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The association of lead and cadmium exposure with periodontitis: a systematic review and meta-analysis

Saiyan Yang[1], Jun Li[1] and Yousheng Wu[1*]

Abstract

Objective Periodontitis, a microbiome-driven chronic inflammatory disease that destroys the supporting structures of the teeth, is influenced by various environmental factors, including exposure to heavy metals such as lead and cadmium. This systematic review and meta-analysis aimed to evaluate the association between exposure to lead and cadmium and periodontitis.

Methods A comprehensive literature search was conducted in PubMed, Web of Science, Scopus, and Embase up to February 1, 2025, following PRISMA guidelines. Observational studies examining the association between lead and/or cadmium exposure and periodontitis were included. Required clinical data were extracted, and study quality was assessed using the Newcastle-Ottawa Scale. Random-effects models were used to compute either standardized mean differences (SMD) of concentration or pooled adjusted odds ratios (aORs). Heterogeneity was assessed with I^2.

Results Fourteen studies (13 datasets for either lead or cadmium) comprising 72,467 participants were eligible for inclusion. The meta-analysis found that cadmium and lead exposure were significantly associated with higher odds of periodontitis, with pooled aORs of 1.22 (95% CI: 1.08–1.37) and 1.85 (95% CI: 1.42–2.41), respectively. Sensitivity analyses confirmed the robustness of the findings.

Conclusion This study provides evidence that exposure to lead and cadmium is significantly associated with periodontitis. These findings highlight the importance of reducing environmental exposure to these heavy metals as part of preventive strategies for periodontal disease. Further research is needed to explore the underlying biological mechanisms and evaluate potential interventions to reduce exposure-associated periodontitis.

Keywords Periodontitis, Lead exposure, Cadmium exposure, Heavy metals, Meta-analysis

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Introduction

Periodontitis is a chronic inflammatory condition influenced by the oral microbiome that damages the supportive structures of the teeth, and can eventually result in tooth loss if not treated [1]. It is a prevalent condition, affecting more than one billion of adults worldwide [2], with severe forms impacting approximately 11% of the global [3]. Based on Global Burden of Disease study, the global age-standardized incidence rate of periodontitis in 2019 was 1,120 per 100,000 people. Additionally, the global disability-adjusted life years (DALYs) attributed to periodontitis in 2019 were 7,090,390.3 years, reflecting a 98.8% increase since 1990 [3]. The etiology of periodontitis is multifactorial, involving bacterial dysbiosis, genetic predisposition, and environmental factors, including exposure to heavy metals [4].

Heavy metals such as lead (Pb) and cadmium (Cd) are widespread environmental pollutants with well-documented toxic effects on human health [5]. These metals are primarily enter the human body through occupational exposure, contaminated food and water, and air pollution [6]. Lead is known for its neurotoxic, nephrotoxic, and cardiovascular effects, while cadmium is a recognized carcinogen associated with renal dysfunction and bone demineralization [7, 8]. Emerging evidence suggests that both lead and cadmium may also play a role in the pathogenesis of periodontitis, potentially through mechanisms involving oxidative stress, immune dysregulation, and bone metabolism disruption [9]. Lead exposure has been linked to alterations in inflammatory responses, increased oxidative stress, dysregulation of cytokines, and adverse effect on bone metabolism which may contribute to periodontal tissue destruction [10]. Similarly, cadmium has been shown to impair bone metabolism by inhibiting osteoblast activity and stimulating osteoclastogenesis, potentially exacerbating alveolar bone loss in periodontitis [11]. Epidemiological studies have reported associations between elevated blood levels of these metals and an increased risk of periodontal disease [12, 13], but the evidence remains inconsistent, warranting a comprehensive systematic review and meta-analysis to clarify the relationship.

To our knowledge, no systematic review and meta-analysis has yet synthesized the available epidemiological data on the association between exposure to lead and cadmium and periodontitis. Given the widespread presence of these metals in the environment and their potential impact on oral health, understanding their role in periodontitis is crucial for public health and preventive strategies. Therefore, this study aims to systematically review and quantitatively synthesize existing evidence to assess the relationship between lead and cadmium exposure and periodontitis.

Methods

Search strategy

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14]. This systematic review and meta-analysis followed the PECOS framework to define its scope: Participants were general populations included in observational studies; Exposure comprised lead and/or cadmium levels measured via validated biomarkers; Comparison groups were individuals with lower or no heavy metal exposure, as defined by each original study; Outcomes included periodontitis diagnosed using standardized criteria; and Study designs were restricted to observational studies.

A thorough literature search was performed across PubMed/MEDLINE, Web of Science, Scopus, and Embase, covering all peer-reviewed published studies up to February 1, 2025. The search strategy incorporated Medical Subject Headings (MeSH) and keywords related to lead, cadmium, heavy metal exposure, and periodontitis, using Boolean operators as follows (Figure S1): (("heavy metals" OR "heavy metal exposure" OR "lead" OR "cadmium") AND ("periodontitis" OR "periodontal diseases" OR "gingivitis" OR "periodontal inflammation" OR "periodontal attachment loss" OR "gum disease") AND ("risk" OR "risk factors" OR "association" OR "odds ratio")). No language restrictions were applied, and reference lists of relevant articles were manually screened to identify additional eligible studies. Non-English papers were translated using ChatGPT or Google Translate. Additionally, we searched the first 20 pages of Google Scholar to identify grey literature.

Eligibility criteria

Studies were included if they were observational in design (cross-sectional, case-control, or cohort studies) and assessed the association between lead and/or cadmium exposure and periodontitis risk. Eligible studies included general populations and measured lead and/or cadmium exposure using validated biomarkers such as blood, urine, or saliva. The outcome of interest was periodontitis, diagnosed based on recognized clinical criteria using definitions from the Centers for Disease Control and Prevention (CDC)/American Academy of Periodontology (AAP), or other established classifications [15–17]. Studies were required to report mean concentration of lead and cadmium or effect estimates such as odds ratios (ORs) with 95% confidence intervals (CIs) or provide sufficient data for their calculation. Exclusion criteria included non-human studies, reviews, editorials, conference abstracts, case reports, studies on other heavy metals, studies without a comparison group, and those lacking relevant exposure or outcome data or sufficient statistical information.

Study selection, data extraction and quality assessment

Two independent reviewers screened the titles and abstracts of all identified studies. Full-text articles were then evaluated for eligibility, and any disagreements were resolved through discussion or by consulting a third reviewer (YW). Data extraction was performed in duplicate using a standardized form, collecting information on study characteristics (first author, publication year, country, study design, sample size), population characteristics (mean age, sex distribution, periodontal disease definition), exposure data (biomarkers and levels of lead/cadmium), outcome data (prevalence/incidence of periodontitis, diagnostic criteria), effect estimates (adjusted/unadjusted ORs, RRs, or HRs with 95% CIs), mean concentration; and covariates considered for adjustment (e.g., smoking, diabetes, socioeconomic status). The Newcastle-Ottawa Scale (NOS) was used to assess the methodological quality of studies [18]. The NOS evaluates studies based on three key domains: selection of study groups (maximum of four stars), comparability of groups (maximum of two stars), and ascertainment of exposure or outcome (maximum of three stars), with a total score ranging from 0 to 9. Studies scoring ≥ 7 were considered high quality, those scoring 5–6 were considered moderate quality, and those scoring ≤ 4 were classified as low quality. Two independent reviewers assessed the quality of each included study, and discrepancies in scoring were resolved through discussion or consultation with a third reviewer if necessary.

Statistical analysis

All statistical analyses in this study were performed using Stata version 17. Random-effects models were used to calculate the pooled standardized mean differences (SMDs) and adjusted ORs (aORs), respectively, in order to account for high expected heterogeneity across studies [19]. Heterogeneity was assessed using I^2, τ2, and Cochran's Q test [20]. Sensitivity analyses were conducted to evaluate the influence of individual studies on pooled estimates, employing a leave-one-out approach to ensure robustness. Publication bias was assessed using funnel plots, complemented by Egger's test to statistically evaluate asymmetry and potential underrepresentation of small studies with null effects [21]. We used restricted maximum likelihood (REML) method for random-effects models and Hedges's g for SMD calculations to adjust for small sample biases [22]. Subgroup analyses or meta-regression were not performed due to insufficient data, but sensitivity analyses were prioritized to explore sources of heterogeneity. The statistical approach was designed to provide a comprehensive evaluation of the association between heavy metal exposure and periodontitis, while addressing potential biases and variability inherent in meta-analytic studies.

Results

Study selection and main characteristics of included studies

The initial search yielded a total of 4,910 records, with 2,215 duplicates removed, leaving 2,695 unique records for screening. After reviewing titles and abstracts, 2,610 irrelevant records were excluded as they did not meet the eligibility criteria. Common reasons for exclusion included: (1) studies not investigating lead/cadmium exposure; (2) non-human or in vitro studies; (3) review articles, editorials, or conference abstracts without original data; and (4) studies that did not investigate periodontitis as an outcome. The remaining 85 full-text articles were assessed for eligibility. Of these, 46 studies were excluded for focusing on other heavy metals, and 25 other studies were excluded due to reasons indicated in Fig. 1. Ultimately, 14 studies [12, 13, 23–34] containing 26 datasets (13 for cadmium and 13 for lead) were included in the systematic review and meta-analysis. The detailed search and selection process are illustrated in Fig. 1. The included studies comprised a total of 72,467 participants including 22,274 individuals with periodontitis and 41,003 individuals without periodontitis. The sample sizes for studies ranged from 40 to 11,412 individuals. The studies were conducted in various countries, including the United States, South Korea, India, Iraq, and Türkiye. The majority of the studies ($n = 9$) were conducted in the United States, followed by South Korea ($n = 4$), and one study each in India, Iraq, and Türkiye. The included studies were primarily cross-sectional ($n = 10$), with a few cohort ($n = 3$) and case-control ($n = 1$) studies. All studies were classified as high-quality based on NOS. Detailed study characteristics are presented in Table 1. Additionally, Table S1 provides a comprehensive summary of all covariates adjusted for in the included studies.

Association between cadmium exposure and periodontitis

Thirteen datasets from 10 studies examined the association between cadmium exposure and periodontitis. Ten datasets were having enough data for calculating pooled ORs and nine datasets also have enough data for pooling mean concentration. Cadmium exposure was measured using blood ($n = 6$), urine ($n = 5$), saliva ($n = 1$), and teeth ($n = 1$). The studies included in the meta-analysis, published from 2009 to 2024, comprised 14,724 participants with periodontitis and 28,33 individuals without periodontitis.

Cadmium concentration in cases vs. Controls

The forest plot comparing cadmium concentrations between participants with periodontitis (cases) and those without periodontitis (controls) revealed a pooled standardized mean difference (SMD) of 0.57 (95% CI: [-0.12, 1.26]; Figure S2) using a random-effects model. This

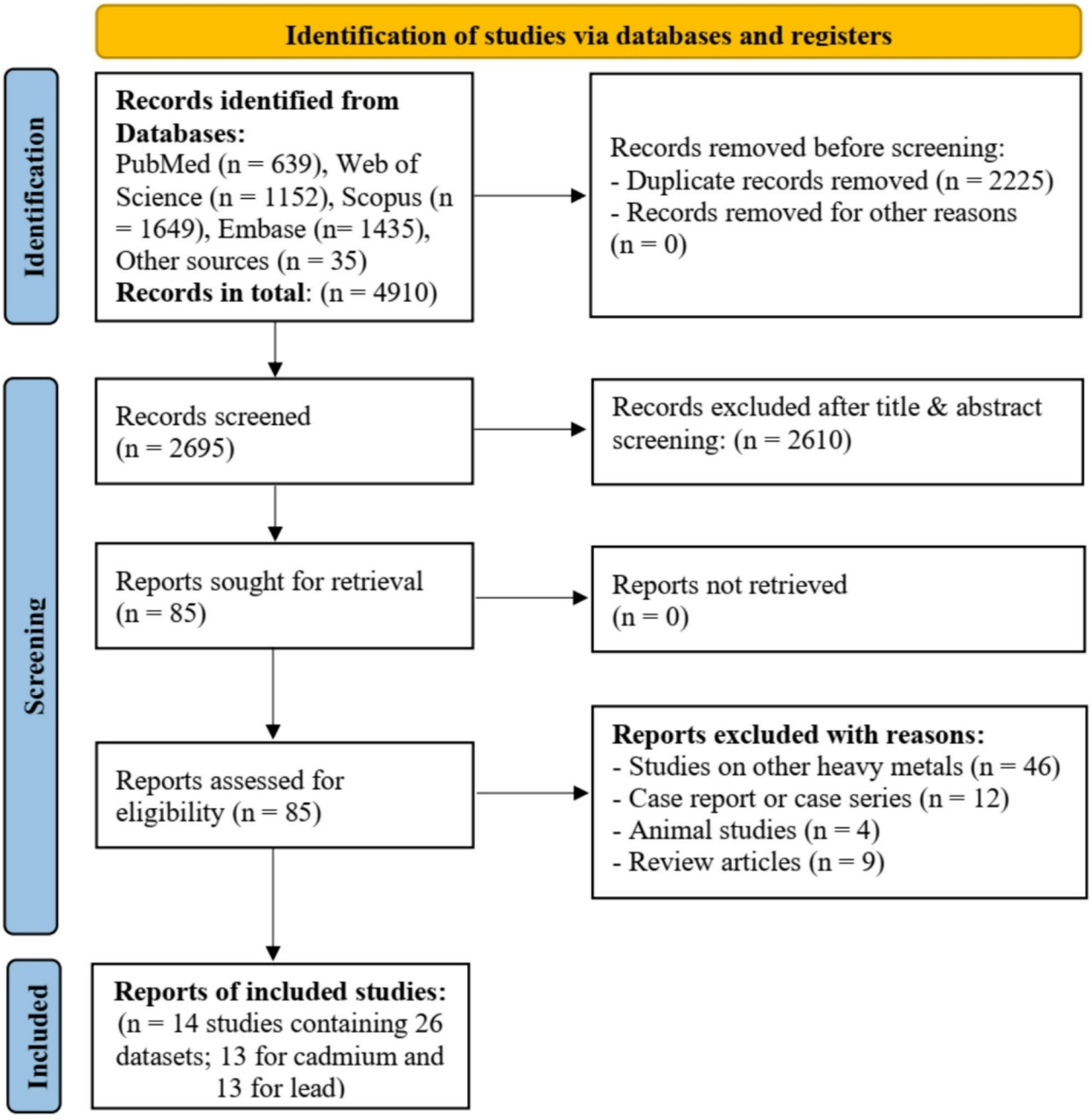

Fig. 1 PRISMA flow chart showing study selection process (https://www.prisma-statement.org)

indicates a trend toward higher cadmium levels in individuals with periodontitis, although the result was not statistically significant ($z = 1.62$, $p = 0.11$). Heterogeneity among the studies was extremely high ($I^2 = 99.83\%$; $p < 0.001$), suggesting substantial variability in cadmium concentrations across the included studies.

Notably, the study by Abd et al., 2015 reported the highest SMD of 2.70 (95% CI: [1.93, 3.48]), indicating a strong association between elevated cadmium levels and periodontitis in this population. In contrast, Ramesh et al., 2013 reported a negative association (SMD = -1.24, 95% CI: [-1.67, -0.82]), which may reflect differences in study populations or methodologies. A sensitivity analysis was conducted to assess the influence of individual studies on the pooled results, particularly focusing on the study by Ramesh et al., 2013, which reported a negative association between cadmium levels and periodontitis. When this study was excluded from the analysis, the pooled standardized mean difference (SMD) increased to 0.78 (95% CI: [0.19, 1.38]; Figure S3), indicating a

Table 1 Main characteristics of studies included regarding the association between cadmium exposure and periodontitis

Authors	Study period	Study design	Country	Biological sample	Total Population	People with Periodontitis	Mean Concentration	People without Periodontitis	Mean Concentration	Adjusted OR
Cadmium										
Arora et al. (2009)	ND	CS	USA	Urine	11,412	1,758	0.50 ± 0.27 µg/g	9,654	0.30 ± 0.00 µg/g	1.54 (1.26–1.87)
Won et al. (2012)	2009	CS	South Korea	Blood	1,966	646	ND	1,320	ND	1.57 (1.03–2.38)
Han et al. (2013)	2008–2010	CS	South Korea	Urine	4,716	1,316	1.83 ± 2.48 µg/l	3,400	1.43 ± 1.91 µg/l	1.12 (0.98–1.28)
Kim et al. (2013)	2008–2009	CS	South Korea	Blood	1,995	451	1.35 ± 1.16 µg/l	1,544	1.02 ± 0.765 µg/l	1.096 (0.78–1.52)
Kim et al. (2013)	2008–2009	CS	South Korea	Blood	2,001	381	1.86 ± 1.94 µg/l	1,620	1.25 ± 1.04 µg/l	1.094 (0.8–1.49)
Ramesh et al. (2013)	ND	CS	India	Urine	100	50	0.41 ± 0.16 µg/g	50	0.67 ± 0.246 µg/g	ND
Abd et al. (2015)	ND	CC	Iraq	Salivary	48	24	0.18 ± 0.02 µg/dl	24	0.11 ± 0.03 µg/dl	ND
Huang et al. (2022)	2013–2014	CS	USA	Blood	4,964	2,509	ND	2,455	ND	1.06 (1.4–1.8)
Acar et al. (2023)	ND	CC	Türkiye	Teeth	40	20	0.01 ± 0.03 µg/g	20	0.00 ± 0.00 µg/g	ND
Li et al. (2023)	2011–2014	CS	USA	Urine	2,269	928	ND	1,350	ND	0.85 (0.26–1.28)
Dai et al. (2024)	2009–2014	CS	USA	Urine	2,393	1,123	ND	1,270	ND	2.64 (1.13–6.14)
Dai et al. (2024)	2009–2014	CS	USA	Blood	8,993	4,469	0.43 ± 0.37 µg/l	4,524	3.3 ± 2.2 µg/l	1.23 (1.11–1.37)
Yang et al. (2024)	2011–2014	CS	USA	Blood	2,148	1,049	0.33 ± 0.71 µg/l	1,099	0.26 ± 0.31 µg/l	1.73 (1.12–2.66)
Lead										
Saraiva et al. (2007)	1988–1994	CS	USA	Blood	2,500	ND	ND	ND	ND	1.70 (1.02–2.85)
Saraiva et al. (2007)	1988–1994	CS	USA	Blood	2,399	ND	ND	ND	ND	3.80 (1.66–8.73)
Won et al. (2012)	2009	CS	South Korea	Blood	1,966	646	ND	1,320	ND	1.31 (0.88–1.96)
Kim et al. (2013)	2008–2009	CS	South Korea	Blood	1,995	451	6.48 ± 11.82 µg/dl	1,544	4.81 ± 7.37 µg/dl	1.69 (1.15–2.5)
Kim et al. (2013)	2008–2009	CS	South Korea	Blood	2,001	381	3.72 ± 4.99 µg/dl	1,620	3.16 ± 4.18 µg/dl	1.24 (0.83–1.85)
Han et al. (2013)	2008–2010	CS	South Korea	Urine	416	1,316	4.33 ± 5.77 µg/dl	3,400	3.53 ± 4.70 µg/dl	1.6 (1.15–2.21)
Huang et al. (2022)	2013–2014	CS	USA	Blood	4,964	2,509	ND	2,455	ND	1.07 (0.2–49.17)
Huang et al. (2022)	2013–2014	CS	USA	Blood	4,964	2,509	ND	2,455	ND	4.14 (1.2–13.9)
Huang et al. (2022)	2013–2014	CS	USA	Blood	4,964	2,509	ND	2,455	ND	28.1 (7.1–111.3)
Acar et al. (2023)	ND	CC	Türkiye	Teeth	40	20	2.14 ± 0.88 µg/g	20	0.07 ± 0.31 µg/g	ND
Dai et al. (2024)	2009–2014	CS	USA	Blood	8,600	ND	ND	ND	ND	2.02 (1.15–2.57)
Dai et al. (2024)	2009–2014	CS	USA	Urine	2,393	1,123	ND	1,270	ND	2.08 (1.67–2.6)
Yang et al. (2024)	2011–2014	CS	USA	Blood	2,148	1,049	1.26 ± 8.51 (µg/dl)	1,099	0.92 ± 6.17 (µg/dl)	1.18 (1.03–1.36)

stronger and statistically significant positive association between cadmium exposure and periodontitis.

Odds of periodontitis associated with cadmium exposure

The forest plot assessing the odds of periodontitis associated with cadmium exposure demonstrated a pooled adjusted odds ratio (aOR) of 1.22 (95% CI: [1.08, 1.37]; Fig. 2), indicating a statistically significant positive association between cadmium exposure and periodontitis (z = 3.28, $p = 0.001$). Heterogeneity among the studies was moderate ($I^2 = 75.88\%$; $p < 0.001$), suggesting variability in effect sizes across studies.

The study by Dai, 2024 reported the highest aOR of 2.64 (95% CI: [1.13, 6.15]), while Li, 2023 reported a non-significant protective effect (aOR = 0.85, 95% CI: [0.56, 1.29]). Most studies, however, supported a positive association, with Arora, 2009 (aOR = 1.54, 95% CI: [1.26, 1.88]) and Yang, 2024 (aOR = 1.73, 95% CI: [1.12, 2.67]) showing particularly strong associations. Sensitivity analysis showed that the estimates of the pooled aOR range from 1.15 (95% CI: 1.05, 1.25) to 1.25 (95% CI: 1.10, 1.43), suggesting that no one study is substantially influencing the pooled estimate (Figure S4).

The funnel plot for the association between cadmium exposure and periodontitis odds showed a symmetrical distribution of studies around the pooled effect size, suggesting no significant publication bias (Egger's regression intercept: 1.12, 95%CI: -0.19, 2.44, $p = 0.095$; Figure S5).

Association between lead exposure and periodontitis

Thirteen datasets from 9 studies investigated the association between lead exposure and periodontitis. Twelve datasets were having enough data for calculating pooled ORs and nine datasets also have enough data for pooling mean concentration. Lead exposure was measured using blood ($n = 7$) and urine ($n = 4$). The studies included in the meta-analysis, published from 2007 to 2024, comprised 39,350 participants.

Lead concentration in cases vs. controls

The forest plot comparing lead concentrations between participants with periodontitis (cases) and controls revealed a pooled standardized mean difference (SMD) of 0.66 (95% CI: [-0.40, 1.72]; Figure S6) using a random-effects model. This suggests no statistically significant association between lead levels and periodontitis (z = 1.22, $p = 0.22$). Heterogeneity among studies was extremely high ($I^2 = 99.81\%$; $p = 0.001$), reflecting substantial variability in lead concentrations across populations.

Notably, Acar, 2023 reported a strong positive association (SMD = 3.08, 95% CI: [2.17, 3.98]), while other studies, such as Han, 2013 (SMD = 0.16, 95% CI: [0.10,

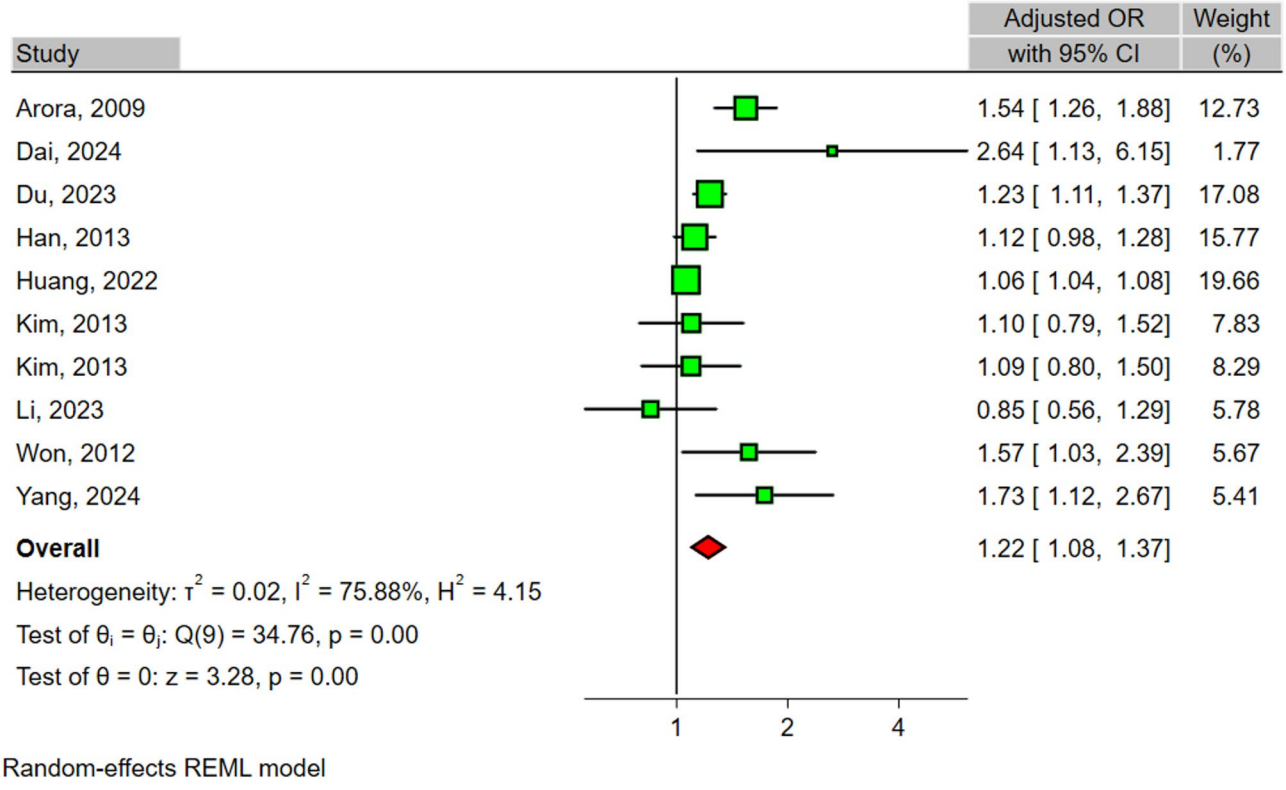

Fig. 2 Forest plot of adjusted ORs, pooled with random effects, regarding the association between cadmium exposure and periodontitis

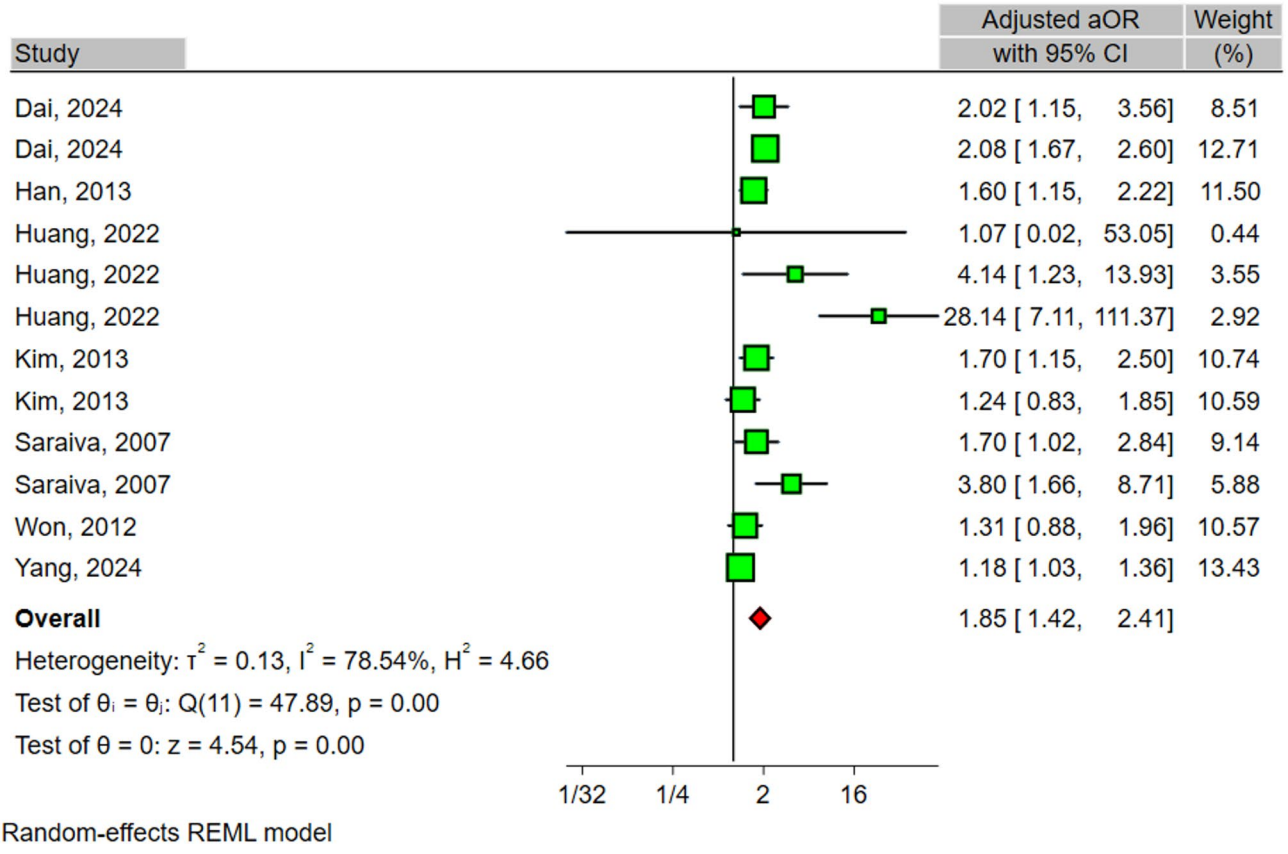

Fig. 3 Forest plot of adjusted ORs, pooled with random effects, regarding the association between lead exposure and periodontitis

0.22]) and Yang, 2024 (SMD = 0.05, 95% CI: [-0.04, 0.13]), showed minimal or non-significant effects. A sensitivity analysis was conducted to evaluate the influence of the Acar, 2023 study on the pooled results for lead concentration and periodontitis. This study reported an exceptionally strong association (SMD = 3.08, 95% CI: [2.17, 3.98]) compared to others in the analysis, likely due to its small sample size ($N = 20$ cases and 20 controls) and extreme mean differences in lead levels between groups (cases: 2.14 ± 0.88 vs. controls: 0.07 ± 0.31). When Acar, 2023 was excluded, the pooled SMD decreased substantially to 0.13 (95% CI: [0.06, 0.19]), indicating a much weaker but statistically significant positive association between lead concentration and periodontitis (Figure S7). This revised estimate suggests that the original pooled SMD (0.66, 95% CI: [-0.40, 1.72]) was disproportionately influenced by the outlier effect of Acar, 2023.

Odds of periodontitis associated with lead exposure

The forest plot assessing the odds of periodontitis demonstrated a pooled aOR of 1.85 (95% CI: [1.42, 2.41]; Fig. 3), indicating a statistically significant positive association between lead exposure and periodontitis (z = 4.54, $p < 0.001$). Heterogeneity was high ($I^2 = 78.54\%$, $p < 0.001$), driven by variability in study effect sizes. Key contributors to the association included Huang, 2022, which reported an extreme aOR of 28.14 (95% CI: [7.11, 111.37]), and Saraiva, 2007 (aOR = 3.80, 95% CI: [1.66, 8.71]). However, several studies, such as Kim, 2013 (aOR = 1.24, 95% CI: [0.83, 1.85]) and Won, 2012 (aOR = 1.31, 95% CI: [0.88, 1.96]), showed non-significant trends. A leave-one-out sensitivity analysis demonstrated that the pooled adjusted odds ratio (aOR) remained stable after sequentially excluding each individual study, indicating robustness of the overall association between lead exposure and periodontitis (Figure S8).

The funnel plot for the association between lead exposure and periodontitis odds [based on visual assessment, showed slight asymmetry, with smaller studies clustering on the right side, suggesting potential publication bias. This could indicate a lack of small studies reporting null effects (Egger's regression intercept: 1.95, 95%CI: 0.72, 3.18, $p = 0.002$; Figure S9).

Discussion

This systematic review and meta-analysis investigated the association between exposure to lead and cadmium and periodontitis, synthesizing data from 14 studies comprising 72,467 participants. The results demonstrated a statistically significant positive association between

both heavy metals and periodontitis. Specifically, cadmium exposure was associated with 22% higher odds of periodontitis (aOR = 1.22), while lead exposure showed a stronger association, with 85% higher odds (aOR = 1.85). Despite differences in study designs, populations, and exposure assessments, the consistency of these results across multiple studies underscores their reliability. Sensitivity analyses further confirmed the stability of the results, indicating that the pooled estimates were not disproportionately influenced by any single study. These findings suggest that environmental exposure to lead and cadmium may play a significant role in the pathogenesis of periodontitis, emphasizing the need to consider heavy metal exposure as a potential risk factor for periodontal disease.

Our results are consistent with a growing body of evidence linking heavy metal exposure to adverse oral health outcomes, including periodontitis. While this study specifically focused on lead and cadmium, other reviews and large-scale original studies have explored the effects of other heavy metals, such as mercury, arsenic, and chromium, on periodontal health. For instance, a scoping review by Coelho et al. (2024) highlighted that heavy metals, including lead and cadmium, contribute to periodontal tissue damage through mechanisms such as oxidative stress, inflammation, and disruption of bone metabolism, which aligns with the findings of this meta-analysis [9] Similarly, a study by Huang et al. (2022) found that elevated blood levels of trace minerals, including heavy metals, were associated with an increased prevalence of periodontitis in a large U.S. population, further supporting the role of environmental pollutants in periodontal disease [12].

In comparison to other heavy metals, the effects of lead and cadmium appear to be particularly pronounced. For example, studies on mercury exposure have shown mixed results, with some reporting a weak association with periodontitis, while others found no significant link [9]. Arsenic, another well-known toxic metal, has been less extensively studied in the context of periodontitis, but preliminary evidence suggests it may also contribute to periodontal inflammation and bone loss, albeit to a lesser extent than lead and cadmium [9]. The stronger association observed for lead and cadmium in this study may be attributed to their well-documented effects on bone metabolism and immune dysregulation, which are central to the pathogenesis of periodontitis [10, 11]. Interestingly, in contrast to the harmful effects of lead and cadmium, zinc—an essential trace element—has been shown to have a protective role in periodontal health [34, 35]. Zinc is known for its anti-inflammatory and antioxidant properties, which can help mitigate the oxidative stress and inflammation associated with periodontitis. Studies have demonstrated that zinc deficiency is associated with an increased risk of periodontal disease, while adequate zinc levels may help reduce periodontal inflammation and promote tissue repair [36, 37]. This contrast between the detrimental effects of toxic heavy metals like lead and cadmium and the beneficial effects of essential trace elements like zinc highlights the complex interplay between environmental exposures and periodontal health. Furthermore, the findings of this study are consistent with global epidemiological data on heavy metal exposure and oral health. For example, similar to our findings, a study by Won et al. (2013) using data from the Korean National Health and Nutrition Examination Survey reported a significant association between cadmium and lead exposure and periodontal disease [13]. Similarly, a cross-sectional study by Arora et al. (2009) in the U.S. found that higher blood cadmium levels were associated with higher odds of periodontitis, further corroborating the findings of this review [24].

This study has several strengths, including the use of a comprehensive search strategy across multiple scientific databases, and the inclusion of high-quality peer-reviewed observational studies. Additionally, the application of random-effects models and sensitivity analyses ensured robust and reliable pooled estimates, accounting for heterogeneity across studies. However, several limitations must be acknowledged. First, the number of available studies on the association between lead, cadmium, and periodontitis was relatively low, with only 14 studies meeting the inclusion criteria. This limited the ability to perform subgroup analyses or meta-regression to explore potential sources of heterogeneity, such as differences in study populations, geographic regions, or exposure measurement methods. The small number of studies also reduced the statistical power to detect more subtle associations and may have influenced the generalizability of the findings. Second, there was significant variability in the methodologies and reporting of key clinical and demographic information across the included studies. For example, some studies did not provide detailed data on covariates adjusted for in their analyses, such as smoking status, diabetes, or socioeconomic factors, which are known confounders in the relationship between heavy metal exposure and periodontitis. This lack of standardized reporting limited the ability to fully account for potential confounding in the meta-analysis. Third, the measurement of heavy metal exposure varied widely across studies, with some using blood, others urine, and a few using saliva or teeth. While these biomarkers are valid for assessing exposure, differences in their sensitivity, specificity, and half-lives may have contributed to heterogeneity in the results. Additionally, most studies relied on single measurements of heavy metal exposure, which may not accurately reflect long-term or cumulative exposure levels.

Fourth, the majority of included studies were cross-sectional in design, which limits the ability to infer causality. Although two case-control studies were included, their small number restricted the ability to draw stronger conclusions about the relationship between heavy metal exposure and periodontitis. Five, while our meta-analysis demonstrated significant associations between lead/cadmium exposure and periodontitis, the available data were insufficient to conclusively evaluate dose-response relationships. Longitudinal studies with standardized exposure assessments, consistent adjustment for confounders, and repeated measures of both exposure and outcome are needed to better establish causality. Finally, publication bias may have influenced the findings, particularly for lead exposure, where the funnel plot suggested some asymmetry. This could indicate that smaller studies with null or negative results were underrepresented in the literature, potentially leading to an overestimation of the association between lead exposure and periodontitis.

Conclusions

The findings of this study demonstrate a significant association between exposure to lead and cadmium and periodontitis. Despite abovementioned limitations, the results underscore the importance of reducing environmental exposure to these metals as part of preventive strategies for periodontitis. Future research should focus on longitudinal studies to establish causality and explore mechanisms, ultimately informing public health interventions to mitigate the oral health risks associated with heavy metal exposure.

Abbreviations

AAP	American Academy of Periodontology
aORs	Adjusted odds ratios
CDC	Disease Control and Prevention
CS	Cross-sectional
CC	Case-control
DALYs	Disability-adjusted life years
ND	Not determined
NOS	Newcastle-Ottawa Scale
OR	Odds ratio
REML	Restricted maximum likelihood
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SMD	Standardized mean differences

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12903-025-06195-9.

Supplementary Material 1

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None.

Author contributions

Author Contributions Conceptualization, S.Y. and W.U.; methodology, S.Y., J.L., and Y.W.; software, S.Y.; validation, Y.W.; formal analysis, S.Y., J.L., and Y.W.; investigation, S.Y., J.L., and Y.W.; resources, Y.W.; data curation, Y.W.; writing—original draft preparation, S.Y., J.L., and Y.W.; writing—review and editing, S.Y., J.L., and Y.W.; visualization, Y.W.; supervision, Y.W.; project administration, Y.W.; funding acquisition, Y.W. All authors have read and agreed to the published version of the manuscript.

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Data availability

We included all data in main manuscript and supplementary files. Further data that supports the findings of this study are available from the corresponding authors upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

All authors have agreed to submit this paper for publication.

Competing interests

The authors declare no competing interests.

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