GRADUATION PROJECT

Degree in Dentistry

THE IMPACT OF PERIODONTAL THERAPY ON SYSTEMIC HEALTH: A REVIEW OF LITTERATURE

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RESUMEN

Introducción: La enfermedad periodontal ha sido asociada con la inflamación sistémica y diversas enfermedades crónicas, lo que sugiere que la salud periodontal puede tener un impacto en la salud sistémica; **Objetivos:** El objetivo principal fue de evaluar el impacto de la terapia periodontal sobre la salud sistémica; los objetivos secundarios fueron de determinar como el tratamiento periodontal puede influir en la prevención, progresión y manejo de las enfermedades sistémicas. **Métodos:** Se definió una pregunta de investigación específica y se realizó una revisión de la literatura utilizando bases de datos científicas, incluyendo ensayos clínicos aleatorizados, estudios de cohortes, estudios de casos y controles y reportes de casos que evaluaban los efectos sistémicos de la terapia periodontal; **Resultados:** utilizando criterios de elegibilidad, varios estudios fueron incluidos en el análisis. Los resultados mostraron que la terapia periodontal no quirúrgica, en particular el raspado y alisado radicular, se asoció con mejoras en los parámetros periodontales y con reducciones en los marcadores inflamatorios sistémicos, como la proteína C reactiva y las citocinas proinflamatorias. Varios estudios también informaron mejoras en parámetros metabólicos, incluido el control glucémico, así como reducciones en el estrés oxidativo; sin embargo, se observó cierta variabilidad entre los estudios; **Conclusiones:** la terapia periodontal no quirúrgica parece aportar beneficios más allá de la salud oral, contribuyendo a la mejora de las condiciones sistémicas. Se necesitan más estudios bien diseñados y con un seguimiento más prolongado, para validar estos resultados y esclarecer mejor los mecanismos biológicos.

PALABRAS CLAVE

Odontología, enfermedades periodontales, periodontitis, terapia periodontal, salud sistémica.

ABSTRACT

Introduction: Periodontal disease, systemic inflammation as well as chronic diseases are closely linked, suggesting that periodontal health may influence systemic health; **Objectives**: The primary objective was to measure the impact of NSPT on systemic health; the secondary objectives were to determine its effects on systemic inflammatory markers, metabolic control and oxidative stress, as well as its potential role in the prevention and management of systematic diseases; **Methods**: A specific research question was defined and a literature review was performed using scientific databases, including randomized controlled trials, cohort studies, case-control studies, and case reports that evaluated the systemic effects of periodontal therapy; **Results**: using eligibility criteria, several studies were included in the analysis. The findings showed that NSPT, particularly SRP, was associated with amelioration in periodontal parameters and a decrease in systemic inflammatory markers as CRP and proinflammatory cytokines. Several studies in addition to these reported improvements regarding metabolic parameters, including glycaemic control, and reductions in oxidative stress; however, some variability between studies was observed; **Conclusions**: non-surgical periodontal therapy appeared to provide benefits beyond oral health, contributing to improvements in systemic conditions. Further well-designed studies with longer follow-up time are necessary to validate these results and clarify the biological mechanisms.

KEYWORDS

Dentistry, periodontal diseases, periodontitis, periodontal therapy, systemic health.

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1. INTRODUCTION

1.1. Periodontitis

Periodontitis is a chronic inflammatory disease of multifactorial origin that affect the periodontal health and surrounding tissue. It is among the most common non-communicable condition. Is defined by the gradual loss of the periodontal supporting structure, known as the periodontium. The principals characteristics of this disease are Bleeding On Probing, and Clinical Attachment Loss with the presence of periodontal pocket > 4mm.

It is produced initially by specific microorganism, leading to the accumulation of plaque and gingival inflammation. This condition is produced after the interaction between bacterial infection and host's immune response. Gingivitis and periodontitis occur due to an imbalance whereby microbial challenge induces a dysregulated host immune response, inducing the secretion of cytokines that ultimately generate tissue breakdown as well as alveolar bone resorption. (1) Moreover, the severity and the disease progression rate will vary according to environmental factor, genetic, and individuals risk factor.

If left untreated, the disease can result in the progressive breakdown bone and surrounding structures, including the periodontal ligament, ultimately leading to tooth loss. This type of disease may have real impact on the life of the patient. His self-esteem, self-confidence and his quality of life are going to be affected. In the study of Bulut et al. (2024), a link has been made between self-esteem and oral hygiene. People with poor self-esteem demonstrate to have a poorer oral hygiene and therefore increases the symptoms of periodontal disease. Lack of self-confidence can exacerbate the vicious circle between bad hygiene, anxiety, depression and progression of the disease. (2)

1.2. Periodontitis and systemic inflammation the role of pro-inflammatory mediators

Periodontal disease is characterized by the local inflammation of the gum, a bacterial biofilm is deposed on the surface of the tooth, provoking an inflammation in the surrounding tissue.

Studies have highlighted the presence of numerous inflammatory markers in periodontal tissues. Periodontitis is associated with increased concentration of pro-inflammatory cells including IL-1β, IL-6, TNF-α, along with C-Reactive Protein (CRP). These molecules are key

mediators of the immune response triggered by infection of tissue damage and are liberated by immune cells.

For example, IL-1 play an important role in the first steps of the immune response and are going to stimulate the liberation of additional inflammatory signals. Although these cytokines are essential to preserve the body, an excessive or prolonged response can lead to chronic inflammation and contribute to various diseases, not only autoimmune disorders but also endothelial dysfunction or diabetes mellitus for example. Therefore maintaining a correct balance is crucial for preserving health.(3)

In some research it has been proven that IL-1β concentration are substantially enhanced in Gingival Crevicular Fluid (GCF) of patient having periodontal disease and decrease following periodontal treatment. This cytokine plays an important role in driving connective tissue destruction and bone loss.

Similarly, interleukin-6 (IL-6) is consistently elevated locally (GCF, tissue, saliva) and correlates with the extent of the illness; its levels could also decrease following treatment.

Additionally, TNF-α concentration are elevated in the diseased periodontium and in the serum of affected patients. Promoting inflammatory progression, osteoclast activation and bone loss.(4)

These inflammatory process involves the stimulation of pro-inflammatory cytokines, which subsequently induce CRP production by hepatocytes. (5) Increased CRP concentration, along with the systemic release of proinflammatory cytokines into systemic circulation, indicate an increase systemic inflammatory burden. Indeed, patients with chronic periodontal disease shows increased CRP amount in blood in comparison with healthy individuals, implying a link between periodontitis and systemic inflammation. High CRP level reflects an increased inflammatory process along with the destruction of the periodontium. Furthermore, after performing periodontal treatment, the level of CRP in blood decrease, implying that reducing periodontal inflammation has beneficial effect on systemic inflammatory status.

In addition to inflammatory mediators, oxidative stress is involved in the pathophysiology in the periodontal disease development and is closely linked to systemic inflammation. Oxidative stress markers reflect a dysregulation among reactive oxygen species (ROS) combined with antioxidant defences.

During periodontal inflammation, immune cells such as macrophages and neutrophils are activated and produce ROS as part of the host defence mechanism. However, excessive ROS production promotes further cytokine release and can stimulate additional ROS generation, generating a self-amplifying cycle involving oxidative stress and inflammation. This interaction

contributes to persistent inflammation leading to further local tissue destruction as well as systemic damage in distant organs. (6)

Thus, this response is not only indicative of periodontal disease, with signs such as gingival inflammation, bleeding, pocket formation, and tooth mobility, but may also contribute to the development of other systemic diseases. (3)

1.3. Periodontitis and its association with systemic diseases

Several studies have demonstrated a link relating periodontitis together with systemic disease like CVD, DM, respiratory disease, arthrosis and cancer.

1.3.1.Cardiovascular diseases

One of the most well-documented systemic links is between periodontitis and cardiovascular disease. As we have seen before, periodontal disease creates a chronic inflammation, and it make an entrance for bacteria from the periodontium to the systemic circulation. This process led to an inflammatory systemic response.

In addition to inflammatory markers such as TNF-α and hs-CRP, plasma homocysteine has also been recognized as an important biomarker associated with systemic inflammation and cardiovascular risk. Elevated homocysteine levels may reflect underlying metabolic dysregulation and oxidative stress, like other inflammatory mediators. Therefore, the reduction of systemic inflammation following NSPT appears to improve plasma homocysteine levels, further supporting the link among periodontal health, metabolic control, and cardiovascular risk. (7)

This inflammation is going to increase the risk of developing cardiovascular condition, like atherosclerosis, AVC ischemic and atrial fibrillation. It has been developed in several studies that people with periodontitis have more than twice the risk of having a cardiovascular accident. (8)

1.3.2.Diabetes mellitus

Another major systemic condition closely connected to periodontitis is diabetes mellitus. Periodontitis and diabetes are closely linked in a bidirectional way. Poorly controlled diabetes increases susceptibility to developing periodontitis (due to an exacerbated inflammatory response and impaired healing). (8) Periodontitis in turn, worsens glycaemic imbalance due to chronic systemic inflammation.

We have seen in several studies a link between periodontal disease and diabetes mellitus relationship, severe periodontitis has been associated to increased serum HbA1c concentration in both, diabetic and non-diabetics individuals (5).
Therefore, it is crucial to take care of periodontal health and join management between doctors and dentist to improve diabetes control and prevent further complications.

1.3.3.Respiratory diseases

Beyond metabolic and cardiovascular effect, periodontitis has also been linked to several respiratory disease. Oral bacteria present in periodontal disease are inhaled through the respiratory system leading to pulmonary inflammation or aggravating existing infection.
Patient with periodontitis exhibit a reduction in respiratory capacity of 5% in comparison to healthy individuals . (8)
Periodontal disease is defined as a chronic inflammatory disease having an impact on the systemic health.

1.3.4.Cancers

More recently, scientific interest has turned toward the association of periodontal diseases with certain cancers. Study have shown a causal and effect relationship between periodontitis and the risk of developing breast cancer. Being one of the most prevalent malignant pathology among women in the world. (9) The result present that women suffering periodontitis have 20% to 30% more risk developing breast cancer compared to women without periodontal disease. Studies suggest that periodontal bacteria like *Porphyromona gingivalis* can go through the systemic circulation and increasing systemic inflammation of the body. Inflammatory state of the body can lead to an increase in cellular proliferation, oxidative stress and gene mutation that are factors involved in cancer development. (10) It is a bidirectional relationship, oxidative stress appears to participates to the development of periodontal disease, signalling pathway are stimulated which are going to activates a systemic inflammatory response.(11)

1.4. Periodontal therapy

The periodontal therapy is based on different step with objective of reducing the infection and stopping the inflammation process. One consists in eliminating the risk factor. Controlling the potential risk factors contribute substantially to reduce periodontal disease development.

The first step of periodontal treatment is to control the apparition of supragingival biofilm. Either at home with technique of brushing applicated by the patient or at the dental office. Depending on the level of the disease, only the first step could be sufficient. At gingivitis stage, control of supragingival biofilm is enough to stop the inflammatory process. For patient diagnosed with periodontitis, a more complete treatment is needed.

The second step of the treatment is focus on removing subgingival biofilm and calculus. Subgingival instrumentation, or scaling and root planing may be performed. Studies have shown an improvement of the periodontal condition with these two steps of treatments. With an improvement in periodontal clinical outcomes. (12) In some cases, the outcomes of the two steps periodontal therapy are not sufficient, and more advanced treatments are required to achieve optimal results.

If the inflammation is still present two options are available to us. We can either repeat the last step, the scaling and root planing procedures or proceed with periodontal surgery. (12)

Periodontal therapy improves the systemic health, reducing the systemic inflammation, leading to an improvement in the management of diabetes and other cardiovascular disease.

Further studies have presented a periodontal - systemic inflammation association. The objective of the present literature is to analyse the power of periodontal therapy on systemic health and to determine how periodontal treatment may influence the prevention, progression and management of systemic diseases.

2. OBJETIVES

Further studies have presented a significant link between periodontal disease and systemic inflammation. The objective of the present literature is to analyse the power of periodontal therapy on systemic health and the secondary objectives are to determine how periodontal treatment may influence the prevention, progression and management of systemic diseases.

3. MATERIAL AND METHODS

3.1.Identification of the PICO question

The documentary research was conducted to answer the following question:
In patients suffering periodontal diseases, how does periodontal therapy have an impact on systemic health?

PICO question:
In patients suffering periodontal disease, how does periodontal therapy compared to the non-treatment affect the level of inflammatory markers on systemic health?

P (patient)	**I** (intervention):	**C** (comparison)	**O** (outcomes)
Which group of patients will be studied?	**Which intervention is to be researched?**	**What is the alternative or control group in the research?**	**What results are expected from the intervention?**
Adults having periodontitis #1 periodontal disease **OR** #2 periodontal patients	Non-surgical or surgical periodontal therapy #3 periodontal therapy OR #4 basic periodontal therapy #5 surgical periodontal therapy	Non treated patients	Improvement in the levels of inflammatory marker #6 systemic inflammatory markers

Table 1. Search according to the PICO question.

3.2 Eligibility criteria

3.2.1 Inclusion criteria

The inclusion criteria consist of:

- **Study design:** Randomized control trial and controlled clinical trial, cohort or case control studies, and meta-analysis. Publication in English after 2015.
- **Patients:** All patients (adults > 18 years old) diagnosed with periodontal disease.
- **Intervention:** Periodontal therapy including non-surgical periodontal therapy and surgical periodontal therapy.
- **Outcomes variables:** Studies evaluating systemic health outcomes associated with periodontal therapy such as, C-reactive protein level, HbA1c level and inflammatory biomarkers level, pregnancy outcomes.

3.2.2. Exclusion criteria

Exclusion criteria consist of:

- **Study design:** Case report, case series, letter and comment to the editor, narrative review, expert report. Studies published earlier than 2014.
- **Patients:** Experimental studies in vitro and in animal, studies involving participants under 18 years old and studies including patients without periodontal disease.
- **Intervention:** Studies not involving periodontal therapy.
- **Outcomes variables:** Studies that does not evaluates systemic health outcomes associated with periodontal therapy.

3.3. Sources of information

A systematic and comprehensive literature review was done using the following database, PubMed and Medline Complete.

3.4. Search strategy

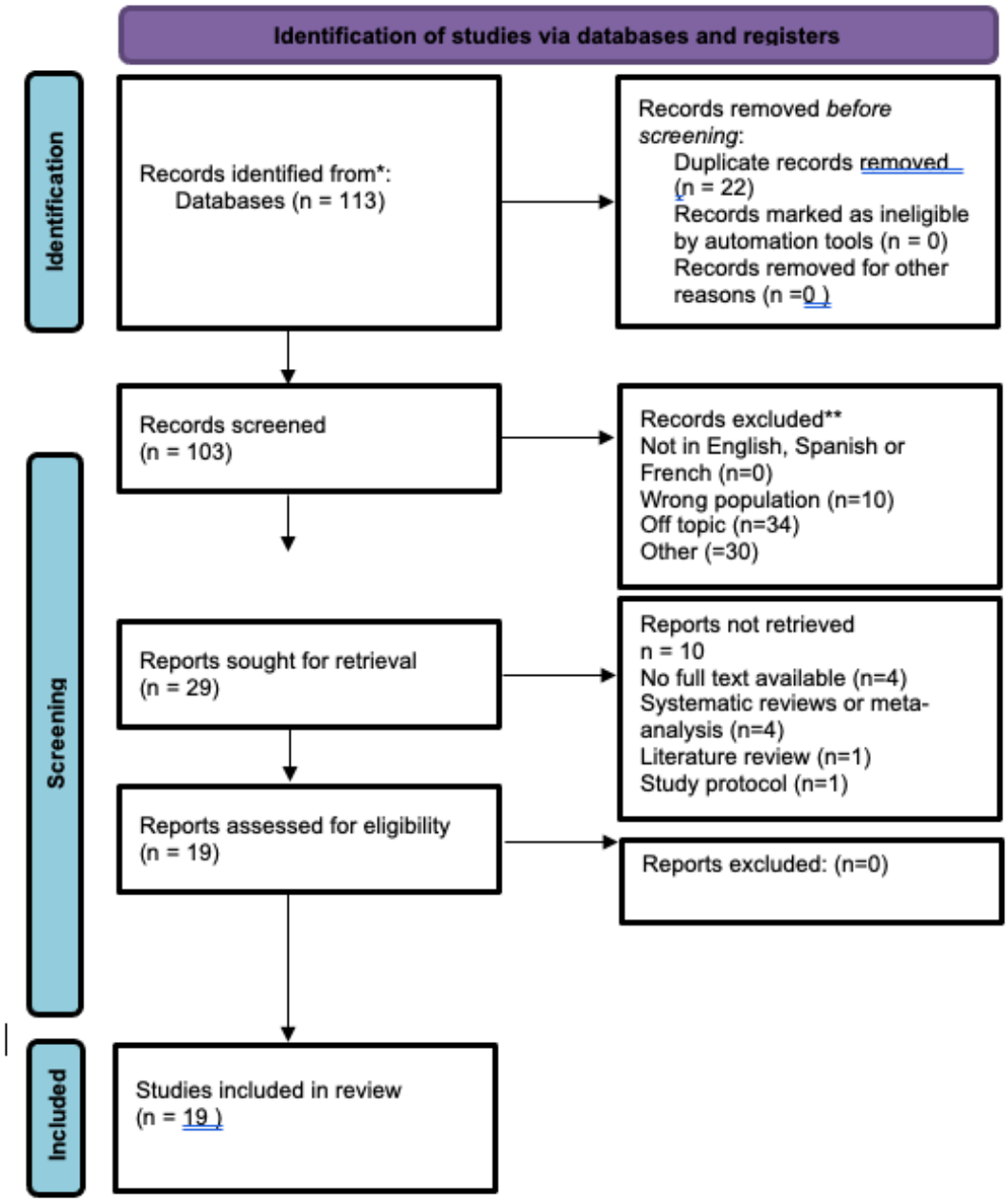
For the research we used key words of the PICO question. Each terms were added to the "query box" in PubMed. Boolean operators (AND, OR, NOT) were used to increase the specificity and sensitivity of the search. Firstly, for the patients "periodontal patients" will be added, for the intervention "periodontal therapy" OR "basic periodontal therapy" OR "surgical periodontal therapy" will be added and for the outcomes "systemic inflammatory markers" will be added. The primary search through PubMed was constructed as follow: ("periodontal disease"), ("periodontal treatment"), (systemic inflammation), ("systemic inflammatory markers). To finally obtain the final search equation: ((((periodontal patients) AND (periodontal therapy)) OR (surgical periodontal therapy)) OR (basic periodontal therapy)) AND (systemic inflammatory markers). To ensure an up-to-date review, only studies published after 2020 were included.

The final search question was the following: ((((periodontal patients) AND (periodontal therapy)) OR (surgical periodontal therapy)) OR (basic periodontal therapy)) AND (systemic inflammatory markers).

4. RESULTS

4.1 – Study selection

103 articles were obtained from primary research on PubMed (n=103). Among them 29 become eligible by title and abstract. However, some were excluded if they were not in English, if there were of topic or were published before 2015. The full text article was then obtained and carefully assessed. As result 19 met the inclusion criteria and were included in this review.



Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

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Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Nair S, Nisha KJ., 2025(13)	Interventional clinical study	n = 60 30 healthy individuals and 30 patients with generalized stage II–IV periodontitis	NSPT	Healthy group vs periodontitis group; baseline vs post-treatment	Salivary and serum prolactin (PRL)	3 Months	PRL levels higher in periodontitis patients. PRL levels decreased after periodontal therapy. Salivary PRL decreased from 8.96 to 6.30 ng/mL and serum PRL from 13.09 to 8.10 ng/mL after treatment.
Kolte r.a. Et al., 2023(14)	Randomized clinical trial (interventional study)	n = 60 60 patients with type 2 diabetes mellitus and Stage III periodontitis (30 intervention group, 30 control group)	NSPT	Intervention group (NSPT) vs control group (supragingival scaling only	IL-10, TNF-α, hs-CRP, fasting plasma glucose, post-meal glucose, HbA1c; periodontal parameters (PPD, CAL, BOP)	6 months (clinical parameters also assessed at 3 months)	NSPT improved periodontal parameters (PPD and CAL), reduced systemic inflammatory markers (TNF-α, hs-CRP), improved glycemic control (decrease in fasting glucose, post-meal glucose and HbA1c), and increased anti-inflammatory cytokine IL-10 compared with control group.

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Shrivastava d. Et al., 2024(15)	Randomized controlled trial (RCT)	n=100 100 adults with moderate to severe chronic periodontitis (30–65 years)	NSPT	Treatment group (n=50) vs control group without treatment (n=50)	CRP, IL-6, TNF-α and Framingham Risk Score	6 months	Periodontal therapy significantly reduced systemic inflammatory markers (CRP −30%, IL-6 −25%, TNF-α −28%) Decreased cardiovascular risk score compared with the control group.
Martínez-herrera et al., 2020(16)	Pilot interventional study (before–after design)	n = 49 49 obese patients with periodontitis (mean age 43.7 ± 8.5 years)	NSPT	Baseline vs 12 weeks after treatment; comparison between patients with dietary therapy vs without	Oxidative stress and inflammatory markers: ROS, superoxide production, intracellular Ca^{2+}, SOD activity, TNF-α, RBP4, P-selectin	12 weeks	Periodontal therapy I improved periodontal parameters and reduced oxidative stress markers (ROS, superoxide, intracellular Ca^{2+}).

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Lopez-oliva et al., 2026(17)	Randomized clinical study + cross-sectional analysis	Total sample size n = 159 n = 100 RA with periodontitis, n = 22 RA without periodontitis, n = 18 periodontitis without RA, n = 19 healthy controls	Intensive NSPT (PMPR: full-mouth professional mechanical plaque removal)	Intensive periodontal therapy vs oral hygiene instruction only	Cytokines in gingival crevicular fluid (IL-1β, IL-8, IL-9, IL-10, IL-12, IL-15, TNF-α, VEGF), antibodies to oral pathogens, microbiome composition	3 and 6 months	Periodontal therapy restored host-microbial balance, reduced inflammatory cytokines and circulating antibodies to oral bacteria. Improved rheumatoid arthritis activity markers (DAS28, ESR, CRP).
Parihar a.s. Et al., 2024(18)	Randomized Controlled Trial (RCT)	n = 2500 2500 adults with chronic respiratory diseases (COPD or asthma) and moderate to severe periodontitis	NSPT combined with pulmonary rehabilitation	Pulmonary rehabilitation (PR) alone vs PR + periodontal therapy	Systemic inflammatory markers: CRP and IL-6; clinical periodontal parameters (probing depth, CAL, bleeding on probing)	5 years	PR + periodontal therapy group showed greater improvement in lung function (FEV1 +220 mL vs +150 mL), better quality of life scores, and a larger reduction in systemic inflammatory markers (CRP and IL-6) compared with PR alone.

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Rabelo m.s. Et al., 2021(19)	Clinical interventional study	n = 60 divided into four groups: healthy controls, normoglycemic with generalized periodontitis, pre-diabetes with generalized periodontitis, and type 2 diabetes with generalized periodontitis	NSPT	Baseline vs 30 days after treatment; comparison between glycemic status groups	Cytokines in GCF, saliva and serum: IL-1β, IL-2, IL-6, IL-8, IL-4, IL-5, IL-10, IFN-γ, GM-CSF, TNF-α	30 days	Periodontal therapy reduces inflammatory markers (especially IL-1β and IFN-γ) in gingival crevicular fluid and saliva. No significant changes were observed in systemic serum cytokine levels.

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Kaveri a. Et al., 2024(20)	Prospective randomized clinical study	n = 60 60 patients with rheumatoid arthritis and chronic periodontitis receiving DMARD therapy	NSPT	Intervention group (periodontal therapy) vs control group (no periodontal treatment during study period)	Systemic inflammatory marker: ESR; Rheumatoid disease activity parameters: DAS28, tender joint count (TJC), swollen joint count (SJC), VAS score; periodontal parameters (PPD, CAL, BOP)	3 months	Periodontal therapy significantly reduced rheumatoid disease activity (DAS28), ESR levels, and clinical periodontal parameters compared with the control group.
Rajaratinam h. Et al., 2025(21)	Comparative prospective cohort study	n = 60 60 participants divided into 3 groups: CKD patients with periodontitis (CKD-P, n=20), periodontitis only (P, n=20), healthy participants (HP, n=20)	NSPT	Baseline vs post-treatment; comparison between CKD-P, P and healthy groups	Systemic inflammatory markers: IL-6, TGF-β1; renal function indicators: creatinine, urea, electrolytes, eGFR; periodontal parameters (PPD, CAL, GBI, plaque score)	6 weeks	NSPT significantly improved periodontal parameters in both CKD-P and P groups. IL-6 levels significantly decreased after treatment. TGF-β1 decreased significantly in CKD-P patients. Renal function improved with a significant increase in eGFR after therapy.

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Suvan j. Et al., 2021(22)	Cohort study	n = 115 115 individuals with periodontitis: 58 obese (BMI ≥30) and 57 nonobese (BMI <25), without diabetes	Intensive NSPT (full-mouth mechanical debridement + oral hygiene instructions)	Baseline vs 2 months and 6 months after treatment; comparison between obese and nonobese groups	Glucoregulatory hormones: GLP-1, GIP, insulin, glucagon; inflammatory marker hs-CRP; oxidative stress marker malondialdehyde (MDA); metabolic markers	2 months and 6 months	Periodontal treatment improved periodontal parameters and significantly increased incretin hormones (GLP-1 and GIP). Increase in GLP-1 occurred more rapidly in obese patients. Insulin and glucagon levels did not significantly change after treatment.
Seinost g. Et al., 2020(23)	Randomized controlled trial	n = 90 90 patients with peripheral arterial disease (PAD) and severe periodontitis	NSPT with or without systemic antibiotics	Two treatment groups (therapy with antibiotics / therapy without antibiotics) vs control group without periodontal treatment	Vascular inflammation measured by **18F-FDG PET/CT**, systemic biomarkers (CRP, IL-6), periodontal parameters (PISA, BOP, CAL, PPD)	3 months	Periodontal therapy significantly improved periodontal parameters but did not significantly reduce vascular inflammation or systemic biomarkers compared with the control group.

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Markou n. Et al., 2023(24)	Randomized controlled trial	n = 60 60 patients with stage III/IV periodontitis	NSPT (FM-SRP) + adjunctive Nd:YAG laser therapy	Control group (FM-SRP alone) vs Laser A vs Laser B	CRP, IL-1β, IL-6, IL-8, IL-12, IFN-γ	12 months	Nd:YAG laser therapy prevented the increase of IL-6 in the control group at 6 weeks and reduced IL-1β levels at 6 months.
Johnston w. Et al., 2020(25)	Randomized controlled trial	n = 39 39 patients with periodontitis	FMD using ultrasonic instrumentation	FMD using hand instrumentation	CRP, IL-6, TNF-α	Baseline, Day 1, Day 7, Day 90	CRP and IL-6 increased transiently at Day 1 after treatment but returned to baseline by Day 7. No significant differences were observed between hand and ultrasonic instrumentation for systemic inflammatory markers.
Orlandi m. Et al., 2021(26)	Randomized controlled trial	n = 49 49 patients with generalized periodontitis	Remote ischemic preconditioning (RIPC) before intensive periodontal therapy	Control group receiving sham procedure before periodontal therapy	hs-CRP, IL-1β, IL-6, IL-8, IL-10, IL-12, TNF-α, IFN-γ, oxidative stress markers	Baseline, Day 1, Day 7	RIPC attenuated endothelial dysfunction and reduced the inflammatory response induced by periodontal therapy.

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Toy v.e. Et al., 2023(27)	Controlled clinical study	n = 39 39 patients with periodontitis (20 obese, 19 non-obese)	NSPT	Obese vs non-obese patients with periodontitis	TNF-α, leptin, adiponectin, resistin, MPO, NO, SOD, TAS, TOS	3 months	Periodontal therapy improved clinical parameters in both groups. Obese patients showed higher systemic inflammatory and oxidative stress markers.
Tarrad et al., 2024(28)	Case-control study	n = 45 45 systemically healthy participants (15 periodontitis, 15 gingivitis, 15 healthy controls)	NSPT	NSPT in periodontal patients	Galectin-1 and Galectin-3 levels in gingival crevicular fluid (GCF)	4 weeks	Non-surgical periodontal therapy significantly reduced Gal-1 and Gal-3 levels and improved clinical periodontal parameters.

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Hermenejildo et al., 2026(29)	Interventional pre–post study (prospective clinical study)	n = 80 80 patients with chronic periodontitis	NSPT + oral hygiene instructions)	Baseline vs 12 weeks after treatment	Mitochondrial ROS, GPX1, PGC-1α, mitochondrial membrane potential, mitochondrial respiratory capacity, TNF-α	12 weeks	Periodontal therapy improved mitochondrial function in circulating immune cells, reducing oxidative stress and increasing mitochondrial bioenergetic capacity.
Leira y. Et al., 2021(30)	Case-control study and randomized clinical trial (secondary analysis)	50 patients with severe periodontitis (n = 50) and 50 healthy controls (n = 50). Intervention study including patients with severe periodontitis (n = 69)	Intensive periodontal therapy (IPT): full-mouth supra- and subgingival debridement with local minocycline microspheres	IPT vs CPT: supragingival scaling and polishing only	Circulating bacterial endotoxin and soluble triggering receptor expressed on myeloid cells-1 (sTREM-1)	Baseline, 1 day, 1 month and 6 months	Advanced periodontitis is linked with significantly higher circulating endotoxin and sTREM-1 concentration. Intensive periodontal therapy significantly reduced sTREM-1 levels after 6 months. Endotoxin levels did not significantly change.

Table 2. Characteristics of the studies reviewed.

REFERENCES	STUDY TYPE	SAMPLE	PERIODONTAL THERAPY (INTERVENTION)	COMPARISON	BIOMARKERS EVALUATED	FOLLOW-UP TIME	OUTCOMES
Penmetsa et al., 2020 (7)	Longitudinal case-control clinical study	n = 60 (30 chronic periodontitis / 30 healthy controls)	Non-surgical periodontal therapy (scaling and root planing)	Periodontitis patients vs healthy controls + before/after therapy	Plasma homocysteine (Hcy) levels	12 weeks	Plasma homocysteine levels were higher in periodontitis patients and decreased significantly after periodontal therapy.

5. DISCUSION

The study demonstrates that NSPT, particularly scaling and root planing, impact periodontal tissue status as well as systemic inflammatory and metabolic biomarkers. Across multiple randomised control trials, cohort studies, case control studies and case reports included in this analysis, periodontal treatment was consistently link with improvements in periodontal parameters and, in many cases, reductions in systemic inflammatory biomarkers.

5.1. The impact of NSPT in relation to Systemic Inflammatory Markers

Several studies reported a reduction in systemic inflammatory markers after NSPT. For instance, Shrivastava et al. (2024) observed significant reductions in C-reactive protein (CRP), IL-6, and TNF-α levels after performing non-surgical periodontal treatment. (15) These are accompanied by an improvement in cardiovascular risk scores. This results were in accordance with the one found in the randomized clinical study written by López-Oliva et al. (2026) which demonstrated that intensive periodontal therapy reduced inflammatory cytokines and improved systemic disease activity in patients with rheumatoid arthritis.(31) These two different studies highlight that the inflammation of the periodontium appears to play a role to systemic inflammation load. Furthermore, additional clinical evidence suggests that the inflammatory response can be modulated. The RCT by Marco Orlandi et al. (2021) demonstrated that remote ischemic preconditioning performed prior to periodontal therapy attenuated endothelial dysfunction and reduced circulating inflammatory cytokines. (26). This highlights the potential for adjunctive strategies to augment the systemic benefits of periodontal therapy. On another hand Markoun. Et al Have demonstrated that Nd:Yag laser therapy prevented the increase of IL-6 and reduced IL-1β levels at 6 months.(24) In opposition, Seinost g. Et al. have found that periodontal therapy did not significantly reduce vascular inflammation or systemic biomarkers compared to the control group.(25)

5.2. The impact of NSPT on Metabolic Control

The impact of NSPT on metabolic markers has also been demonstrated in several studies. In the study written Kolte et al**.** (2023) studying patients having type 2 diabetes mellitus as well as stage III periodontitis, reported improvements in periodontal parameters along with considerable reductions in TNF-α, hs-CRP, fasting blood glucose, and HbA1c concentration

following six months of therapy have been demonstrate.(32) These findings suggest that periodontal treatment may contribute to better glycaemic control by reducing systemic inflammation. Similarly, Suvan et al. (2021) reported metabolic improvements following intensive periodontal therapy, including increases in incretin hormones such as GLP-1 and GIP, which modulate glucose metabolism.(22) In line with these findings, Toy V.E. et al. (2023) also demonstrated that NSPT resulted in enhanced clinical periodontal parameters in both obese and non-obese patients. However, their results further suggest that systemic conditions such as obesity may modulate this response, as obese patients exhibited higher levels of systemic inflammatory and oxidative stress markers. But the results demonstrate that despite the elevated inflammatory marker levels observed in obese individuals, non-surgical periodontal therapy continues to produce significant reductions in these systemic biomarkers.(27) This supports the concept that, although periodontal therapy can improve both periodontal and metabolic outcomes, the magnitude of systemic benefits may be influenced by underlying metabolic status.

5.3. Role of Periodontal therapy in Oxidative stress and Immune response

Other studies highlighted the impact of NSPT on oxidative stress and immune regulation. Martínez-Her rera et al. (2020) found that NSPT reduced oxidative stress markers such as reactive oxygen species and superoxide production, while also improving antioxidant activity(8). In another hand Hermenejildo et al. (2026) reported improvements in mitochondrial function and reductions in oxidative stress in circulating immune cells following periodontal therapy, suggesting that periodontal treatment may influence systemic cellular metabolism and inflammatory pathways.(33) Additionally, Toy et al. (2023) reported that non-surgical periodontal therapy improved oxidative stress markers such as SOD, TAS and reduced TOS and MPO levels, further supporting the contribution of NSPT in modulating systemic oxidative balance, as well as in metabolically compromised patients.

Consistently, Penmetsa et al. (2020) observed that plasma homocysteine, endothelial dysfunction and systemic inflammation were significantly elevated in periodontal patients and decreased following periodontal therapy. These results presents that the benefits of periodontal treatment are extend beyond periodontium and have an effect on systemic redox balance and inflammatory burden. (7)

Further supporting the systemic impact of periodontal therapy, Lopez-Oliva et al. (2026) reported that periodontal treatment restored host–microbial balance and reduced inflammatory cytokines and circulating antibodies against oral bacteria. Importantly, these changes were associated with improvements in rheumatoid arthritis activity markers, including DAS28, ESR, and CRP, highlighting the impact of NSPT over systemic inflammatory diseases and oxidative stress.(31). In this context, bacterial-derived circulating endotoxins, particularly lipopolysaccharides from periodontal pathogens, play a key role in triggering systemic inflammation by activating immune responses and promoting cytokine release. Supporting this mechanism, Leira Y. et al. (2021)(30) found that advanced-stage periodontal disease was linked to significantly higher concentration of circulating endotoxin and sTREM-1 levels, a marker of innate immune activation. Following intensive periodontal therapy, sTREM-1 levels were significantly reduced after six months, although endotoxin levels did not show significant changes. This suggests that, while periodontal treatment effectively modulates host inflammatory response, the persistence of endotoxins may reflect a more complex or delayed systemic clearance, reinforcing the multifactorial nature of inflammation associated with periodontal disease.

5.4 Variability between studies

However, the findings across studies are not entirely consistent. Some studies reported limited or no significant changes in systemic biomarkers after periodontal therapy. For example, Rabelo et al. (2021) observed reductions in local inflammatory markers in GCF and saliva but did not detect significant changes in systemic cytokine levels in serum.(19) , Seinost et al. (2020) found that while periodontal parameters improved significantly, systemic vascular inflammation and biomarkers such as CRP and IL-6 are not modified compared to control.(34) These discrepancies may be explained by differences in study populations, systemic health conditions, follow-up duration, or the severity of periodontal disease.

5.5 Interaction between periodontal disease and systemic conditions

Another important aspect emerging from the included studies is the potential influence of systemic conditions on treatment outcomes. For example, Rajaratinam et al. (2025) showed that Non-Surgical Periodontal Therapy decrease renal function markers concentration as well as reduced inflammatory cytokines in CDK patients.(21) Likewise, in two different studies, Kaveri et al. (2024) and Lopez-oliva et al., (2026) demonstrated that NSPT reduced rheumatoid arthritis activity markers(20)(31)

Parihar a.s. Et al., 2024, showed that periodontal therapy showed a greater improvement in lung function in the PR + periodontal therapy group. These findings highlight the complex bidirectional relationship between periodontitis and systemic diseases.(35)

From another perspective, Shrivastava D. et al. (2024) support that periodontal therapy considerably decreased cardiovascular risk scores, suggesting a beneficial effect on systemic cardiovascular health.(15) In contrast, Seinost G. et al. (2020) reported that NSPT does not have an impact on vascular inflammatory condition, highlighting inconsistencies in the current evidence regarding the impact of periodontal therapy on vascular outcomes.(34)

5.6 Study limitations

Despite the promising evidence, some limitations should be considered. The selected studies exhibit variation in design, sample size, follow-up duration, but also biomarkers evaluated. Additionally, some studies used short follow-up periods, which may not fully capture long-term systemic effects of periodontal therapy. Heterogeneity in patient populations and therapeutic protocols also makes direct comparisons difficult.

Overall, the evidence suggests that non-surgical periodontal therapy plays a significant role in reducing periodontal inflammation and may contribute to improvements in systemic inflammatory status, metabolic control, and oxidative stress. However, expanded large-scale randomized clinical trials with prolonged follow-up time remain necessary to elucidate the systemic benefits of NSPT and clarify the mechanisms underlying these effects.

6. CONCLUSIONS

In conclusion, the present literature review highlights a significant association between periodontal disease and systemic inflammation, reinforcing the concept that periodontal health is closely related with systemic health. Different studies shows that NSPT improves periodontal conditions as well as contributes to the reductions in systemic inflammatory markers, metabolic control and the modulation of oxidative stress. These effects appear to play a role in the prevention and management of some systemic conditions.

However, variability observed among studies present that the systemic impact of periodontal therapy may depend on several factors, including patient characteristics, disease severity, and study design. While the evidence supports a beneficial role of periodontal treatment in reducing systemic inflammatory burden, further well-designed, large-scale randomized controlled trials with extended duration of follow-up are required with the aim of better understand the underlying mechanisms and to confirm its long-term effects on systemic health.

Overall, this review supports the growing recognition of periodontal therapy as a potential adjunctive strategy in preventing and managing systemic diseases, emphasizing the clinical relevance of integrating oral health into comprehensive patient care.

7. SUSTAINABILITY

The sustainability of the results obtained in this review point out the broader impact of NSPT beyond individual patient outcomes. From an economic perspective, early and effective non-surgical periodontal treatment may reduce long-term healthcare costs by preventing the progression of systemic diseases such as diabetes and cardiovascular conditions and decreasing the need for more complex and expensive medical interventions.

From a social standpoint, improving periodontal health contributes to better quality of life, reduced morbidity, and increased understanding of oral - systemic health association, supporting more equitable access to preventive care. Environmentally, non-surgical approaches such as scaling and root planing represent minimally invasive interventions with relatively low resource consumption compared to surgical procedures or long-term pharmacological treatments. These aspects align with the principles of the United Nations Sustainable Development Goals, especially Goal 3 (Good Health and Well-being) and as well as Goal 12 (Responsible Consumption and Production). Therefore, integrating periodontal care into general healthcare strategies reflects a sustainable and ethically responsible approach with long-term benefits for both individuals and healthcare systems.

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9. ANNEXES