcitriol synthesis and decreased urinary calcium excretion, and hypocalcemia has been proposed as a potential risk factor for periodontal disease [18, 19].

Inflammatory biomarkers represent another important link between periodontitis and CKD. C-reactive protein (CRP), a well-established marker of systemic inflammation in CKD, shows a strong independent association with the extent of periodontitis [20]. Interleukin-6 (IL-6), a multifunctional cytokine involved in immune regulation and inflammation, is typically elevated in CKD patients with poorer periodontal status [21]. Interleukin-17 (IL-17), a cytokine that bridges T-cell activation and neutrophil responses, is also elevated in the gingival crevicular fluid of patients with both aggressive and chronic periodontitis [22] and correlates with the progression of kidney disease [23]. While these cytokines are associated with the severity of both periodontitis and CKD, they are also elevated in several other systemic inflammatory disorders [24].

Among emerging renal biomarkers, cystatin C, a low-molecular-weight protein freely filtered by the glomerulus, has been proposed as another potential mediator linking periodontal disease and CKD. Beyond reflecting renal function [25], cystatin C inhibits cathepsin K, an enzyme involved in bone resorption [26]. Evidence indicates that cystatin C concentrations in gingival crevicular fluid and serum are elevated in patients with

periodontitis compared with healthy controls [27], and successful periodontal therapy may lead to improvements in cystatin C levels [28]. Neutrophil gelatinase-associated lipocalin (NGAL) has also attracted attention for its sensitivity in detecting early kidney injury. Serum NGAL and urinary NGAL (uNGAL) reflect tubular damage and correlate with renal function, making them useful biomarkers for the early diagnosis and prognosis of both acute kidney injury and CKD [29].

Other emerging biomarkers related to kidney function have been proposed to provide a more specific and comprehensive assessment of renal function and CKD progression, thereby enabling earlier diagnosis and more accurate risk stratification [30,31]. These include beta-trace protein (BTP), kidney injury molecule-1 (KIM-1), N-acetyl- β -D-glucosaminidase (NAG), uromodulin (Tamm–Horsfall protein), Klotho, and Dickkopf-3 (DKK-3).

In addition, several inflammatory biomarkers [30], such as ficolins, the NLRP3 inflammasome, tumor necrosis factor receptors 1 and 2 (TNFR1 and TNFR2), calprotectin, the systemic inflammation response index (SIRI), the neutrophil-to-lymphocyte ratio (NLR), and the CRP-to-albumin ratio (CAR), serve not only as indicators of systemic inflammation but also as important predictors of adverse renal and cardiovascular outcomes.

Overall, although numerous biomarkers have been proposed to elucidate the systemic and local interplay between periodontal inflammation and CKD, only a limited number—such as estimated glomerular filtration rate (eGFR), serum creatinine, blood urea nitrogen (BUN), albuminuria (urine albumin-to-creatinine ratio, UACR), cystatin C, and neutrophil gelatinase-associated lipocalin (NGAL)—are currently applicable in clinical practice for evaluating renal function. In contrast, biomarkers such as C-reactive protein (CRP) primarily reflect systemic inflammation and cardiovascular risk

rather than direct renal impairment, underscoring the importance of developing comprehensive biomarker panels in future investigations [24].

There is some evidence suggest that periodontal inflammation may contribute to systemic inflammation in CKD patients [32]. Therefore, periodontal therapy may not only improve oral health but also provide systemic benefits, including potential improvements in renal function. Some studies have reported that non-surgical periodontal therapy (NSPT) led to significant improvements in eGFR in both CKD and non-CKD individuals [33]. Chambrone *et al.* [9] supported this finding, indicating a positive impact of periodontal therapy on renal function. Furthermore, Tonetti *et al.* [34] showed that periodontal therapy improved endothelial function six months after treatment. However, more recent reviews suggest that the evidence remains inconclusive regarding the benefits of NSPT in CKD patients with periodontitis [35].

Given these limitations, the association between periodontal therapy and CKD outcomes remains uncertain. Prior reviews have primarily focused on non-surgical interventions. Therefore, this systematic review and meta-analysis was designed to evaluate the effects of all types of periodontal interventions, including both surgical and non-surgical approaches, on renal function and systemic outcomes in CKD patients with periodontitis. However, after applying the predefined inclusion and exclusion criteria, only studies investigating non-surgical periodontal therapy (e.g., scaling and root planing) met the eligibility criteria. Compared with prior reviews, this study extends the existing evidence base by incorporating more recent trials, performing subgroup analyses of pre-dialysis and dialysis patients, and integrating additional systemic inflammatory biomarkers. The aim is to provide more comprehensive and updated evidence to support the integration of periodontal care into multidisciplinary CKD management.

Materials and Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [36]. The study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42021232030). As this study was a systematic review and meta-analysis based on previously published data, ethical approval was not required.

A comprehensive literature search was conducted in four electronic databases: PubMed, Embase via Elsevier, Scopus via Elsevier, and the Cochrane Library for studies published up to 31 October 2025. Only studies with titles and abstracts in English were included. The search strategy was developed using a combination of controlled vocabulary (Medical Subject Headings [MeSH] and Emtree terms) and free-text keywords related to periodontal disease and chronic kidney disease. Boolean operators (AND, OR) were used to combine search terms, and the search syntax was adapted for each database.

For PubMed, MeSH terms and text words were used to identify relevant studies related to periodontal disease and chronic kidney disease. The search strategy was as follows:

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("Periodontitis"[MeSH] OR periodontitis  
[Title/Abstract] OR "periodontal disease"  
[Title/Abstract]  
OR "periodontal therapy"[Title/Abstract]  
OR "periodontal treatment"[Title/Abstract]  
OR "scaling and root planing"[Title/Abstract]  
OR "dental scaling"[Title/Abstract]  
OR "periodontal debridement"[Title/Abstract]  
OR "subgingival scaling"[Title/Abstract])  
AND  
("Kidney Failure, Chronic"[MeSH] OR "Renal  
Insufficiency"[MeSH])
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OR "chronic kidney disease"[Title/Abstract]
 OR "renal insufficiency"[Title/Abstract]
 OR "kidney failure"[Title/Abstract] OR "end-stage
 renal disease"[Title/Abstract]
 OR "hemodialysis"[Title/Abstract] OR
 "peritoneal dialysis"[Title/Abstract]
 OR "renal replacement therapy"[Title/Abstract])

For Embase via Elsevier, the corresponding
 Emtree terms and keywords were used as follows:

('periodontitis'/exp OR 'periodontal disease':
 ti,ab,kw OR 'periodontal therapy':ti,ab,kw
 OR 'periodontal treatment':ti,ab,kw OR
 'scaling and root planing':ti,ab,kw
 OR 'dental scaling':ti,ab,kw OR 'periodontal
 debridement':ti,ab,kw
 OR 'subgingival scaling':ti,ab,kw)
 AND

('chronic kidney disease'/exp OR 'renal
 insufficiency'/exp
 OR 'end stage renal disease'/exp OR
 'hemodialysis'/exp
 OR 'peritoneal dialysis'/exp OR 'renal
 replacement therapy'/exp)

For Scopus, the search was performed using
 the title, abstract, and keyword fields as follows:

TITLE-ABS-KEY("periodontitis" OR "periodontal
 disease" OR "periodontal therapy"
 OR "periodontal treatment" OR "scaling
 and root planing" OR "dental scaling"
 OR "periodontal debridement" OR "subgingival
 scaling")
 AND

TITLE-ABS-KEY("chronic kidney disease"
 OR "chronic kidney diseases"
 OR "renal insufficiency" OR "kidney failure"
 OR "end-stage renal disease"
 OR "hemodialysis" OR "peritoneal dialysis"
 OR "renal replacement therapy")

For the Cochrane Library, free-text search
 terms and equivalent controlled vocabulary were
 applied as follows:

("periodontal therapy" OR "periodontitis therapy"
 OR "periodontal treatment"
 OR "periodontitis treatment" OR "scaling and
 root planing" OR "dental scaling"
 OR "periodontal debridement" OR "subgingival
 scaling")

AND

("chronic kidney disease" OR "CKD" OR
 "renal insufficiency" OR "kidney failure"
 OR "end-stage renal disease" OR "hemodialysis"
 OR "peritoneal dialysis"
 OR "renal replacement therapy")

Reference lists of the included studies
 and relevant reviews were also hand-searched
 to identify additional eligible articles. In addition,
 clinical trial registries (ClinicalTrials.gov and
 the World Health Organization International
 Clinical Trials Registry Platform [WHO ICTRP])
 were screened to identify relevant grey literature.

The titles and abstracts of all retrieved articles
 were screened to determine their eligibility based
 on the predefined inclusion criteria. Review articles
 and meta-analyses were excluded. The full texts of
 potentially eligible studies were then retrieved and
 assessed for final inclusion.

Characteristic and study selections

PICO question

Population: Adults with CKD (KDIGO G1–G5,
 with or without dialysis) diagnosed with periodontitis
 using accepted clinical criteria (AAP 1999 or AAP
 2017 classification).

Intervention: Periodontal therapy (eg. Scaling
 and root planning, surgical treatment, open flap
 debridement) performed in CKD patients

Comparison: For randomized controlled trials
 (RCTs) or controlled clinical trials, comparisons
 were made between patients receiving periodontal
 treatment and those without periodontal treatment.

For before–after studies, comparisons were made between pre-treatment and post-treatment measurements. These study designs were analyzed separately in the meta-analysis.

Outcome: Primary outcome: renal function-parameter (eGFR, creatinine, BUN, NGAL, UACR)

Secondary outcome: periodontal parameter (PD, CAL, BOP)

Focus question

In patients with chronic kidney disease and periodontal disease, does periodontal treatment improve renal function?

Inclusion and exclusion criteria

Eligible studies included adults with chronic kidney disease (CKD stages G1–G5, with or without dialysis) who were diagnosed with periodontitis using accepted clinical criteria (AAP 1999 or AAP 2017 classification). Interventions comprised non-surgical periodontal therapy (scaling and root planing with or without adjunctive therapy) or comprehensive periodontal therapy completed within the study period. Studies were required to have a follow-up period of ≥ 1 month after treatment and to report at least one renal function-related outcome (e.g., eGFR, serum creatinine, BUN, UACR, NGAL, or cystatin C). Studies were included if they enrolled ≥ 10 participants or provided a justified sample size calculation. Non-English articles with English titles and abstracts were included and translated using Google Translate.

Studies were excluded if they did not involve periodontal treatment, did not include patients with both CKD and periodontitis, involved renal transplant recipients, or lacked sufficient data on renal outcomes.

Selection of study

Two authors (CS and RK) independently screened the titles and abstracts of all articles

retrieved from the database search according to the predefined inclusion criteria. If the title and abstract did not provide sufficient information for eligibility assessment, the full text was obtained and reviewed. Disagreements at any stage were first resolved through discussion between the two reviewers. If consensus could not be reached, a third author (SN) was consulted to make the final decision. The final selection of studies was based strictly on the predefined inclusion and exclusion criteria.

Data extraction and quality assessment

Data extraction was performed independently by two authors (CS and RK). The extracted data included study characteristics, CKD stage, dialysis modality, definition of periodontitis, treatment protocol, and outcomes at all reported time points. For studies with multiple follow-up assessments, the latest time point was prespecified for the primary analyses to avoid double counting. Any disagreements between the two reviewers were resolved through discussion. If consensus could not be reached, a third author (SN) was consulted to resolve the disagreement.

The National Institutes of Health (NIH) Quality Assessment Tool for Controlled Intervention Studies was used to evaluate randomized controlled trials (RCTs) and other studies with a control group. For before–after studies without a control group, the NIH Quality Assessment Tool for Before–After Studies with No Control Group was applied. The controlled intervention tool includes 14 checklist items, whereas the before–after tool includes 12 items. Each item was rated as “Yes,” “No,” or “Unclear” (cannot determine/not applicable/not reported). These tools assess the potential risk of selection bias, information bias, measurement bias, and confounding.

Data analysis

Meta-analyses of continuous outcomes were conducted by pooling renal function-related

parameters across studies using standardized mean differences (SMDs). For RCTs, the SMD between the intervention and control groups was calculated. For before–after studies, the standardized mean change (SMC) between baseline and follow-up measurements was estimated. Mean changes in renal function–related parameters from baseline to follow-up were pooled across studies.

If the mean and standard deviation (SD) of change scores were not reported, they were estimated from the sample size and available summary statistics (e.g., median, minimum–maximum values, interquartile range, or the 25th and 75th percentiles) according to previously described methods [37,38]. Meta-analyses were performed separately for RCTs and before–after studies using R statistical software (R Core Team, 2023) and RStudio version 2023.12.0.369 (Posit Software, PBC, Boston, MA, USA) with the meta package.

A random-effects model was applied to account for potential heterogeneity across studies. Statistical heterogeneity was assessed using Cochran's Q test and the inconsistency index (I^2). Pooled effect estimates with 95% confidence intervals (CIs) were presented using forest plots. Reporting bias was evaluated using funnel plots.

Subgroup analyses were conducted to evaluate the effect of periodontal treatment in patients with CKD at different stages of disease progression. The pre-dialysis group included patients with CKD stages 1–5 who were not receiving dialysis therapy. The dialysis group included patients undergoing maintenance dialysis, including both hemodialysis and peritoneal dialysis. Because only a limited number of studies reported outcomes separately by dialysis modality, hemodialysis and peritoneal dialysis were combined into a single dialysis subgroup for analysis.

Results

The electronic search of four databases yielded 2,378 articles (PubMed: 333; Embase: 1,005; Scopus: 1,006; Cochrane Library: 34). After removing duplicates, 1,413 articles remained. Screening of titles and abstracts reduced this number to 34 articles. Following full-text evaluation, 24 articles were excluded for not meeting the inclusion criteria. Reasons for exclusion included absence of an intervention, studies not conducted in humans, studies not involving periodontitis, studies not involving CKD patients, and lack of renal function outcomes, as shown in Figure 1. Ten articles were ultimately included in the systematic review, comprising three randomized controlled trials (RCTs) (Table 1) and seven before-after studies (Tables 2 and 3). All ten studies were included in the meta-analysis.

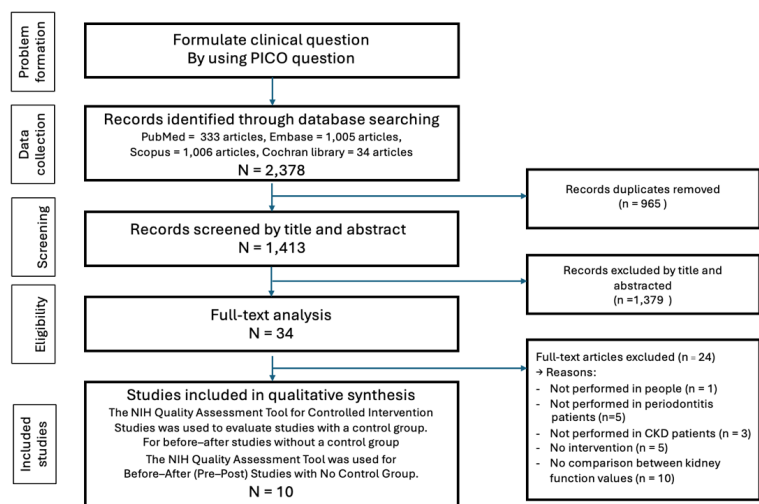


Figure 1 PRISMA flow diagram illustrating the process of study identification, screening, eligibility assessment, and final inclusion in the systematic review and meta-analysis.

Table 1 Characteristics and outcomes of randomized controlled trials evaluating periodontal therapy in patients with chronic kidney disease.

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention (Test Group)	Intervention (Control Group)	PD, CAL, BOP Results	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Fang <i>et al.</i> [42] Dialysis / ESRD Patients undergoing maintenance Hemodialysis (HD).	Enrolled: 100 patients 97 patients Intervention Group: 48 patients. Control Group: 49 patients	Clinical diagnosis of chronic periodontitis (AAP 1999: Clinical attachment loss ≥ 1 mm), ESRD requiring administration HD 3 times/ week At least 16 teeth (excluding 3rd molars)	Systemic disease that could influence periodontal disease course (including Diabetes) Antibiotic administration within previous 3 months Periodontal therapy in previous 12 months	Non-Surgical Periodontal Therapy (NSPT) consisting of OHI, supra- and subgingival scaling and root planing (SRP) using ultrasonic and hand instruments, completed within 24 hours. Supragingival prophylaxis at 3-month follow-up. Extraction of hopeless teeth at baseline	No intervention or formal oral hygiene instructions until the end of the study. (Delayed treatment approach)	PPD, CAL, BOP, PLI: Significant improvement (reduction) in the Intervention Group vs. the Control Group at follow-ups (6 weeks, 3 & 6 months) ($p < 0.001$)	Serum Creatinine (mg/ dL): Significantly higher in Intervention Group vs. Control Group at 6 weeks, 3 and 6 months (6 months: 11.44 vs 10.18 mg/dL, $p <$ 0.001) BUN (mg/dL): Significantly higher in Intervention Group vs. Control Group at 3 & 6 months (6 months: 77.67 vs 74.02 mg/ dL, $p = 0.035$)	NSPT effectively improved periodontal, circulating inflammatory (hsCRP, IL-6, Ferritin), and nutritional status (Albumin, Cr, BUN) in ESRD patients, suggesting beneficial systemic effects

Table 1 Characteristics and outcomes of randomized controlled trials evaluating periodontal therapy in patients with chronic kidney disease.
(continued)

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention (Test Group)	Intervention (Control Group)	PD, CAL, BOP Results	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Lu <i>et al.</i> [43] Dialysis / Uremia Patients with uremia undergoing Peritoneal Dialysis	Enrolled: 33 patients Intervention Group: 16 patients Control Group: 17 patients	Clinical diagnosis of chronic periodontitis (AAP1999: Clinical attachment loss ≥ 1 mm), ESRD receiving peritoneal dialysis (eGFR < 10 mL/min/1.73 m ²) Age 18–65 years.	Complete edentulous ridge Liver cirrhosis or malignant tumors Antibiotic/ immunosuppressive therapy within 3 months Other infectious diseases within 6 months	Concurrent Periodontal Therapy (basic treatment) using an ultrasonic dental scaler	Conventional Peritoneal Dialysis only.	PLI, BI, CAL: Significantly reduced in the Experimental Group compared to the Control Group at 1, 3 and 6 months ($p < 0.05$). PPD: Showed a positive correlation with serum creatinine.	Serum Creatinine (mg/ dL): Significantly lower in the Experimental Group vs. Control Group at 1, 3 and 6 months (6 months: 12.4 vs 10.8 mg/dL, $p = 0.017$)	NSPT can improve local periodontal inflammation and systemic inflammatory conditions (hsCRP, Scr) in patients with periodontitis undergoing peritoneal dialysis.

Table 1 Characteristics and outcomes of randomized controlled trials evaluating periodontal therapy in patients with chronic kidney disease. (continued)

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention (Test Group)	Intervention (Control Group)	PD, CAL, BOP Results	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Vachhani <i>et al.</i> [45]	Enrolled: 100 patients Completed: 80 patients	Clinical diagnosis of generalized moderate to severe periodontitis	ESRD requiring RRT. Immunosuppressive medications. History of infective local anesthesia, endocarditis or prosthetic heart valve.	Intensive NSPT (Scaling and Root Planing, SRP) under local anesthesia, Oral Hygiene Instructions (OHI)	Oral Hygiene Instructions (OHI) only.	PPD, CAL, BOP: Significantly decreased in the NSPT group (Group 1) compared to the OHI-only group (Group 2) at 3 and 6 months ($p < 0.001$).	eGFR: Significantly increased in Group 1 vs. Group 2 at 3 and 6 months ($p < 0.001$) UACR: Significantly decreased in Group 1 vs. Group 2 at 3 and 6 months ($p < 0.001$)	NSPT resulted in improved periodontal health, significant decreases in hs-CRP and UACR, and an increase in eGFR in pre-dialysis CKD patients, demonstrating that periodontitis treatment can hinder systemic inflammation and potentially slow CKD progression.
Pre-dialysis CKD Patients in CKD stages 3 and 4 (eGFR < 60 mL/min/1.73 m ² , excluded m ² , excluded ESRD)	Group 1 (NSPT): 47 completed Group 2 (Control): 33 completed	(cumulative PPD ≥ 40 mm, excluding PPDs < 5 mm.), CKD stage 3 or 4 (eGFR < 60 mL/min/1.73 m ² for at least 3 months) and Urine albumin- to-creatinine ratio (UACR) ≥ 70 mg/gCr on 3 consecutive occasions	Periodontal treatment in previous year.	Extraction of hopeless teeth at baseline		PISA Score: Decreased significantly in Group 1 vs. Group 2 ($p < 0.001$)		

Table 2 Characteristics and outcomes of before–after studies evaluating periodontal therapy in patients with chronic kidney disease.

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention	PD, CAL, BOP Results (Post- Treatment vs. Pre-treatment)	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Artese <i>et al.</i> [33] Pre-dialysis (only group I: eGFR 15–89 mL/ min/1.73 m ²)	Enrolled/ Completed: 21 CKD patients (Group 1).	Clinical diagnosis of chronic periodontitis (Clinical attachment loss ≥ 4 mm with BOP); Pre-dialysis patients (eGFR 15–89 mL/min) with conservative treatment Age 35–76 years and at least 15 teeth;	HIV, pregnancy, lupus, RA, antibiotic use in 6 months.	Scaling and Root Planing (SRP) by manual instruments by sextant over 6–8 weeks.	PD/CAL: Significant Decrease in severe sites ($p < 0.001$). BOP: Significant Decrease (60.4% to 46.2%, $p = 0.002$).	eGFR: Significant Increase (46.5 to 50.7 mL/min, $p = 0.04$). Serum Creatinine (mg/dL): Not Significant (2.0 to 2.1 mg/dL)	CKD pre-dialysis patients showed a good periodontal response, and periodontal treatment had a statistically significant positive effect on eGFR

Table 2 Characteristics and outcomes of before–after studies evaluating periodontal therapy in patients with chronic kidney disease. (continued)

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention	PD, CAL, BOP Results (Post- Treatment vs. Pre-treatment)	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Almeida <i>et al.</i> [44] Pre-dialysis (CKD Stages 3 or 4)	Enrolled/ Completed: 26 patients.	Clinical diagnosis of severe chronic periodontitis (≥30% of periodontal site with PD >4 mm. and > 2 sites with Clinical attachment level > 6 mm. and PD > 5mm.). CKD stages 3 and 4 (eGFR 20–70 mL/ min/1.73 m ²) for 6 months with regular control Age ≥ 30 years and at least 12 teeth	Pregnancy Previous periodontal therapy Systemic conditions that contraindicated periodontal therapy or might affect the progression or treatment of periodontitis History of endocarditis Antibiotic/ anti-inflammatory drugs in last 3 months	NSPT (SRP) over 4–6 sessions within 2 weeks Performed by single experienced periodontist	PPD/CAL: Significant Decrease in PPD 4–5 mm., > 6 mm and CAL level 4–5 mm., > 6mm (<i>p</i> < 0.001) BOP: Significant Decrease (<i>p</i> < 0.001)	eGFR: Median Significant Increase at 3 and 6 months (6 months from 34.6 to 37.6 mL/min/1.73 m ² , <i>p</i> < 0.05) increasing eGFR and reducing ADMA.	Periodontal treatment suggests a benefit to the course of CKD by significantly increasing

Table 2 Characteristics and outcomes of before–after studies evaluating periodontal therapy in patients with chronic kidney disease. (continued)

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention	PD, CAL, BOP Results (Post- Treatment vs. Pre-treatment)	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Tasdemir <i>et al.</i> [40] Dialysis (only Group III: CAPD/Diabetic Nephropathy)	Enrolled: 20 CAPD patients (group III)	Clinical diagnosis of moderate to severe periodontitis (at least 5 teeth with PD $\geq$ 5 mm., Clinical attachment level $\geq$ 2 mm. and BOP) Diabetic Nephropathy (macro albuminuria $\geq$ 300 mg in 24 h. with abnormal serum creatinine or eGFR) Age $\geq$ 25 years and at least 15 teeth	Antibiotic/ anti-inflammatory drugs use in last 6 months Smoking/alcohol Pregnancy/Lactation	Full mouth SRP and OHI within 24 hours Extraction necessary teeth Performed by same investigator ($p < 0.001$)	PD/CAL: Significant Decrease ($p < 0.001$) BOP : Significant Decrease ($p < 0.001$)	SCr: Not Significant changed (6.9 to 7.7 mg/dL) BUN : Not Significant changed (52.9 to 53.4 mg/dL)	NSPT was successful, and inflammatory markers (PTX-3, IL-6, Hs-CRP, TNF- α) significantly reduced in CAPD patients

Table 2 Characteristics and outcomes of before–after studies evaluating periodontal therapy in patients with chronic kidney disease. (continued)

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention	PD, CAL, BOP Results (Post- Treatment vs. Pre-treatment)	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Grubbs <i>et al.</i> [37] Pre-dialysis (only Intensive periodontal treatment group: eGFR 15–60 mL/min/1.73 m ²)	Enrolled: 34 patients (Intensive periodontal treatment group) Completed: 30 patients.	Clinical diagnosis of moderate to severe periodontitis (≥ 2 teeth with PD ≥ 5 mm., Clinical attachment loss ≥ 4 mm. and BOP ≥ 30%) CKD (CKD stage 3 or 4; eGFR 15–60 mL/ min/1.73 m ² reported for past 12 months)) Age 20–75 years	Dialysis, recent AKI (eGFR increase > 50%) Allergy to minocycline/ tetracycline Infective endocarditis/ prosthetic heart valve. Medication: anticoagulants, long term immunosuppressive drugs	Full mouth SRP and Local Minocycline antibiotic in deep pockets Extraction of hopeless teeth at baseline	PD/CAL: Improvement observed; PD sites ≥5 mm decreased BOP: Improvement observed; patients with BOP>30% decrease	eGFR: Not Significant changed (43.4 to 42.4 mL/min/1.73 m ²) Median UACR: Not Significant changed (116 to 182 mg/g) Median Serum NGAL: Not Significant changed (12.1 to 33.4 ng/mL) Median Urine NGAL/Cr: Not Significant changed (142 to 140 ng/g)	Pilot study demonstrated feasibility but was unsuccessful in establishing a significant magnitude of effect on kidney and inflammatory biomarkers (ADMA, IL-6, hs-CRP); slightly improvement but not significant

Table 2 Characteristics and outcomes of before–after studies evaluating periodontal therapy in patients with chronic kidney disease. (continued)

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention	PD, CAL, BOP Results (Post- Treatment vs. Pre-treatment)	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Vrinda <i>et al.</i> [39] Dialysis (HD, only Group I: dialysis < 1 yr; group II: dialysis > 1yr)	Enrolled: 40 CKD patients (Group I = 20, Group II = 20).	Clinical diagnosis of periodontitis ($\geq 30\%$ of teeth affected with attachment loss ≥ 5 mm. with BOP) ESRD undergoing Hemodialysis (HD)	Smokers/alcoholics Pregnant/lactation Receiving periodontal therapy in last 6 months.	NSPT (SRP by ultrasonic/ Gracey curettes) and OHI	PPD/CAL: Not Significant changed BOP: Significant Decrease in both groups ($p < 0.05$)	eGFR: Not Significant changed in both group (Group I: Slightly increase; Group II: Slightly iron indices in decrease). SCr: Not Significant changed in both group	NSPT contributed to improvement in acute-phase reactants (hs-CRP) and iron indices in HD patients.
Chaudhry <i>et al.</i> [38] Pre-dialysis (only group II: CKD Stages 3 and 4)	Enrolled/ Completed: 33 CKD patients (group II).	Clinical diagnosis of moderate to severe periodontitis (Clinical attachment loss ≥ 1 mm. and PPD > 3 mm) CKD Stage 3 or 4 (eGFR: 15–60 mL/min/1.73 m ²) At least 12 teeth	CKD patients with HbA1c $\geq 7.5\%$ Antibiotic/ corticosteroids/ statin/aspirin use in past month, Pregnant/lactation Patients with condition that required antibiotic prophylaxis	NSPT (SRP by ultrasonic/hand scalers) + OHI + 0.2% Chlorhexidine irrigation	PPD/CAL: Significant Decrease ($p < 0.001$) GBI: Significant Decrease ($p < 0.001$)	eGFR Not Significant changed at 6 weeks (25.96 to 27.18 mL/ min/1.73 m ²) Serum urea: Not Significant changed (12.57 to 12.30 mmol/L)	Pre-dialysis CKD patients showed good clinical periodontal and inflammatory response after NSPT (significant reduction in hs-CRP and IL-6)

Table 2 Characteristics and outcomes of before–after studies evaluating periodontal therapy in patients with chronic kidney disease. (continued)

Study	Participants (Enrollment/ Completion))	Inclusion Criteria	Exclusion Criteria	Intervention	PD, CAL, BOP Results (Post- Treatment vs. Pre-treatment)	eGFR, Serum Creatinine, BUN, UACR, NGAL	Study Conclusion
Rajaratnam <i>et al.</i> [41] Pre-dialysis (only CKD-P group: CKD stage 3 and 4)	Enrolled/ Completed: (Study period: 1 year, follow-up: 6 weeks) 20 CKD patients (group I). 1.73 m ² for at least 3 months and not on dialysis) HbA1c < 7.0% Age ≥ 18 years with at least 8 teeth	Clinical diagnosis of periodontitis (AAP 2017) CKD stage 3 or 4 (eGFR ≥ 30 and < 60 mL/min/ 1.73 m ² for at least 3 months and not on dialysis) HbA1c < 7.0% Age ≥ 18 years with at least 8 teeth	Antibiotics within the past 2 weeks On steroids, anti- inflammatory, or immunosuppressant drugs History of infective endocarditis risk (e.g., prosthetic heart valves);	NSPT (Full mouth SRP) using ultrasonic and hand scalers + OHI + 0.2% Chlorhexidine irrigation	PPD, CAL, GBI, and PS: significantly Decreased (<i>p</i> < 0.0001) in the CKD-P group post NSPT	eGFR: Median eGFR significantly Increased at 6 weeks by 16.81% (22.60 (11.97) to 26.40 (13.15) Creatinine, Urea (BUN): Post-treatment changes not reported in the results summary	NSPT is effective in enhancing periodontal health, improving renal function (eGFR), and decreasing systemic inflammation (IL-6, TGF-1) in CKD patients with periodontitis

Table 3 Mean $\pm$ standard deviation values of renal biomarkers in pre-dialysis CKD patients before and after non-surgical periodontal therapy.

Study Author/Year	Follow up time	Biomarker	Pre-treatment/ control	Post-treatment/ Intervention
Artese <i>et al.</i> [33] /2010 Before-After study	3 months	eGFR (mL/min/1.73 m ²)	46.50 $\pm$ 21.30	50.70 $\pm$ 26.80
		serum creatinine(mg/dl)	2.00 $\pm$ 1.40	2.10 $\pm$ 1.80
Almeida <i>et al.</i> [44] /2017 Before-After study	6 months	eGFR (mL/min/1.73 m ²)	35.49 $\pm$ 13.88	40.96 $\pm$ 21.49
Grubb <i>et al.</i> [37] /2020 Before-After study	12 months	eGFR (mL/min/1.73 m ²)	43.40 $\pm$ 14.70	42.40 $\pm$ 18.30
		UACR (mg/gCr)	143.77 $\pm$ 110.22	215.18 $\pm$ 149.24
		Urine NGAL/creatinine, ng/g	144.77 $\pm$ 23.67	143.80 $\pm$ 23.04
		Serum NGAL (ng/mL)	13.83 $\pm$ 6.74	32.45 $\pm$ 9.46
Vachhani <i>et al.</i> [45] /2021 RCT	6 months	UACR (mg/gCr)	218.94 $\pm$ 202.29	138.4 $\pm$ 143.69
		eGFR (mL/min/1.73 m ²)	16.06 $\pm$ 9.39	25.04 $\pm$ 11.53
Chaudhry <i>et al.</i> [38] /2022 Before-After study	1.4 months	eGFR (mL/min/1.73 m ²)	25.96 $\pm$ 10.56	27.18 $\pm$ 12.17
		BUN (mg/dl)	35.76 $\pm$ 11.84	33.40 $\pm$ 11.34
Rajaratnam <i>et al.</i> [41] /2025 Before-After study	1.4 months	eGFR (mL/min/1.73 m ²)	22.60 $\pm$ 8.87	26.40 $\pm$ 9.75

Table 4 Mean $\pm$ standard deviation values of renal biomarkers in ESRD patients undergoing dialysis before and after non-surgical periodontal therapy.

Study Author/Year	Follow up time	Biomarker	Pre-treatment/ control	Post-treatment/ Intervention
Tasdemir <i>et al.</i> [40] /2018 Before-After study	3 months	serum creatinine (mg/dl)	6.90 $\pm$ 2.90	7.70 $\pm$ 3.10
		BUN (mg/dl)	52.90 $\pm$ 16.10	53.40 $\pm$ 14.40
Vrinda <i>et al.</i> [39] /2021 Before-After study	dialysis	eGFR (mL/min/1.73 m ²)	7.40 $\pm$ 1.98	7.70 $\pm$ 2.69
	<1yr 3 months	serum creatinine (mg/dl)	8.71 $\pm$ 1.98	8.46 $\pm$ 2.31
	dialysis	eGFR (mL/min/1.73 m ²)	11.20 $\pm$ 6.32	9.45 $\pm$ 5.94
	>1yr 3 months	serum creatinine (mg/dl)	6.69 $\pm$ 2.68	8.17 $\pm$ 3.95
Fang <i>et al.</i> [42] /2015 RCT	6 months	BUN (mg/dL)	74.02 $\pm$ 8.84	77.67 $\pm$ 8.52
		serum creatinine (mg/dL)	10.18 $\pm$ 1.67	11.44 $\pm$ 1.70
Lu <i>et al.</i> [46] /2020 RCT	6 months	serum creatinine (mg/dL)	12.4 $\pm$ 3.0	10.8 $\pm$ 1.8

In the present analysis, data were extracted from specific subgroups of each included study according to study design and relevance to the objective of evaluating changes in renal function before and after non-surgical periodontal therapy (NSPT) in patients with chronic kidney disease (CKD). For the study by Grubbs *et al.* [37], only the immediate intensive treatment group was included. In the study by Chaudhry *et al.* [38], only the subgroup of CKD patients was analyzed. For Vrinda *et al.* [39], only Groups 1 and 2, which comprised CKD patients, were included. In Tasdemir *et al.* [40], only Group 3 (patients with diabetic nephropathy undergoing continuous ambulatory peritoneal dialysis) was selected for analysis. In Rajaratnam *et al.* [41], only the CKD-P group was included. Across all included subgroups, renal function parameters were compared before and after scaling and root planing.

Study characteristic

The ten included studies varied in their inclusion and exclusion criteria, baseline CKD severity, and definitions of periodontitis, which may have influenced the observed outcomes. In seven studies [33,38,40-44], the exclusion criteria included the use of antibiotics within the previous six months. Six studies [33, 37, 38, 41, 44, 45] were conducted in pre-dialysis CKD patients, while four studies [39,40,42,43] included end-stage renal disease (ESRD) patients undergoing either hemodialysis or peritoneal dialysis.

Definitions of periodontitis also differed across studies. Three studies applied the diagnostic criteria of the American Academy of Periodontology (AAP) [41-43], One study [45], periodontal prognosis was determined based on cumulative probing pocket depth (PPD). Two studies [33,39] diagnosed periodontitis based on bleeding on probing (BOP) and

clinical attachment level (CAL). Other studies [37, 38, 40, 44] used a combination of probing depth (PD), CAL, and BOP as diagnostic parameters. The proportion of participants with diabetes mellitus (DM) also varied among studies. One study [40] included only CKD patients with diabetic nephropathy, whereas several studies specifically excluded patients with diabetes [38, 42, 44].

Among the ten included studies, seven were before–after (pre–post) studies [33, 37-41, 44] and three were randomized controlled trials (RCTs). The seven before–after studies comprised a total of 190 CKD patients with periodontitis, with sample sizes ranging from 20 [40, 41] to 40 [39] participants, all aged ≥ 18 years. Five studies [33, 39-41, 44] reported formal sample size calculations. Artese *et al.* [33] estimated an α -error of 5% and a β -error of 20% to detect a 32% variation in probing depth (PD) ≥ 7 mm between groups, requiring 19 participants. Almeida *et al.* [44] conducted two separate power analyses: one for MDRD-estimated glomerular filtration rate (eGFR) with 80% power at a significance level of 0.05 to detect a 10% increase in eGFR (requiring 24 participants), and another for periodontal parameters with 80% power to detect a 50% reduction in mean probing pocket depth (PPD) and clinical attachment level (CAL) ≥ 6 mm (requiring 22 participants). Three additional studies [39-41] calculated their sample size based on data from previous reports. Studies were conducted in San Francisco [37], Turkey [45], India [39], Malaysia [38,41], and Brazil [33, 44].

For the three RCTs, only one study provided formal sample size calculations. Fang *et al.* [42] based their sample size on a pilot study using high-sensitivity C-reactive protein (hsCRP) as the primary outcome. Using a two-sided hypothesis test with an α -error of 5% and statistical power of 85%, the required sample size was calculated to be 42 participants per group. To account for potential dropouts, 50 participants were recruited

per group. These RCTs were conducted in China [42,43] and India [45].

Across all included studies, periodontal treatment consisted of non-surgical periodontal therapy (NSPT), including scaling, root planing, and oral hygiene instruction (OHI). Treatment protocols varied considerably among studies. In some studies [37, 38, 41] adjunctive antibiotics were administered at deep-pocket sites. The duration to complete full-mouth therapy ranged from 24 hours [40, 42] to 6–8 weeks [33]. However, most studies [37–39, 41, 43, 45] did not specify the exact timeframe required to complete the NSPT procedures, and six studies [33, 38, 39, 41, 43, 44] did not specify whether hopeless teeth were extracted. Only two studies [40,44] explicitly stated that all procedures were performed by a single periodontist to ensure methodological consistency, whereas the remaining studies did not provide details regarding the operators involved.

Biochemical parameters related to renal function varied across studies, reflecting differences in study design and CKD severity. The renal biomarkers assessed included eGFR [33, 37–39, 41, 44, 45], BUN [38, 40, 42], Scr [33, 39, 40, 42, 43], UACR [37, 45], NGAL, and uNGAL [37]. Because different studies used different biochemical markers to represent renal function, values were standardized where possible.

For studies reporting data as median (range or interquartile range [IQR]) [37, 41, 44], values were converted to mean and standard deviation using the method proposed by Luo *et al.* [47] and Wan *et al.* [48] to enable inclusion in the quantitative synthesis. However, minor inaccuracies may exist due to possible deviations from normal data distribution.

Overall, substantial methodological and clinical heterogeneity was observed among the

included studies, particularly in CKD staging, periodontal parameters, treatment protocols, and follow-up duration. These variations were carefully considered during data analysis and subgroup analyses to ensure interpretability and validity of pooled estimates.

Assessment risk of bias

The NIH Quality Assessment Tool for Controlled Intervention Studies was applied to randomized controlled trials (RCTs), while the NIH Tool for Before–After Studies Without a Control Group was used for pre–post studies. Quality was categorized as good, fair, or poor based on the responses to the assessment criteria. Studies with major methodological limitations or a high risk of bias in critical domains were rated as poor quality, whereas studies with minimal bias and sound methodology were rated as good quality. Studies with some concerns that were not sufficient to invalidate their results were classified as fair quality.

Good-quality studies clearly described the study population, setting, interventions, and comparison groups; used valid methods for participant allocation; reported low dropout rates with transparent explanations for withdrawals; implemented appropriate measures to minimize bias; and used valid outcome assessment methods.

Fair-quality studies showed some susceptibility to bias, but not to an extent that would invalidate their findings. Although these studies did not meet all criteria for a “good” rating, there was no strong indication that methodological limitations introduced substantial bias. Some information may have been missing, making it difficult to fully evaluate potential limitations. The “fair” category therefore includes studies ranging from valid to probably valid, with varying methodological strengths and weaknesses.

Poor-quality studies contained significant flaws in study design, analysis, or reporting, such as high levels of missing data, inconsistencies in reporting, or concerns regarding intervention delivery that could invalidate the results. Consequently, their findings may reflect methodological weaknesses rather than true differences between study groups.

The results of the risk of bias assessment are presented in Table 5. Bias assessments for the seven before-after studies were performed using the National Institutes of Health (NIH) quality assessment tool for before-after studies with no control group. Three of the seven studies explicitly excluded participants who had previously received periodontal therapy or antibiotic treatment prior to recruitment and clearly specified the timeframe required to complete the NSPT procedures, thereby ensuring transparency and reproducibility of the intervention protocol. These studies were therefore rated as having a low risk of bias in this domain. In contrast, the remaining four studies were classified as having a moderate risk of bias because the authors did not report participants' prior history of periodontal therapy and did not clearly indicate whether or when the NSPT procedures were completed. In addition, some studies did not provide explanations for participant dropouts, which may further affect the reliability of the outcome assessment.

For the three RCTs presented in Table 6, blinding of participants was not feasible due to the nature of the intervention. One study [43] was rated as having a high risk of bias because the method of randomization was not clearly described. Another study [45] was assessed as having a moderate risk of bias, as it employed appropriate randomization methods; however, the dropout rate was significantly higher in the control group than in the intervention group. The remaining study [42] was judged to have a low risk of bias in this domain.

Table 5 Risk of bias assessment of before-after studies

	Artese <i>et al.</i> 2010	Almeida <i>et al.</i> 2017	Tasdemir <i>et al.</i> 2018	Grubbs <i>et al.</i> 2020	Vrinda <i>et al.</i> 2021	Chaudhry <i>et al.</i> 2022	Rajatinam <i>et al.</i> 2025
1. Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Yes	Yes	Yes	Mixed	Yes	Yes	Yes
4. Were all eligible participants that met the prespecified entry criteria enrolled?	Cannot Determine	No	No	No	Cannot Determine	No	No

Table 5 Risk of bias assessment of before-after studies (continued)

	Artese <i>et al.</i> 2010	Almeida <i>et al.</i> 2017	Tasdemir <i>et al.</i> 2018	Grubbs <i>et al.</i> 2020	Vrinda <i>et al.</i> 2021	Chaudhry <i>et al.</i> 2022	Rajatinam <i>et al.</i> 2025
5. Was the sample size sufficiently large to provide confidence in the findings?	No	No	No	No	No	No	No
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	Yes	Yes	Yes	No	No	No	No
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	Cannot Determine	Yes	Cannot Determine	No	Cannot Determine	Cannot Determine	Cannot Determine
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	No	Yes	No	Yes	No	No	No
12. If the intervention was conducted at a group level did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	NA (No)	NA (No)	NA (No)	NA (No)	NA (No)	NA (No)	No
	Good	Good	Good	Fair	Fair	Fair	Fair

Table 6 Risk of bias assessment of RCT studies

	Fang 2015	Lu <i>et al.</i> 2021	Vachhani 2021
1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?	Yes	Yes	Yes
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	Yes	Cannot Determine	No
3. Was the treatment allocation concealed (so that assignments could not be predicted)?	Yes	No	No
4. Were study participants and providers blinded to treatment group assignment?	No	No	No
5. Were the people assessing the outcomes blinded to the participants' group assignments?	Yes	Cannot Determine	Yes
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	Yes	Yes	Yes
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	Yes	Cannot Determine	Yes
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	Yes	Cannot Determine	No
9. Was there high adherence to the intervention protocols for each treatment group?	Yes	Yes	Yes
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	Yes	Yes	Yes
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	Yes	Yes	Yes
12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	Yes	No	No
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	Cannot Determine	Cannot Determine	Cannot Determine
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?	Yes	No	No
	Good	Poor	Fair

Effect of periodontal treatment

Ten studies assessed renal function using at least one of the following parameters: eGFR, BUN, serum creatinine, UACR, NGAL, and urinary NGAL.

Among pre-dialysis patients, three before-after studies [33, 41, 44] and one randomized controlled trial [45] reported statistically significant improvements ($p < .05$) in eGFR or UACR. Conversely, two before-after studies [37, 38] reported no statistically significant changes in eGFR, BUN, UACR, or NGAL after periodontal treatment.

For dialysis patients, the outcomes related to renal parameters were mixed. One randomized controlled trial involving patients undergoing peritoneal dialysis [43] reported a significant decrease in serum creatinine levels. In contrast, another randomized controlled trial involving hemodialysis patients [42] observed a statistically significant increase in both serum creatinine and BUN levels after treatment. Furthermore, two before-after studies [39,40] found no significant changes in serum creatinine, BUN, or eGFR in the dialysis groups.

Meta-analysis and quality of evidence assessments

The meta-analysis of renal function-related parameters included ten studies. Seven before-

after studies and three RCTs were analyzed separately. For the before-after studies, paired analysis methods were applied by calculating the standardized mean change (SMC) between baseline and follow-up measurements after periodontal treatment. The effect size was estimated using the mean difference between pre- and post-treatment values and the corresponding standard deviations, assuming a correlation coefficient of 0.5 between baseline and follow-up measurements. For RCTs, the standardized mean difference (SMD) between intervention and control groups was calculated.

Funnel plots with pseudo 95% confidence limits were generated to visually assess potential publication bias. The funnel plots for both study designs appeared asymmetrical, with studies more widely scattered in the lower part of the plots (Figure 2). However, given the limited number of included studies—particularly in the RCT subgroup—the interpretation of funnel plot asymmetry should be made with caution. The observed pattern may reflect small-study effects, clinical heterogeneity, or methodological variability rather than true publication bias. This observation is consistent with the moderate heterogeneity identified in the meta-analysis.

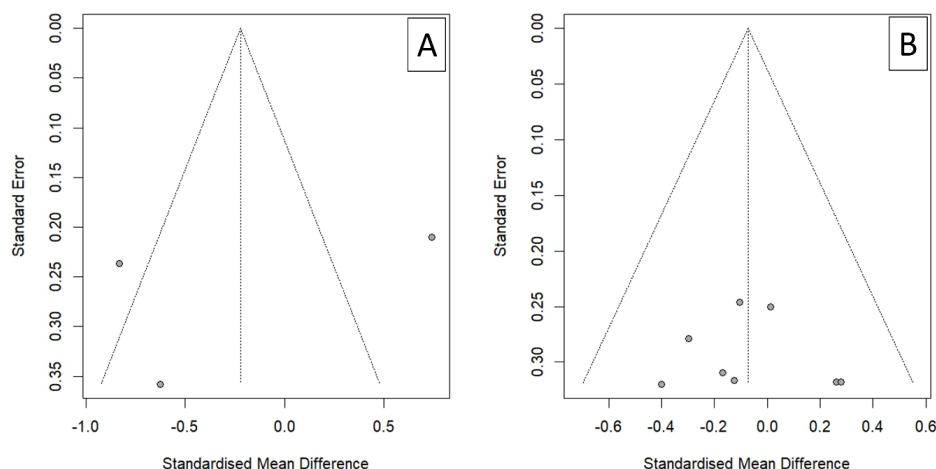


Figure 2 Funnel plots: A; RCTs studies, B; before-after studies

Cochran's Q test and the inconsistency index (I^2) were calculated for both pre-post studies and RCTs. According to Cochrane thresholds, no significant heterogeneity was detected in the pre-

post studies group ($I^2 = 16.9\%$, $p = .297$), whereas considerable heterogeneity was observed in the RCT group ($I^2 = 92.8\%$, $p < .001$), as shown in Figures 3 and 4.

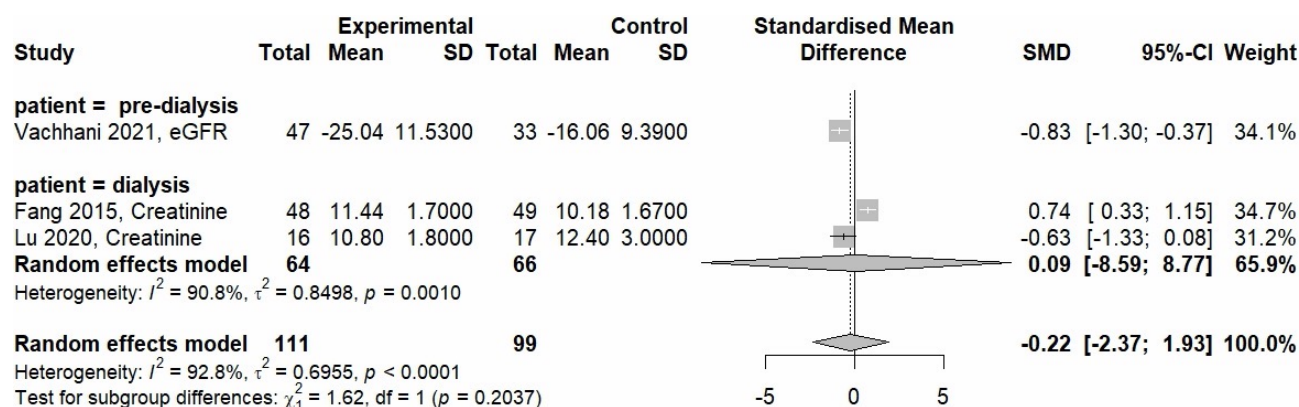


Figure 3 Forest plot of RCTs studies showing the standardized mean differences (SMDs) in renal function parameters

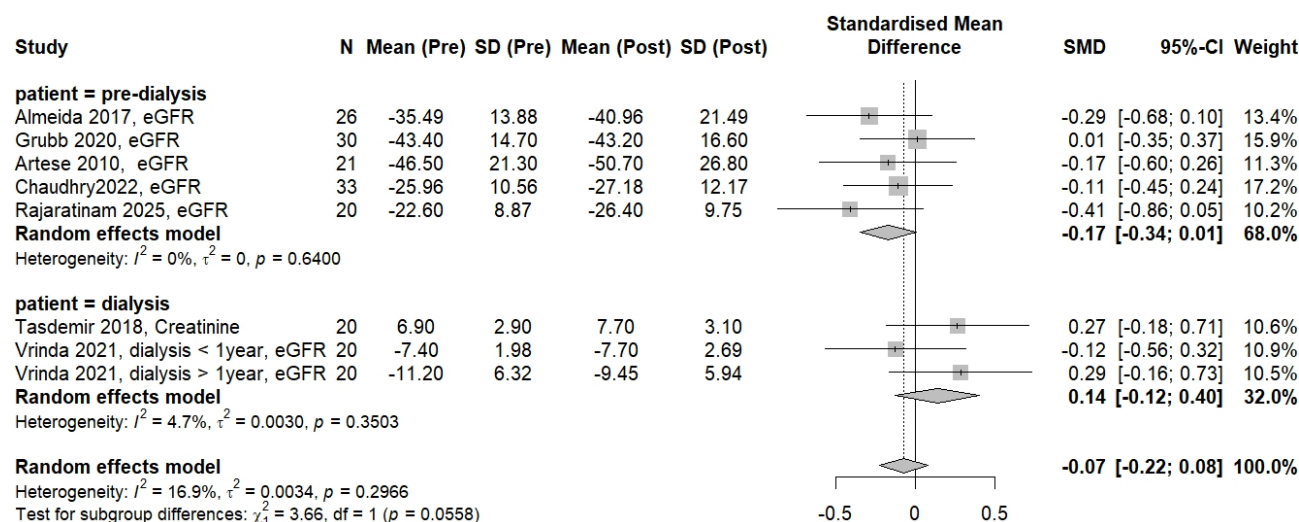


Figure 4 Forest plot of before-after studies showing the standardized mean differences (SMDs) in renal function parameters

A negative standardized mean difference (SMD) was defined as an improvement in renal function. To ensure consistent interpretation of effect direction across renal biomarkers in the meta-analysis, changes in eGFR were multiplied by -1 so that improvements across biomarkers

were aligned in the same direction as changes in serum creatinine. This transformation was applied solely for statistical pooling and does not alter the biological interpretation of eGFR, where higher values indicate better kidney function. Pooled effects were estimated using a random-effects

model, and heterogeneity across studies was expressed as I^2 .

In the RCT group, three studies [44, 45, 47] assessing eGFR (reversed for interpretability) and serum creatinine showed non-significant improvements in renal function following periodontal therapy.

In the before–after studies group, pooled data from eight comparisons derived from seven studies [33, 39–43, 46] were analyzed. In the pre-dialysis subgroup, the results indicated a slight but non-statistically significant improvement in eGFR levels after treatment. In contrast, pooled data in the dialysis subgroup indicated a non-statistically significant worsening in eGFR and serum creatinine levels.

These findings suggest that periodontal therapy may be associated with a modest, non-significant trend toward improved renal function in pre-dialysis patients. However, no measurable benefit was observed in dialysis patients, and the pooled results indicated a tendency toward worsening renal parameters after treatment.

Discussion

This systematic review and meta-analysis aimed to evaluate the effect of non-surgical periodontal therapy (NSPT) on renal function in patients with chronic kidney disease (CKD). Based on updated subgroup analyses stratifying patients into pre-dialysis and dialysis cohorts, the overall pooled findings indicate that periodontal treatment does not significantly improve traditional renal function parameters, including eGFR, and serum creatinine. These findings are consistent with recent reviews [35] suggesting that the evidence supporting the direct renal benefits of periodontal therapy remains inconclusive.

In the pre-dialysis subgroup, NSPT effectively improved local periodontal conditions, such as probing depth (PD) and clinical attachment level (CAL). However, the pooled analysis demonstrated only a small and statistically non-significant trend toward improvement in renal parameters. Although some individual studies, such as Vachhani *et al.* [45] and Almeida *et al.* [44], reported statistically significant improvements in eGFR and UACR, the overall pooled data lacked statistical significance. This discrepancy may be explained by the progressive and largely irreversible nature of nephron loss in CKD [49]. While reducing oral inflammation may help lower systemic inflammatory burden [50, 51], it is likely insufficient to reverse established structural renal damage within the relatively short follow-up periods (typically 3–6 months) observed in the majority of the included studies. Furthermore, evaluation of tubular injury markers, such as NGAL, showed only slight, non-significant post-treatment improvements [37].

For the dialysis (end-stage renal disease) subgroup [39, 40, 42], periodontal therapy similarly failed to yield significant improvements in serum creatinine or BUN levels. In this population, where residual renal function is minimal or absent, serum creatinine and BUN are predominantly influenced by dialysis adequacy, dietary protein intake, and muscle mass rather than actual renal filtration capacity [51]. Therefore, using these conventional biomarkers to assess the systemic impact of periodontal treatment in dialysis patients may not be physiologically appropriate. Interestingly, some studies [42] reported post-treatment increases in these markers, which could paradoxically reflect improved nutritional status [52]—for example, elevated serum albumin levels following the resolution of oral inflammation—rather than restoration of renal filtration function.

Despite the lack of significant changes in renal filtration markers, a consistent and important finding across both subgroups was the significant reduction in systemic inflammatory markers, including CRP, IL-6, and TNF- α . Given that chronic systemic inflammation is a major contributor to cardiovascular morbidity and mortality in the CKD population [49], the anti-inflammatory effects of NSPT remain clinically meaningful. Therefore, integrating periodontal care into the multidisciplinary management of CKD is important, primarily for its role in mitigating systemic inflammatory burden rather than restoring renal filtration.

This systematic review has several limitations. Most of the included studies were before-after designs with small sample sizes. The overall certainty of the evidence is substantially compromised by the moderate to high risk of bias observed across several included studies. The absence of proper control groups in observational designs makes them highly susceptible to unmeasured confounding variables. During follow-up, changes in nephroprotective medications, dietary protein intake, or dialysis regimens may independently affect renal outcomes, thereby obscuring the true effect of periodontal therapy [53]. Even within the included randomized controlled trials, challenges in achieving double blinding for dental interventions and potential limitations in allocation concealment may have introduced performance and detection bias. These methodological issues contribute to clinical heterogeneity in the meta-analysis and may lead to overestimation of systemic treatment effects, thereby reducing the strength and generalizability of the findings [54].

There was also considerable methodological variability in the definition of periodontitis, treatment intensity, and duration of follow-up. The included studies relied mainly on conventional renal biomarkers such as eGFR, BUN, serum creatinine,

and UACR. This not only increased clinical heterogeneity but also posed diagnostic limitations, as traditional markers like serum creatinine are relatively insensitive to early or subtle structural kidney changes. Except for one pilot study by Grubbs *et al.* [37] that evaluated NGAL, there is a notable lack of trials evaluating NSPT using more sensitive emerging biomarkers such as cystatin C and KIM-1. Cystatin C is freely filtered by the glomerulus and less affected by muscle mass, while KIM-1 is a specific marker of early proximal tubular injury. Consequently, the current literature's reliance on conventional biomarkers may mask subtle early-stage renal benefits of periodontal therapy.

In addition, follow-up periods varied widely, ranging from 1.4 months to 12 months, with most studies lasting 3–6 months. Although such durations may be sufficient to observe reductions in systemic inflammatory markers, they are likely too short to detect meaningful long-term structural changes in kidney function or to accurately assess CKD progression. Given the slow and progressive nature of CKD, longer follow-up periods and the use of sensitive biomarkers are necessary to determine whether periodontal therapy can slow the rate of renal decline.

Considering the irreversible nature of nephron loss, future longitudinal studies should focus primarily on the pre-dialysis population. In this group, the primary clinical outcome should emphasize slowing the rate of eGFR decline over time, thereby delaying CKD progression, rather than expecting absolute improvement in renal filtration [55, 56]. Large-scale, well-designed randomized controlled trials with extended follow-up and the incorporation of sensitive novel biomarkers such as cystatin C and KIM-1 are needed to clearly determine the impact of periodontal therapy on renal outcomes.

The overall certainty of the pooled estimates should be interpreted with caution in light of the methodological quality of the included studies. Although the majority of studies were rated as good or fair quality, one study was classified as poor quality due to substantial methodological limitations and a high risk of bias in key domains. The inclusion of fair-quality studies may have introduced moderate bias and contributed to heterogeneity, potentially affecting the precision of the pooled effect estimates. Furthermore, the poor-quality study may have exerted additional influence on the overall results. Nevertheless, no consistent pattern suggesting systematic overestimation or underestimation of treatment effects was observed. Therefore, while the meta-analysis findings provide useful evidence regarding the effect of periodontal treatment on renal outcomes, they should be interpreted with caution in light of the underlying study quality. Sensitivity analyses were not performed because the number of available studies was limited, which may restrict the assessment of the robustness of the pooled estimates. Future studies including a larger number of trials are needed to confirm these findings.

Conclusion

In conclusion, this systematic review and meta-analysis demonstrates that non-surgical periodontal therapy does not produce statistically significant improvements in traditional renal function parameters in patients with chronic kidney disease, regardless of whether they are in the pre-dialysis or dialysis stage. The current evidence base is limited by short follow-up durations and a reliance on conventional biomarkers that may lack sufficient sensitivity to detect early renal changes.

However, periodontal treatment consistently and significantly reduces systemic inflammatory mediators across all CKD stages. Given the substantial role of chronic inflammation in cardiovascular complications and overall disease progression in CKD, periodontal therapy remains an important component of comprehensive patient care.

Future well-designed, long-term randomized controlled trials incorporating highly sensitive novel biomarkers (e.g., cystatin C and kidney injury molecule-1 [KIM-1]) and standardized methodologies are needed to better determine the systemic impact of periodontal therapy in this population.

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Declaration of interest

The authors report no conflict of interest.

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