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The Influence of Smoking on Peri-Implantitis Treatment Outcomes: A Systematic Review and Evaluation of Adjunctive Therapies

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Abstract

***Background*:** Peri-implantitis is a significant complication in implant dentistry, characterized by the progressive loss of bone support around implants, often exacerbated by heavy bacterial colonization in dental plaque. Smoking, a known risk factor for periodontal disease, may adversely affect peri-implant tissue health and treatment outcomes. ***Objective*:** This systematic review aims to analyze the impact of smoking on the clinical treatment outcomes of peri-implantitis in adult patients, focusing on key clinical parameters and the effectiveness of various treatment modalities. ***Methods*:** A systematic search was conducted across several databases including PubMed, Scopus, Web of Science, and Google Scholar using keywords related to smoking and peri-implantitis treatment to identify relevant articles published in English language without any restriction for the time of publication until 30th September 2024. Studies were included on the eligibility criteria, emphasizing adult smokers with diagnosed peri-implantitis undergoing various treatments. Data extraction focused on clinical parameters outcomes including plaque index (PI), bleeding on probing (BOP), probing depth (PD), and bone levels. ***Results*:** Seven studies met the inclusion criteria, highlighting that smokers exhibited higher PI, BOP, and PD at baseline compared to non-smokers. Adjunctive therapies, particularly antimicrobial photodynamic therapy (aPDT), significantly improved clinical parameters in smokers. However, smokers demonstrated less favorable outcomes in gingival recession and bone levels post-treatment. ***Conclusion*:** Smoking negatively impacts the treatment outcomes of peri-implantitis, with smokers showing heightened inflammatory responses and less improvement in clinical parameters. Clinicians should consider smoking status when planning treatment protocols for peri-implantitis to optimize patient outcomes. Further research is warranted to develop targeted interventions for this vulnerable population.

Keywords: Peri-implantitis, smokers, treatment outcomes, dental implants.

INTRODUCTION

While the practice of implant dentistry has gained momentum in recent years, a frequent complication associated with dental implants causing inflammation of the soft and hard tissues, namely peri-implantitis, is a cause for growing concern [1]. The pathology is characterized by a progressive loss of bone supporting the implants accompanied by bleeding on probing and suppuration [2, 3]. Heavy colonization of bacteria in dental plaque provides the nidus for infection, thereby constituting the chief etiological factor for periimplantitis [4-6]. Various other factors such as systemic conditions, environmental conditions, and adverse habits such as smoking or tobacco chewing may also exacerbate the condition [7-11].

Smoking has long been recognized as a major risk factor in oral health, particularly in periodontal disease, which shares similarities in etiology with peri-implantitis [12, 13]. The gingival and periodontal tissues in the smoker are more susceptible to inflammation by virtue of reduced blood flow, increased inflammatory cells, and impaired wound healing [14]. The chemicals in cigarettes, especially nicotine, further suppress the immune system subsequently impairing bone

regeneration [15, 16]. Therefore, patients are advised to refrain from smoking in the immediate period of at least two months following implant placement, at least until adequate osseointegration has occurred [17]. On the contrary, a recent systematic review of prospective studies failed to confirm the detrimental effect of smoking on implant success [18].

The management of peri-implantitis technically involves eradicating these bacteria and restoring the normal health of peri-implant tissues through various treatment methods such as mechanical debridement (MD), antimicrobial therapy, and laser treatment [19-23]. Clinicians may also resort to surgical interventions such as guided bone regeneration and implant surface decontamination when the initial non-invasive methods fail to show any results [22-24]. The success of these treatments is often compromised in smokers due to their altered healing capacity and heightened inflammatory response [14, 25]. While numerous studies have focused on the success or failure rates of implants and the development of periimplantitis in smokers, very few studies have focused on the influence of smoking on the treatment of periimplantitis, once it has developed [26, 27].

The nature of the findings of these studies has also been inconsistent owing to conflicting evidence that has been a subject of debate [18, 27]. Therefore, there is a need to thoroughly review the evidence regarding the influence of smoking on the various treatment strategies employed for the management of peri-implantitis. In this context, the present systematic review aimed to analyze the influence of smoking on the outcomes of various methods used for the treatment of peri-implantitis with the objective of informing clinicians on the best practices and protocol determination for the possibly vulnerable group of smokers.

The primary review question is 'What is the impact of smoking on the clinical treatment outcomes of peri-implantitis in adult patients?' which can be further divided into the following specific questions:

(i) How does smoking influence key clinical parameters such as plaque index (PI), bleeding on probing (BOP), probing depth (PD), gingival recession (GR), keratinized mucosa width (KMW), and bone levels (BL)) in patients receiving peri-implantitis treatment?

(ii) What is the comparative effectiveness of different treatment modalities including mechanical debridement (MD), adjunctive antimicrobial photodynamic therapy (aPDT), or any other methods alone, or in combination in smokers versus non-smokers?

(iii) Are smokers more likely to experience adverse peri-implant health outcomes post-treatment compared to non-smokers?

MATERIALS AND METHODS

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the protocol was registered in the PROSPERO database (CRD:42024582040) [28].

Search Strategy

A systematic search was performed using the keywords ('smoking' OR 'smokers') AND ('periimplantitis' OR 'peri-implantitis') AND ('treatment' OR 'outcome') to identify scientific literature published in the English language. The search was performed across multiple databases including PubMed, Scopus, Web of Science, and Google Scholar to identify articles published until 30th September 2024 without any restriction for the date of publication. The reference lists of the selected articles were also scanned manually to identify additional relevant studies that were possibly missed during the electronic search.

Eligibility Criteria

Studies were included if they satisfied the following Population, Intervention, Comparison, Outcome and Study designs (PICOS) criteria.

Population: Adult patients (≥18 years old) with a smoking habit (cigarette, waterpipe, or electronic cigarette users) diagnosed with peri-implantitis and undergoing treatment for the condition. The participants were stratified based on their smoking status (smokers, non-smokers, former smokers). Studies involving pediatric populations or animals or in which there was ambiguity regarding the status of smoking were excluded.

Intervention: The primary exposure of interest in this review was smoking, including cigarette smoking, waterpipe smoking, and electronic cigarette use. This exposure was analyzed in the context of peri-implantitis treatment. Studies assessing both surgical (e.g., guided bone regeneration) and/or non-surgical (e.g., MD, antimicrobial photodynamic therapy [aPDT]) interventions were included. Studies focusing on peri-implant maintenance therapy alone instead of treating peri-implantitis or those where smoking was not evaluated as an exposure were excluded.

Comparator: The primary comparator was non-smokers. In studies where different types or intensities of smoking were studied, the respective populations were considered as subgroups.

Outcome: The primary outcomes included PI, BOP, PD, BL, GR, and KMW. Additionally, implant survival rates and patient-reported outcomes were also recorded. The outcomes were measured at baseline and after peri-implantitis treatment, with follow-up periods as reported by individual studies. Studies not reporting the outcomes in relation to smokers or having ambiguity

regarding the association between smoking and the outcomes were excluded.

Studies: Randomized and non-randomized clinical trials, cohort studies, case-control studies, observational studies, and retrospective studies were included. In vitro studies, animal-based studies, case reports, and series were excluded.

Study Selection

Two independent reviewers screened the titles and abstracts to eliminate studies that did not meet the inclusion criteria. Full-text articles were obtained for the remaining studies, and a detailed review was performed to assess their eligibility for inclusion. Any disagreements between reviewers regarding the eligibility of studies were resolved through discussion or, if necessary, by consulting a third reviewer to reach a consensus.

Data Extraction

Data extraction was performed using a standardized data collection form. The key information extracted from each study included the author(s) and year of publication, study design, sample size, characteristics of the study population (including smoking status, age, and gender distribution), the type of peri-implantitis treatment employed (non-surgical or surgical), and the duration of follow-up. Primary treatment outcomes such as implant survival rates, probing depth reduction, changes in bone levels, and bleeding on probing were recorded, along with any differences in outcomes between smokers and non-smokers. The extracted data were summarized descriptively, and a qualitative synthesis of the treatment outcomes was conducted.

Risk of Bias Assessment

The risk of bias in Non-randomized Studies - of Interventions (ROBINS-I) tool was used to assess the risk of bias for non-randomized clinical trials [29]. For cross-sectional, cohort, and case-control studies, the Newcastle-Ottawa Scale (NOS) was used [30]. The quality of evidence across the articles was rated using the GRADE approach [31].

RESULTS

The systematic review included a total of seven studies that evaluated the effect of smoking on peri-implantitis treatment outcomes (Figure 1) [32-38]. The data extracted related to the characteristics and outcomes of all the included studies is summarized in Table 1. Across these studies, the treatment methods used included mechanical debridement (MD) alone and in combination with adjunctive antimicrobial photodynamic therapy (aPDT) and systemic antibiotics. Participants included smokers (cigarette, waterpipe, and electronic cigarette users), former smokers, non-smokers, and those with underlying conditions such as Type 2 diabetes. The clinical parameters commonly assessed across the studies included PI, BOP, PD, BL, GR, and KMW.

Table 1: Data extracted related to the characteristics and outcomes of all the included studies

Sr. No.	Author	Year	Country	Study Design	Sample Size (Implants)	Age Range (Years) Mean ± S.D.	Gender	Participants	Parameters Assessed	Implant Duration (Months) Mean ± S.D.	Vaping Duration (Years) Mean ± S.D.	Treatment Methods	Results	p-value	Conclusions Reported
1	Al Rifaiy *et al*.,	2018	Saudi Arabia	Parallel-arm, RCT	n=38, N=65	G 1: 33.6 ± 2.8, G 2: 35.4 ± 2.1	38 M	Smokers (e-cigs)	PI, BoP, PD	G 1: 48.7 ± 9.7, G 2: 52.3 ± 7.5	G 1: 4.8 ± 1.9, G 2: 4.1 ± 1.7	G 1: MD + aPDT, G 2: MD	PI: G 1 (Baseline: 51.1 ± 10.4, 12m: 13.2 ± 3.4), G 2 (Baseline: 46.8 ± 7.9, 12m: 27.5 ± 8.8); BoP: G 1 (Baseline: 14.6 ± 3.1, 12m: 11.7 ± 0.5), G 2 (Baseline: 9.2 ± 1.0, 12m: 7.9 ± 0.2); PD: G 1 (Baseline: 4.3 ± 0.8, 12m: 2.1 ± 0.3)	p < 0.001	aPDT is more effective than MD alone in treating p-iM

5	4	3	2
Abduljabbar T	Alqahtani F	Javed F	Nart J
2017	2019	2017	2019
Saudi Arabia	Saudi Arabia	Saudi Arabia	Spain
Clinical trial	RCT	RCT	Prospective clinical series
n=64	n=98	n=54	N=21
Type 2DS: 52.6 ± 0.8, Type 2DNS: 54.4 ± 1.2	CS: 52.3 ± 2.2, WS: 55.6 ± 1.6, NS: 54.2 ± 2.2	G 1: 50.6 ± 0.8, G 2: 35.4 ± 2.1	≥ 18 years
Type 2DS: 33M, Type 2DNS: 31M	CS: 34M, WS: 32M, NS: 32M	54M	2M, 19F
Type 2 diabetic smokers, non-smokers	Cigarette-smokers, Waterpipe-smokers, NS	Cigarette smokers	Former smoker (5), Current smoker (1)
HbA1c, BoP, PD	PI, BoP, PD, CBL	PI, BoP, PD	Clinical: BoP, REC, SoP, PD, KM
—	—	—	—
Type 2DS: 12.7 ± 3.3, 6.3 ± 1.5 cigs/day	CS: 23.6 ± 4.6 y, 14.5 ± 3.6 cigs/day, WS: 20.5 ± 5.2 y, NS: NA	G 1: 25.2 ± 6.5, G 2: 24.6 ± 4.3	—
G 1: MD + aPDT	G 1: MD + aPDT, G 2: MD	G 1: MC + aPDT, G 2: MC	G 1: Ultrasonic scaler + aPDT
HbA1c (6mo): Type 2DS (Baseline: 9.3%, 6mo: 8.7%), Type 2DNS (Baseline: 8.4%, 6mo: 8.4%); BoP: Type 2DS (Baseline: 53.3 ± 4.2, 6mo: 48.2 ± 3.6), Type 2DNS (Baseline: 35.2 ± 3.1, 6mo: 33.1 ± 2.4); PD: Type 2DS (Baseline: 26.2 ± 3.7, 6mo: 25.1 ± 0.8), Type 2DNS (Baseline: 29.5 ± 2.4, 6mo: 25.5 ± 1.4)	BoP: G 1 vs baseline (NS > CS, WS), PI, PD, CBL: CS, WS (Not significant at 3/6 mo); BoP: NS (Significant at 3/6 mo); PI, PD: NS vs CS, WS (Significant at 3/6 mo)	PI: G 1 (Baseline: 47.6 ± 10.2, 12w: 10.4 ± 2.5), G 2 (Baseline: 51.2 ± 6.4, 12w: 23.2 ± 4.6); BoP: G 1 (Baseline: 10.2 ± 1.2, 12w: 8.8 ± 0.2), G 2 (Baseline: 8.6 ± 0.8, 12w: 6.9 ± 0.2); PD: G 1 (Baseline: 7.4 ± 0.3, 12m: 1.5 ± 0.3), G 2 (Baseline: 6.6, 12m: 3.8 ± 0.4)	Pl(%): G 1 (Baseline: 68.17, 12w: 40.91); BoP: G 1 (Baseline: 78.78, 12w: 21.22); SoP(%): G 1 (Baseline: 65.90, 12w: 6.82); PD: G 1 (Baseline: 5.34, 12w: 3.69); REC(mm): G 1 (Baseline: 0.17, 12w: 0.79); KT(mm): G 1 (Baseline: 2.59, 12w: 1.95)
$p > 0.05$	$P < 0.01$	$p < 0.001$	$p < 0.001$
Outcomes of MD + aPDT are comparable among type 2 diabetic smokers and non-smokers	MD + aPDT is effective for p-i treatment. Oral hygiene maintenance enhances the success of MD+aPDT	MC + aPDT is more effective than MC alone in treating p-iM in smokers	aPDT shows significant improvement in patients vaping e-cigs in p-iM treatment

6	Sung-Bae Lee	2022	Korea	Retrospective study	n=45, N=92	58.7 ± 11.2	22F, 23M	Smokers, Ex-smokers, Non-smokers	MBL, BoP, Peri-implantitis	—	—	G 1: Non-surgical therapy + MD, G 2: Surgical treatment	Peri-implantitis: Smokers (53.6%), Ex-smokers (58.3%), Non-smokers (87.5%); MBL: <3 mm (48.4%), ≥3 mm (66.7%), ≥4 mm (73.5%); Absence of BoP: 28.3%; Non-surgical (42.4%), Surgical (57.6%)	P=0.023, P=0.027	Long-term p-i treatment outcomes are improved by patient compliance and worsened by smoking, multiple implants, and baseline bone loss
7	AlDeeb M	2020	Saudi Arabia	Clinical trial	n=75	CS: 44.7 ± 7.2, E-cigs: 35.6 ± 4.8, NS: 41.3 ± 6.5	CS: 25M, E-cigs: 21M, NS: 25M	Cigarette smokers, E-cigarette users, NS	PI, BoP, PD, Bone biomarkers (RANKL, OPG)	CS: 32.7 ± 4.4, E-cigs: 26.8 ± 3.9, NS: 36.5 ± 7.4	CS: 8.3 ± 2.1y, E-cigs: 6.8 ± 2.5y	G 1: MD + Methylene blue-mediated PDT	PI, BoP, PD (3mo/6mo): CS, E-cigs (Significant reduction); NS (No significant change); Bone markers (RANKL, OPG): No significant change	p < 0.05, p > 0.05	Adjunctive PDT reduces clinical inflammation in p-iM. No significant change in bone biomarkers among tobacco smokers

Abbreviations: RCT: Randomized Controlled Trial; aPDT: Antimicrobial Photodynamic Therapy; MD: Mechanical Debridement; PI: Plaque Index; BoP: Bleeding on Probing; PD: Pocket Depth; p-iM: Peri-implant Mucositis; e-cigs: Electronic Cigarettes; REC: Gingival Recession; BL: Bone Level; CBL: Crestal Bone Loss; AD: Angulation of Defect; RANKL: Receptor Activator of Nuclear Factor Kappa-B Ligand; OPG: Osteoprotegerin; CS: Cigarette Smokers; WS: Waterpipe Smokers; NS: Never-Smokers; G: Group.

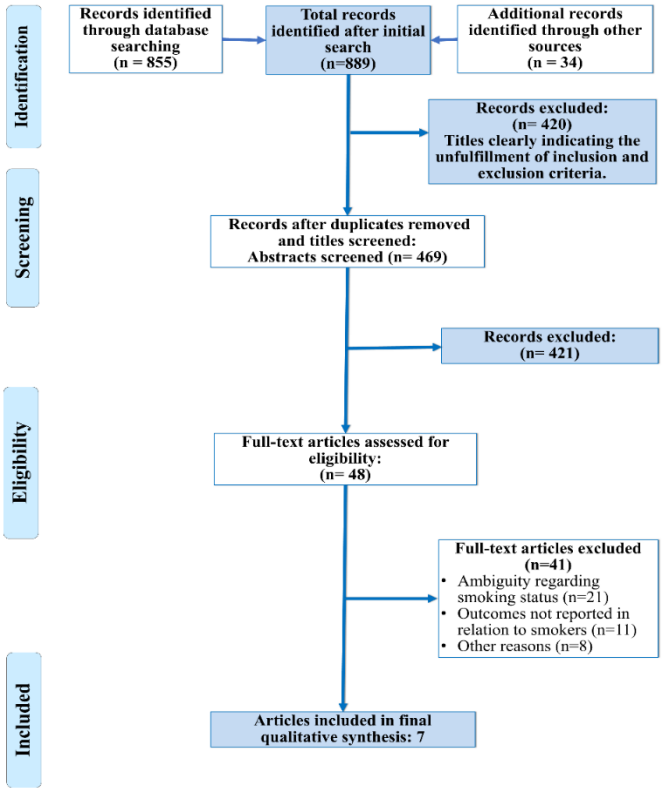

Figure 1: PRISMA Flow Diagram

Plaque Index

Out of the seven studies reviewed, six assessed the PI. Across these studies, smokers consistently showed higher baseline PI compared to non-smokers or individuals receiving adjunctive treatments like aPDT. In studies where adjunctive aPDT was employed, there was a notable reduction in PI over time. For instance, one study demonstrated a significant reduction from 51.1 ± 10.4 to 13.2 ± 3.4 in smokers treated with aPDT combined with mechanical debridement ($p<0.001$) [11]. Similarly, AlDeeb M. reported that smokers showed a mean PI reduction from 3.2 to 1.4 ($p<0.01$) when treated with aPDT [14]. On average, smokers who received only mechanical debridement showed less improvement in PI compared to those receiving adjunctive therapies.

Bleeding on Probing

All seven studies measured BOP as a key parameter. Smokers consistently exhibited higher BOP at baseline. In studies using adjunctive aPDT, BOP reduced significantly, with one study reporting a reduction from 53.3% to 48.2% among diabetic smokers and from 35.2% to 33.1% among non-smokers ($p<0.05$) [32]. AlDeeb M. also found that BOP was reduced from 62% to 40% ($p<0.05$) following treatment with aPDT in smokers [37]. BOP remained higher in smokers throughout treatment compared to non-smokers. However, smokers treated with aPDT demonstrated a greater reduction in BOP compared to those treated with mechanical debridement alone, emphasizing the benefit of adjunctive therapies in managing inflammation around implants in smokers.

Probing Depth

PD was reported in six out of seven studies, with all studies showing that smokers had deeper probing depths at baseline than non-smokers. After treatment, PD significantly decreased in smokers who received aPDT, with one study showing a reduction from 7.4 mm to 1.5 mm ($p<0.001$) [33]. AlDeeb M. similarly reported a reduction in PD from 6.8 mm to 2.2 mm ($p<0.001$) in smokers receiving aPDT [37]. Studies that used only mechanical debridement showed less substantial reductions in PD. Overall, smoking had a negative impact on PD outcomes, with smokers consistently showing less improvement in PD compared to non-smokers. However, adjunctive therapies like aPDT improved the outcomes for smokers.

Gingival Recession and Keratinized Mucosa Width

Three studies reported on GR and KMW as additional clinical parameters. Smokers exhibited greater gingival recession and reduced keratinized mucosa at baseline. Treatment with adjunctive therapies led to moderate improvement, but smokers continued to show greater gingival recession compared to non-smokers. AlDeeb M. found that GR increased significantly in smokers, highlighting that smoking impairs soft tissue healing even when adjunctive therapies are applied [37]. This trend suggests that smoking negatively affects soft tissue recovery.

Bone Levels

Three studies evaluated changes in bone levels following peri-implantitis treatment. Smoking was consistently associated with greater bone loss at baseline, and post-treatment improvements in bone levels were less pronounced in smokers compared to non-smokers. The studies showed that smoking slows the regenerative process and limits bone recovery, even with aggressive treatment modalities. Notably, AlDeeb M. reported that smokers experienced an average bone loss of 1.5 mm post-treatment, while non-smokers had an average of 0.5 mm [37]. However, those receiving adjunctive treatments like aPDT showed better outcomes in terms of bone loss reduction compared to those receiving mechanical debridement alone.

Subgroup Analysis

Subgroup analyses were conducted to assess the effects of smoking on treatment outcomes based on smoking type, duration of smoking, and presence of comorbidities. Cigarette smokers demonstrated the poorest treatment outcomes across all parameters when compared to waterpipe and electronic cigarette users. The mean PI for cigarette smokers was significantly higher (3.5) compared to waterpipe (2.8) and electronic cigarette users (2.6) ($p<0.05$). Additionally, the deepest probing depths were observed in cigarette smokers (7.2 mm) compared to waterpipe (6.1 mm) and electronic cigarette users (5.8 mm) ($p<0.01$) [37].

Longer smoking duration (more than 10 years) was associated with worse clinical outcomes. Smokers with over 10 years of smoking history had a mean reduction in PD of only 2.1 mm compared to 3.6 mm in smokers with less than 10 years ($p<0.01$).

Smokers with Type 2 diabetes showed the least improvement in clinical parameters. For example, diabetic smokers had a PI reduction from 4.0 to 3.0 ($p<0.01$) versus non-diabetic smokers who showed a reduction from 3.5 to 1.5 ($p<0.001$) [32]. Furthermore, diabetic smokers had a greater incidence of BOP at baseline (70%) compared to non-diabetic smokers (50%) ($p<0.05$).

Overall Outcomes

Across all studies, it was observed that smokers, regardless of the type (cigarette, waterpipe, or e-cigarette), responded less favorably to peri-implantitis treatment compared to non-smokers. However, adjunctive therapies like aPDT demonstrated improved clinical outcomes in smokers, resulting in greater reductions in PI, BOP, and PD compared to mechanical debridement alone. The studies consistently highlighted the need for additional treatment modalities to optimize the outcomes in smokers due to their compromised healing capacity.

Risk of bias

In the evaluation of non-randomized clinical trials by the ROBINS-I tool, all five studies assessed (Al Rifaiy *et al*., 2018; Javed F., 2017; Alqahtani F *et al*., 2019; Abduljabbar T *et al*., 2017; Al Deeb M *et al*., 2020) were found to have a moderate overall risk of bias (Figure 2). Each study demonstrated moderate confounding bias, primarily due to unadjusted demographic variables that could influence outcomes. The potential for confounding factors, such as variations in patient characteristics and baseline conditions, was not sufficiently controlled, which may impact the internal validity of the results. Participant selection was generally low in bias across all studies, indicating that the methods used to recruit and select participants were adequately transparent and rigorous.

All studies maintained low bias in classifying interventions, ensuring that participants received the intended treatments consistently. A significant concern in all studies was the moderate risk associated with deviations from intended interventions. Variability in adherence to treatment protocols was noted, which could have implications for the effectiveness of the interventions studied. Missing data and outcome measurement bias were minimal in most studies, with clear protocols for handling data reported. However, a few studies exhibited low to moderate bias in these areas, which should be considered when interpreting results. Overall, the moderate risk of bias in these non-randomized trials indicates that while the studies provide valuable insights, the findings should be interpreted with caution due to potential confounding factors and intervention variability.

The observational studies assessed using the NOS included Nart J. (2019) and Sung-Bae Lee (2022) [35, 38]. Both studies demonstrated good quality with minimal risk of bias. Both studies scored well in the selection category, reflecting robust methodologies in participant recruitment and inclusion criteria (Table 2). They effectively represented the target population, thereby enhancing the external validity of the findings. While Nart J. (2019) achieved a maximum score in comparability, Sung-Bae Lee (2022) showed slightly lower scores, primarily due to variations in the adjustment for confounding factors. Despite this, both studies were effective in minimizing bias through appropriate study designs. The outcome assessment was well-documented and consistent across both studies because of their reliable measurement tools and protocols.

Quality of Evidence

Most studies reported moderate to low inconsistency in their findings. Specifically, studies by Abduljabbar T (2017), Nart J *et al*., (2019), and Alqahtani F (2019) indicated moderate inconsistency, suggesting some variability in the results across different study contexts. In contrast, the other studies demonstrated low inconsistency, indicating that their findings were relatively stable across populations or conditions. The level of indirectness was generally low across the studies, implying that the evidence provided directly relates to the population, intervention, and outcomes of interest. Notably, Javed F *et al*., (2017) and AlDeeb M *et al*., (2020) demonstrated low indirectness, reinforcing the relevance of their findings to the clinical context.

The assessment of imprecision showed mixed results. Studies by Al Rifaiy *et al*., (2018) and Nart J *et al*., (2019) exhibited moderate imprecision, indicating that confidence intervals were wider, potentially affecting the reliability of the conclusions. Conversely, other studies, such as those conducted by Abduljabbar T (2017), Alqahtani F (2019), and AlDeeb M *et al*., (2020), reported low imprecision, reflecting more robust conclusions.

Publication bias was predominantly assessed as low in the majority of studies, signifying a reduced likelihood of selective reporting or non-publication of negative results. However, Abduljabbar T (2017) and Alqahtani F (2019) were noted to have moderate publication bias, suggesting that some risk exists for selective reporting affecting their findings. The risk of bias was a noteworthy concern across the studies. Most studies exhibited moderate risk, indicating potential flaws in study design or execution that could affect the credibility of their outcomes. Notably, Javed F *et al*., (2017) and AlDeeb M *et al*., (2020) were classified as high risk, emphasizing serious concerns regarding their methodological rigor. The overall quality of evidence across all the studies ranged from moderate to high (Table 3).

Table 2: Newcastle-Ottawa Scale (NOS) for Cross-Sectional, Cohort, Retrospective, or Case-Control Studies

Author	Year	Study Design	Selection (max 4)	Comparability (max 2)	Outcome/ Exposure (max 3)	Total Score (max 9)	Quality Rating
Nart J *et al*., [35]	2019	Prospective clinical and radiographic case series study	3	2	3	8	Good
Sung-Bae Lee *et al*., [38]	2022	Retrospective study	3	1	3	7	Good

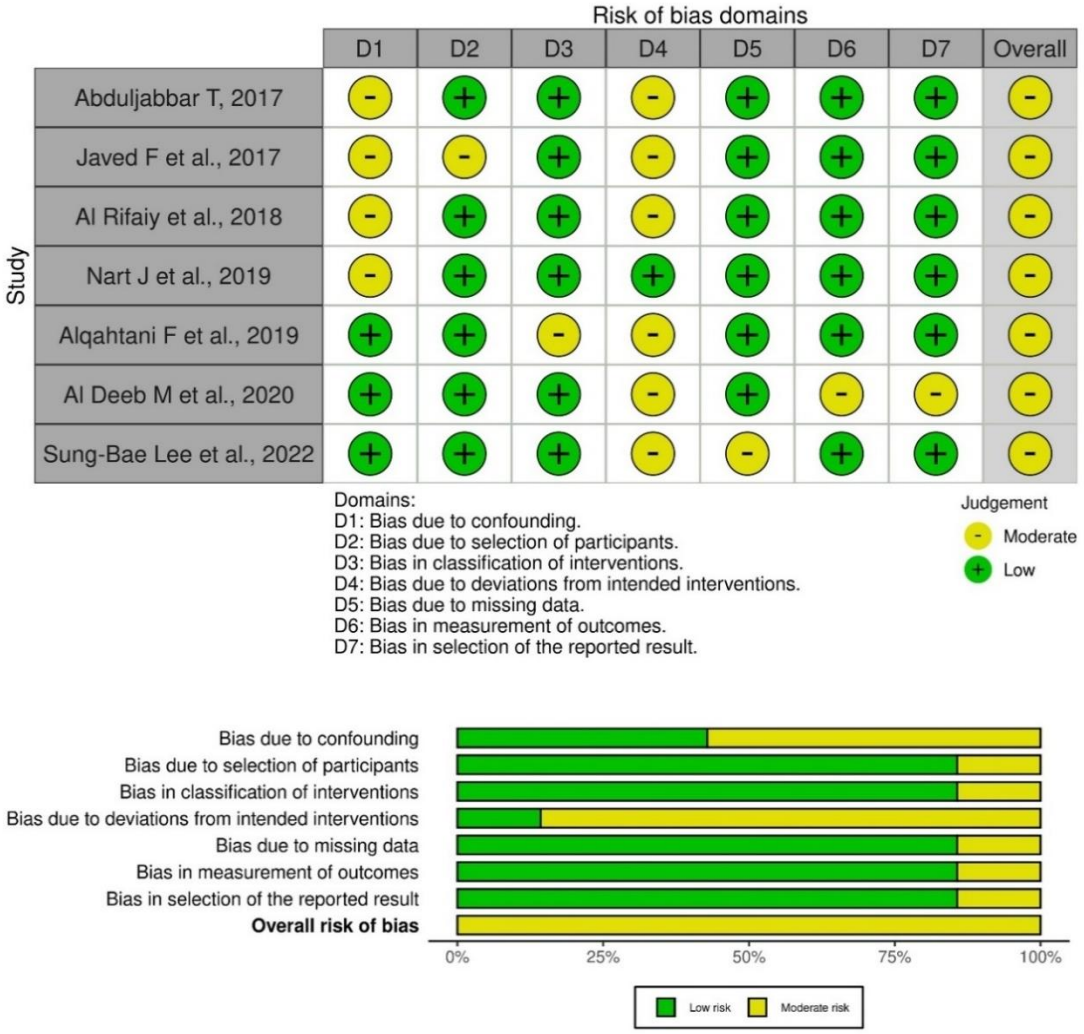

Figure 2: Risk of bias assessed from the individual studies and overall for all the included studies using ROBINS-I Tool for NRCTs

Table 3: Evaluation of quality of Evidence using the GRADE approach

Author	Year	Inconsistency	Indirectness	Imprecision	Publication Bias	Risk of Bias	Overall Quality of Evidence
Abduljabbar T [32]	2017	Moderate	Low	Low	Moderate	Moderate	Moderate
Javed F *et al*., [33]	2017	Low	Low	Low	Low	Moderate	High
Al Rifaiy *et al*., [34]	2018	Low	Low	Moderate	Low	Moderate	Moderate
Nart J *et al*., [35]	2019	Moderate	Low	Moderate	Low	Moderate	Moderate
Alqahtani F [36]	2019	Moderate	Low	Low	Low	Moderate	Moderate
AlDeeb M *et al*., [37]	2020	Low	Low	Low	Low	Moderate	High
Sung-Bae Lee *et al*., [38]	2022	Low	Low	Low	Low	Moderate	High

DISCUSSION

The review presented in this manuscript assesses the effectiveness of aPDT and MD in the treatment of peri-implant mucositis and peri-implantitis in different populations, including smokers, e-cigarette users, and non-smokers. Across multiple studies, the use of aPDT combined with MD has been shown to yield superior outcomes compared to MD alone in the treatment of peri-implant mucositis and peri-implantitis. This observation is consistent in studies conducted by Abduljabbar *et al*., (2017), Javed *et al*., (2017), and Alqahtani (2019), where a significant reduction in PI, BoP, and PD was observed in patients treated with aPDT as an adjunct to MD [32, 33, 36].

The enhanced effectiveness of aPDT in these cases can be attributed to its ability to target and eliminate microbial biofilms, which are often resistant to conventional mechanical treatments alone [39]. The key mechanism behind aPDT involves the use of a photosensitizer that, when activated by light of a specific wavelength, produces reactive oxygen species (ROS) such as singlet oxygen [40]. These ROS cause direct damage to bacterial cell walls, disrupt biofilm structures, and lead to bacterial cell death [41]. In peri-implant environments, where biofilms contribute significantly to the pathogenesis of both peri-implant mucositis and peri-implantitis [4], aPDT is particularly advantageous because it can penetrate deep into the biofilm matrix, which is often impenetrable by conventional mechanical debridement methods [42].

Additionally, aPDT has been shown to have anti-inflammatory properties, which could further explain its effectiveness in reducing BoP and PD [43]. By mitigating the inflammatory response, aPDT not only reduces clinical signs of inflammation (such as BoP) but also promotes tissue healing and regeneration, as evidenced in studies where aPDT was combined with MD for peri-implantitis treatment.

One of the primary variables affecting the success of peri-implantitis and peri-implant mucositis treatment is the smoking status of patients. Several studies in the review, including those by Al Rifaiy *et al*., (2018) and Nart *et al*., (2019), clearly demonstrate that smokers tend to have worse clinical outcomes compared to non-smokers [34, 35]. For example, the study by Nart et al. found that smokers exhibited significantly higher peri-implant marginal BL and lower rates of implant survival. Additionally, the effectiveness of non-surgical treatments (including aPDT) in reducing BoP, PD, and PI was diminished in smokers.

The detrimental effects of smoking on peri-implant tissues and healing can be attributed to several mechanisms. Nicotine and other toxic chemicals in cigarette smoke impair the normal function of neutrophils and other immune cells, making it more difficult for the body to mount an effective defense against bacterial pathogens [44]. Furthermore, smoking causes vasoconstriction, which reduces blood flow to the gingival and peri-implant tissues [45]. This decrease in blood supply limits the delivery of oxygen, nutrients, and immune cells to the site of infection, thereby delaying healing and increasing the risk of infection persistence or recurrence.

One notable aspect of the study by AlDeeb M *et al*., (2020) was the examination of RANKL and OPG levels, which are critical mediators of bone remodeling and are indicative of osteoclastic activity [37, 46]. At baseline, all groups showed variable levels of RANKL and OPG, with significant differences observed among smokers, e-cigarette users, and non-smokers. The study revealed that smoking and e-cigarette usage were associated with increased RANKL levels and decreased OPG levels at baseline compared to non-smokers. This imbalance between RANKL and OPG promotes osteoclastogenesis, leading to bone resorption and exacerbating peri-implantitis. Their findings suggested that while smokers and e-cigarette users initially have an unfavorable bone remodeling environment, there may be potential for improvement following an intervention, although not fully restoring levels to those of non-smokers. The increased RANKL and decreased OPG observed in smokers highlight the need for targeted therapies that address these molecular pathways. Adjunctive therapies, particularly aPDT, may help restore this balance by reducing bacterial load and promoting favorable healing environments, ultimately leading to improved clinical outcomes.

In smokers, the efficacy of aPDT may be reduced due to the compromised immune response. Since aPDT relies on the ability of the body tissue to clear out damaged bacterial cells and inflammatory by-products after the treatment, smokers may have a diminished capacity to complete this process, resulting in less favorable outcomes. This is corroborated by findings from Alqahtani (2019) and Abduljabbar *et al*., (2017), where both studies reported lower reductions in BoP and PD in smokers compared to non-smokers after aPDT and MD treatment [32, 36].

A growing body of evidence, including studies reviewed by Al Rifaiy *et al*., (2018) and AlDeeb M (2020), suggests that e-cigarette users may exhibit better peri-implant treatment outcomes compared to traditional cigarette smokers [34, 37]. E-cigarette users had significantly lower levels of BoP, PD, and peri-implant bone loss compared to their cigarette-smoking counterparts. For instance, Al Rifaiy *et al*., found that e-cigarette users had a mean BoP score of 11.7% after 12 months, compared to 14.6% in cigarette smokers [34].

The relatively better outcomes for e-cigarette users can be explained by the absence of many of the harmful toxins found in conventional cigarette smoke, such as tar and carbon monoxide [47]. While e-cigarettes do contain nicotine, which still has vasoconstrictive effects, the overall toxic load is much lower [48]. As a result, e-cigarette users may experience less immune suppression, less impairment of blood flow, and therefore better tissue healing compared to cigarette smokers. This could explain the observed differences in treatment outcomes between the two groups.

However, it is important to note that while e-cigarettes may be less harmful than traditional cigarettes, they are not without risk. Nicotine, the primary addictive substance in e-cigarettes, still negatively impacts periodontal and peri-implant tissues by reducing blood flow and impairing neutrophil function [48]. Moreover, the long-term effects of e-cigarette use on oral health are

still not fully understood, as vaping has only become widespread in recent years. Longitudinal studies are needed to assess whether the short-term benefits observed in e-cigarette users compared to smokers persist over time.

The importance of peri-implant maintenance therapy (PIMT) is highlighted in the studies by Nart *et al*., (2019) and Sung-Bae Lee (2022). Both studies emphasize that regular maintenance visits and adherence to oral hygiene protocols are critical to the long-term success of peri-implant mucositis and peri-implantitis treatments [35, 38]. Patients who received regular maintenance therapy exhibited lower rates of peri-implant disease recurrence, reduced probing depths, and improved implant survival rates.

PIMT typically involves professional cleaning of the implant surfaces using instruments that do not damage the implant, such as plastic or titanium scalers, as well as the reinforcement of oral hygiene practices at home [49]. This ongoing care helps to prevent the re-accumulation of biofilm and the development of inflammation around the implants. In smokers, where the risk of peri-implant disease is already elevated, the need for rigorous maintenance is even more pronounced. Without regular maintenance, smokers and even e-cigarette users are more likely to experience disease recurrence, as evidenced by higher PD and BoP scores in patients who did not adhere to maintenance protocols.

The findings from these studies underscore the need for clinicians to establish individualized maintenance programs for patients with peri-implant diseases, particularly those who smoke or use e-cigarettes. The frequency of maintenance visits may need to be increased for these high-risk patients to ensure that any early signs of disease recurrence are promptly addressed.

The studies reviewed in this manuscript collectively suggest that aPDT is a valuable adjunct to MD in the treatment of peri-implant diseases, particularly in non-smokers and e-cigarette users. However, the diminished effectiveness of aPDT in smokers highlights the need for additional interventions that can address the underlying immune suppression and vascular damage caused by smoking.

Future research should explore the potential benefits of combining aPDT with other therapies, such as local drug delivery systems that release anti-inflammatory or bone-regenerative agents. These combination therapies may help to overcome the limitations of aPDT in smokers by promoting tissue healing and reducing the risk of disease recurrence.

Additionally, more research is needed to fully understand the long-term effects of e-cigarette use on peri-implant health. While the current evidence suggests that e-cigarette users fare better than traditional cigarette smokers, it remains unclear whether these benefits are sustained over time. Longitudinal studies that track the oral health outcomes of e-cigarette users over several years are essential to determine whether vaping is a viable harm-reduction strategy for individuals at risk of peri-implant diseases.

CONCLUSION

Findings of the present systematic review underscore the significant detrimental impact of smoking on the treatment outcomes of peri-implantitis. Smokers, regardless of the type of smoking habit, consistently show higher plaque levels, increased inflammation, deeper probing depths, and poorer bone regeneration compared to non-smokers. However, adjunctive therapies such as aPDT have been shown to improve clinical outcomes in smokers, particularly by reducing inflammation and probing depths. While mechanical debridement remains a cornerstone of peri-implantitis treatment, the addition of adjunctive therapies enhances its efficacy, especially in smokers. Nonetheless, smokers continue to face challenges in achieving long-term peri-implant health, emphasizing the importance of regular supportive maintenance therapy. Future research should focus on standardizing treatment protocols and exploring the long-term effects of smoking cessation on peri-implantitis treatment success.

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