Received: 4 August 2023 | Revised: 10 December 2023 | Accepted: 5 January 2024

DOI: 10.1111/jcpe.13950

ORIGINAL ARTICLE

Journal of Clinical Periodontology WILEY

Long-term exposure to ambient fine particulate matter and periodontitis: An observational study using nationally representative survey data

Wenjing Li[1,2] | Na Li[3] | Zhisheng Liang[3] | Xingduo Hou[3] | Yan Si[4] | Xing Wang[5] | Xiping Feng[6] | Baojun Tai[7] | Deyu Hu[8] | Huancai Lin[9] | Bo Wang[5] | Chunxiao Wang[10] | Shuguo Zheng[4] | Xuenan Liu[4] | Wensheng Rong[4] | Weijian Wang[4] | Shengzhi Sun[11] | Huanxing Meng[12] | Zhenyu Zhang[3,13,14]

[1]Beijing Laboratory of Biomedical Materials, Department of Geriatric Dentistry, Peking University School and Hospital of Stomatology, Beijing, China

[2]Institute of Medical Technology, Peking University Health Science Center, Beijing, China

[3]Department of Global Health, School of Public Health, Peking University, Beijing, China

[4]Department of Preventive Dentistry, National Engineering Laboratory for Digital and Material Technology of Stomatology, Beijing Key Laboratory of Digital Stomatology, Peking University School and Hospital of Stomatology, Beijing, China

[5]Chinese Stomatological Association, Beijing, China

[6]Department of Preventive Dentistry, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

[7]School and Hospital of Stomatology, Wuhan University, Wuhan, China

[8]Department of Preventive Dentistry, West China School of Stomatology, Sichuan University, Chengdu, China

[9]Department of Preventive Dentistry, Guanghua School of Stomatology, Hospital of Stomatology, Sun Yet-sen University, Guangzhou, China

[10]Chinese Center for Disease Control and Prevention, Beijing, China

[11]Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, Beijing, China

Abstract

Aim: The rising prevalence of periodontitis imposes substantial burdens on individuals and society. Identifying environmental risk factors for periodontitis may contribute to tackling the global public health burden of it. This study aimed to assess the association between long-term exposure to $PM_{2.5}$ and periodontitis in a nationally representative population from China.

Materials and Methods: In this multi-centre cross-sectional study of 372 communities in 31 provinces of Mainland China, we used data from the Fourth National Oral Health Survey of China in 2015–2016, in combination with high-resolution gridded concentrations of fine particulate matter ($PM_{2.5}$). Logistic regression was applied to assess the relationship between long-term $PM_{2.5}$ exposure and the risk of periodontitis. In addition, we examined whether the association varied by individual characteristics, and estimated the exposure–response relationship and the risk of damaged tooth in each tooth quadrant.

Results: A total of 8391 participants from 96 cities were diagnosed with periodontitis, accounting for 60.04% (8391/13,459) of the participants. For each 10 $\mu g/m^3$ increment in 1-, 3- and 5-year average concentrations of $PM_{2.5}$, the risk of total periodontitis increased by 9.0% (95% confidence interval: 6.0%, 12.0%), 8.0% (6.0, 11·0) and 7.0% (5.0, 10.0), respectively. Mild periodontitis was more strongly associated with $PM_{2.5}$ exposure than moderate and severe periodontitis. The teeth in the lower anterior, lower posterior or upper anterior are more susceptible to the effect of $PM_{2.5}$ on the periodontal pocket, calculus and bleeding gums.

Conclusions: Long-term exposure to $PM_{2.5}$ is significantly associated with an increased risk of periodontitis in the nationally representative Chinese population. Considering the rising prevalence of periodontitis, considerable costs of treatment, and substantially adverse effects on individuals and society, these findings suggest that stricter air quality regulations may help ease the burden of periodontal disease.

Wenjing Li and Na Li contributed equally to this study.

[12]Department of Periodontology, Peking University School of Stomatology, Beijing, China

[13]Institute for Global Health and Development, Peking University, Beijing, China

[14]Institute of Carbon Neutrality, Peking University, Beijing, China

Correspondence
Huanxing Meng, Department of Periodontology, Peking University School of Stomatology, Beijing, China.
Email: kqhxmeng@bjmu.edu.cn

Zhenyu Zhang, Department of Global Health, Peking University School of Public Health, Beijing, China.
Email: zzy@pku.edu.cn

KEYWORDS
chronic air pollution, fine particulate matter, national survey, periodontitis

Clinical Relevance

Scientific rationale for study: Oral diseases, often overlooked in global public health, share risk factors with major non-communicable diseases (NCDs). While air pollution is a known NCD risk factor, its role in periodontitis is plausible yet understudied.

Principal findings: We found that long-term $PM_{2.5}$ exposure is associated with an increased risk of periodontitis and highlights a critical role of air pollution exposure in the development of early-stage periodontitis. Additionally, we observed specific tooth quadrants more vulnerable to the adverse periodontal effects from ambient $PM_{2.5}$ exposure.

Practical implications: Strategies aimed at reducing $PM_{2.5}$ exposure could significantly alleviate the global burden of periodontitis.

1 | INTRODUCTION

Oral diseases are a major but neglected public health problem globally (Peres et al., 2019; Watt et al., 2019). On the one hand, the rising prevalence of oral diseases imposes substantial health burdens and considerable economic burdens on individuals and the broader healthcare system. According to the most recent global report by the World Health Organization (WHO), almost half of the world's population (45% or 3.5 billion people worldwide) are being affected by oral diseases over the life course, of which three quarters live in low- and middle-income countries (LMICs) (World Health Organization, 2022). On the other hand, oral diseases remain primarily untreated due to treatment costs exceeding available resources, especially in LMICs, which can cause severe personal consequences including continuous pain, sepsis, reduced quality of life, decreased work productivity, lost school days and disruption to family life (Peres et al., 2019). Oral disease was rarely regarded as a treatment priority in health policy and became marginalized from mainstream developments in healthcare systems (Benzian et al., 2011). As one of the most prevalent and consequential oral diseases globally, periodontitis is a severe gum infection that damages the tissues surrounding and supporting the teeth, leading to gingival swelling, alveolar bone resorption and tooth loss if not treated promptly (Chapple, 2014; Petersen & Baehni, 2000). Despite being preventable, the prevalence of periodontal disease ranges from 20% to 50% worldwide, and the prevalence rate is as high as 70% among Chinese adults (Dye, 2000; Jiao et al., 2021).

Fine particulate matter (particulate matter with a median aerodynamic diameter equal to or less than 2.5 μm, $PM_{2.5}$) pollution is an established environmental risk for non-communicable diseases (Alexeeff et al., 2021; Xing et al., 2016), including diabetes, cardiovascular disease, dementia and aspiration pneumonia (Hajishengallis & Chavakis, 2021; Hamanaka & Mutlu, 2018; Monsarrat et al., 2016; Pihlstrom et al., 2005). Accumulating evidence has demonstrated that $PM_{2.5}$ exposure was associated with changes in the levels of cytokines and biomarkers related to inflammatory response and endothelial dysfunction, two of the key mechanisms through which $PM_{2.5}$ exposure led to hazardous health outcomes (Block & Calderón-Garcidueñas, 2009; Brunekreef & Holgate, 2002; Hamanaka & Mutlu, 2018; Munzel et al., 2017; Rajagopalan & Landrigan, 2021; Y. Zhang et al., 2016). Periodontitis is a chronic inflammatory disease initiated by plaque bacteria. And the inflammatory response by the host results in excessive levels of pro-inflammatory mediators and enzymes, leading to irreversible loss of periodontal tissue attachment, destruction of alveolar bone, and even tooth mobility and tooth loss (Genco & Williams, 2010). In terms of direct effect, the particulate matter could flow past oral cavity and deposit on teeth and supporting tissue, which opens up the possibility of $PM_{2.5}$ damaging the periodontal tissue and oral microbiota (Manojkumar et al., 2019; Wu et al., 2022). And in terms of indirect effect, inflammation and oxidative stress, the biological mechanism by which air pollutants induce adverse health effects, is also involved in the primary pathogenesis of periodontitis (Møller et al., 2014; Nääv et al., 2020). Meanwhile, a growing body of evidence shows that particulate matter exposure can change the composition and function of gut microbiota (Qin & Wang, 2023) that is demonstrated to facilitate periodontitis (Luo et al., 2023). In view of this, it is biologically plausible that exposure to $PM_{2.5}$ may be associated with the development of periodontitis. However, there is a lack of epidemiological evidence from a nationally representative population that supports the associations between long-term $PM_{2.5}$ exposure and periodontitis. The availability of such evidence would significantly contribute to the development of preventive approaches for periodontal disease and enhance the understanding of its relationship with air pollution.

We sought to evaluate the association of long-term exposure to ambient $PM_{2.5}$ with periodontitis and its clinical manifestations using national representative data from the fourth Oral Epidemiological Survey in China. We hypothesized that long-term exposure to ambient $PM_{2.5}$ would be associated with an increased risk of periodontitis, especially in the early stage of periodontitis.

2 | METHODS

2.1 | Study population

We conducted this study using data from the Fourth National Oral Health Survey of China, launched in 2015 by the Chinese Stomatological Association (CSA). This survey aimed to describe oral health status and investigate Chinese adults' knowledge, attitudes and behaviours towards oral health (Jiao et al., 2021). The survey design and sample selection description were published elsewhere (Jiao et al., 2021). A total of 124 districts (91 cities) were chosen from 31 provinces using probability-proportional-to-size (PPS) with a varied population-sized method. Then, the participants to be examined between 35 and 74 years old were chosen from 372 communities (select three communities for each urban and rural district) by applying the quota sampling method. The sample size was calculated according to the prevalence of periodontal diseases (86%) found in the third National Oral Health Survey in 2005, an acceptable margin of error (10%) and an anticipated response rate of 80% (Jiao et al., 2021). In this study, all the cities surveyed were divided into six geographical regions: East China, South China, North China, Northwest China, Southwest China and Northeast China (Table S1). The ethics committee of the CSA approved this study (approval no. 2014-003). Written informed consent was obtained from each participant at their enrolment.

2.2 | Exposure assessment

Ambient $PM_{2.5}$ exposure levels were estimated and validated based on previously published prediction models (Z. Zhang et al., 2018). Briefly, this prediction model fused ground measurements of $PM_{2.5}$, Community Multiscale Air Quality (CMAQ) $PM_{2.5}$ simulations, Moderate Resolution Imaging Spectroradiometer (MODIS) level-2 aerosol optical depth (AOD) retrievals, Modern-Era Retrospective analysis for Research and Applications, Version 2 (MERRA-2) meteorology parameters and land use information with a two-stage random forest model. The addresses of 373 communities were geocoded to latitude and longitude data. We aggregated geocoded addresses and assigned exposures to individuals based on their residential geocoded addresses. Considering security and privacy issues, the exact addresses of survey participants were not publicly available. As a surrogate, we assigned the $PM_{2.5}$ concentration for each participant according to the geocoded address of their county. We then calculated the average concentrations across days during the 1-, 3- and 5-year periods before the survey for each participant as the proxy for long-term $PM_{2.5}$ exposure.

2.3 | Health outcome assessment

In this study, the diagnoses of periodontitis, attachment loss, calculus, bleeding gums and periodontal pockets were ascertained by licensed dentists through periodontal examinations. Detailed information about the periodontal disease definition and diagnosis criteria has been described elsewhere (Jiao et al., 2021). Briefly, full-mouth periodontal examinations were performed using a community periodontal index probe in a combination of the following four periodontal parameters, including bleeding on probing (BOP), presence of calculus, periodontal probing depth (PPD) and clinical attachment loss (CAL). The probe walked along gingival crevices with a force of ≤20 g to assess BOP, calculus presence, PPD and CAL. For each parameter, the tooth was scored according to the severity of the most severe site. Periodontal disease included (a) calculus (defined by visual examination for supragingival calculus and by probing for subgingival calculus, 0 = absence, 1 = presence, 9 = tooth excluded and X = tooth not present), (b) PPD (0 = 1–3 mm, 1 = 4–5 mm, 2 = ≥6 mm, 9 = tooth excluded and X = tooth not present), (c) BOP (0 = absence, 1 = presence, 9 = tooth excluded and X = tooth not present) and (d) CAL (measured by the distance from the cementoenamel junction to the bottom of the periodontal pocket, 0 = 0–3 mm, 1 = 4–5 mm, 2 = 6–8 mm, 3 = 9–11 mm, 4 = ≥12 mm, 9 = tooth excluded and X = tooth not present). Periodontal disease was diagnosed according to the classification scheme proposed at the 2018 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions as follows: periodontally healthy: <10% BOP-positive teeth and PPD ≤3 mm; gingivitis: ≥10% BOP-positive teeth and PPD ≤3 mm; and periodontitis was staged using the algorithm developed by Graetz et al. (2019). For each tooth, the CAL of the most severe sites was recorded, and a CAL of 1 ∼ 2 mm was defined as stage I, 3–4 mm as stage II and ≥5 mm as stage III. Next, the number of missing teeth was considered (stages I and II, no tooth missing; stage III, ≤4 teeth missing; and stage IV, ≥5 teeth missing; it should be noted that the reasons for tooth missing were not considered here). We also evaluated the complexity of management. Stage II patients were reclassified as stage III if the maximum PPD was ≥6 mm. Stage III patients were reclassified as stage IV if there were fewer than 20 remaining teeth or 10 opposing pairs. The extent of periodontitis was described as localized (<30% of teeth involved) or generalized (≥30% of teeth involved). Periodontitis was staged using the algorithm developed by Graetz et al. (2019), which is described in the Section 2. Then we classified periodontitis severity based on the results of the algorithm, with stage I being mild periodontitis, stage II being moderate periodontitis patients and stage III and above being severe periodontitis.

We classified adult teeth into four quadrants, including upper anterior (UA, four upper incisors, two upper cuspids), upper posterior (UP, four upper bicuspids, four upper molars), lower anterior (LA, four lower incisors, two lower cuspids) and lower posterior (LP, four lower bicuspids, four lower molars). The location of the teeth was indexed with the Fédération Dentaire Internationale Two-Digit System (Keiser-Nielsen, 1971), and the total number of damaged teeth in each quadrant was recorded.

2.4 | Covariates

We selected potential confounders based on a literature review of previous studies (Genco & Borgnakke, 2000; Nazir, 2017). All the

variables were collected using a standard structured questionnaire through face-to-face interviews by trained investigators. Demographic variables included age, sex, ethnicity, types of living area (urban or rural areas) and geographical regions. Socio-economic variables included educational attainment (illiteracy, middle school, high school, college or above). Behavioural variables included smoking status, frequency of alcohol consumption (never, seldom, frequent or former), frequency of dessert consumption (seldom, sometimes or frequent), frequency of sweetened beverage consumption (seldom, sometimes or frequent), domiciliary oral hygiene habits (frequency of tooth brushing, frequency of toothpick use) and professional oral hygiene habit (history of dental cleaning in the past 12 months). The information on dental cleaning history was collected by asking 'Have you had professional dental cleaning in the past 12 months?' Medical history variables included stroke, type 2 diabetes, hypertension, heart disease and chronic obstructive pulmonary disease (COPD). Regarding frequency of dessert and sweetened beverage consumption, 'one to three times a month' was defined as 'sometimes' and 'more than once a week' was defined as 'frequent'.

2.5 | Statistical analysis

Descriptive analyses were conducted for all variables. Continuous variables are described as the mean and standard deviation (SD), and categorical variables are expressed as counts and percentages. Differences in the distribution of baseline characteristics between groups were tested using Student's *t*-tests for continuous variables and the chi-squared test for categorical variables. We used multivariate logistic regression and constructed two models with different covariates to examine the associations of long-term exposure to $PM_{2.5}$ with the risk of periodontal disease. To address confounding, we identified covariates related to both the $PM_{2.5}$ exposure and the outcome of periodontitis and which were not in the causal pathway between the exposure and the outcome. We began with the crude model and then added confounders into the model (fully adjusted model), including current smoking status, current alcohol consumption status, frequency of sweet desserts, frequency of beverage, frequency of tooth brushing, frequency of toothpick use, whether the tooth was cleaned in the past 12 months and medical history of stroke, diabetes, hypertension, heart diseases and COPD. To evaluate non-linear exposure–response associations between 1-, 3- and 5-year $PM_{2.5}$ exposure and the risk of periodontitis, we modelled $PM_{2.5}$ air pollution exposure variables using restricted cubic splines using 4 degrees of freedom with knots at the 10th, 50th and 90th percentiles of the distribution of $PM_{2.5}$ exposure estimates. We presented results as odds ratios (ORs) for periodontal disease per 10 $\mu g/m^3$ increment in $PM_{2.5}$ concentration with corresponding 95% confidence intervals (CIs).

We performed stratified analyses to test the potential effect modifications of sex, age, ethnicity, types of living area, smoking status, alcohol consumption frequency, dessert consumption frequency, sweetened beverage consumption frequency and geographical region, by including an interaction term in the adjusted model. The likelihood ratio tests for models with and without the interaction term were applied to compare difference among stratifications. In addition, to explore possible pathogenic mechanisms by which $PM_{2.5}$ exposure may cause periodontitis, we assessed the associations between long-term $PM_{2.5}$ exposure and risk of clinical manifestations of periodontitis including periodontal pockets, calculus, bleeding gums and attachment loss by four tooth quadrants. For each clinical manifestation of periodontitis, we counted the number of teeth with clinical manifestations in the UA, UP, LA and LP quadrants. The exposure–response relationship between $PM_{2.5}$ and the number of affected teeth (regarded as the continuous variable) was plotted using restricted cubic splines with knots at the 10th, 50th and 90th percentiles of the distribution of 1-year $PM_{2.5}$ exposure estimates adjusting for the same covariates as in the adjusted model. Sensitivity analyses were conducted by separately adding O_3, SO_2 and NO_2, as well as combining them. We chose not to analyse SO_2 and NO_2 together due to their relatively high correlation coefficient (0.64, as indicated in Table S3). All statistical analyses were performed using STATA.

3 | RESULTS

A total of 13,459 participants (representing 459,292,050 adults) from 372 communities in 31 provinces of Mainland China were included in this study. Among them, 8391 participants were diagnosed with periodontitis, accounting for 60.04% of the participants (Table 1). Compared with healthy participants, participants with periodontitis tended to be older (63.54 vs. 60.27, $p < .001$), male (53.9% vs. 43.2%, $p < .001$), possessing lower levels of educational attainment, and smokers and alcohol consumers. Periodontitis patients were also more likely to have a medical history of diabetes (9.2% vs. 6.8%, $p < .001$), hypertension (26.4% vs. 19.9%, $p < .001$) and heart disease (12% vs. 10.2%, $p < .001$) than the healthy participants. The 1-, 3- and 5-year average exposure levels of $PM_{2.5}$ for participants with periodontitis were higher than those for healthy participants. Figure 1 presents the annual mean concentrations of $PM_{2.5}$ across China during 2014–2015 and proportion of individuals diagnosed with periodontitis in the oral health survey. The proportion of individuals diagnosed with periodontitis was generally larger in cities with a higher level of $PM_{2.5}$ concentration than that in cities with lower $PM_{2.5}$ concentrations (Figure 1).

Overall, long-term exposure to $PM_{2.5}$ was significantly positively associated with total periodontitis. In fully adjusted models, the ORs of total periodontitis associated with 10 $\mu g/m^3$ increase in 1-, 3- and 5-year annual $PM_{2.5}$ concentrations were 1.09 (95% CI: 1.06, 1.12), 1.08 (95% CI: 1.06, 1.11) and 1.07 (95% CI: 1.05, 1.10), respectively. From the severity of periodontitis, we found a slightly reduced association for moderate than mild periodontitis per 10 $\mu g/m^3$ $PM_{2.5}$ increase in annual concentration. For example, the OR of mild and moderate periodontitis associated with a 10 $\mu g/m^3$ increase in 1-year average concentration of $PM_{2.5}$ was 1.08 (95% CI: 1.05–1.12) and 1.05 (95% CI: 1.01–1.08). However, no significant associations were observed for severe periodontitis (Table 2).

TABLE 1 Demographic and clinical characteristics of participants.

Characteristics	No periodontitis ($n = 5068$)	Periodontitis ($n = 8391$)	p value[a]
Age, years	60.4 (13.2)	63.5 (11.7)	<.001
Female sex	2880 (56.8)	3870 (46.1)	<.001
Other ethnicities (%)	466 (9.2)	840 (10.0)	.13
Live in rural area	2533 (50.0)	4106 (48.9)	.25
$PM_{2.5}$ exposure, mean (SD)			
1-year	48.6 (1.81)	51.0 (1.91)	<.001
3-year	53.5 (2.03)	55.9 (2.19)	<.001
5-year	56.2 (2.16)	58.5 (2.30)	<.001
Smoking status (%)			<.001
Never smoked	3531 (69.7)	5021 (59.8)	
Current smokes	1120 (22.1)	2427 (28.9)	
Former smoked	416 (8.2)	942 (11.2)	
Frequency of alcohol consumption (%)			<.001
Never	3161 (62.4)	4575 (54.5)	
Seldom	1091 (21.5)	1880 (22.4)	
Frequent	561 (11.1)	1347 (16.1)	
Former	252 (5.0)	585 (7.0)	
Frequency of dessert consumption			<.001
Seldom	3413 (67.3)	6061 (72.2)	
Sometime	1169 (23.1)	1685 (20.1)	
Frequent	486 (9.6)	645 (7.7)	
Frequency of sweetened beverage consumption (%)			<.001
Seldom	4289 (84.6)	7358 (87.7)	
Sometime	593 (11.7)	793 (9.5)	
Frequent	186 (3.7)	240 (2.9)	
Education (%)			<.001
Illiteracy	781 (15.4)	1444 (17.2)	
Middle school	2643 (52.2)	4603 (54.9)	
High school	800 (15.8)	1417 (16.9)	
College	844 (16.7)	926 (11.0)	
Geographical region (%)			<.001
East	1401 (27.6)	1647 (19.6)	
North	736 (14.5)	1411 (16.8)	
Northeast	502 (9.9)	768 (9.2)	
Northwest	707 (14.0)	1516 (18.1)	
South	886 (17.5)	1667 (19.9)	
Southwest	836 (16.5)	1382 (16.5)	
Frequency of tooth brushing (%)			<.001
Seldom/never	258 (5.1)	477 (5.7)	
1–3 times/month	46 (0.9)	111 (1.3)	
1 time/week	56 (1.1)	120 (1.4)	
2–6 times/week	226 (4.5)	505 (6.0)	
1 time/day	2446 (48.3)	4357 (51.9)	
≥2 times/day	2036 (40.2)	2821 (33.6)	
Frequency of toothpick use (%)			<.001
Seldom/never	2802 (55.3)	4123 (49.1)	
1–3 times/month	319 (6.3)	521 (6.2)	

(Continues)

TABLE 1 (Continued)

Characteristics	No periodontitis ($n = 5068$)	Periodontitis ($n = 8391$)	p value[a]
1 time/week	189 (3.7)	344 (4.1)	
2–6 times/week	446 (8.8)	917 (10.9)	
1 time/day	470 (9.3)	871 (10.4)	
≥2 times/day	841 (16.6)	1614 (19.2)	
Dental cleaning in the past 12 months	4818 (95.1)	8030 (95.7)	.11
Comorbidity			
Stroke	75 (1.5)	145 (1.7)	.30
Diabetes	343 (6.8)	769 (9.2)	<.001
Hypertension	1006 (19.9)	2215 (26.4)	<.001
Heart diseases	516 (10.2)	1009 (12.0)	.001
COPD	92 (1.8)	128 (1.5)	.22

Abbreviations: COPD, chronic obstructive pulmonary disease; $PM_{2.5}$, particulate matter with a median aerodynamic diameter of no more than 2.5 μm.
[a]Values were calculated using the chi-squared test for categorical variables and Student's t-test for continuous variables.

The $PM_{2.5}$–periodontitis associations showed a significant heterogeneity in different geographical regions of China. The association between 1-year $PM_{2.5}$ exposure and periodontitis was stronger in North, East and Southwest China regions compared with Northwest China. However, we found non-significant effects on periodontitis in the South and Northwest regions (Table 3). We did not observe any appreciable differences in effect estimates when stratified by sex, age, ethnicity, living region, smoking status, alcohol consumption,

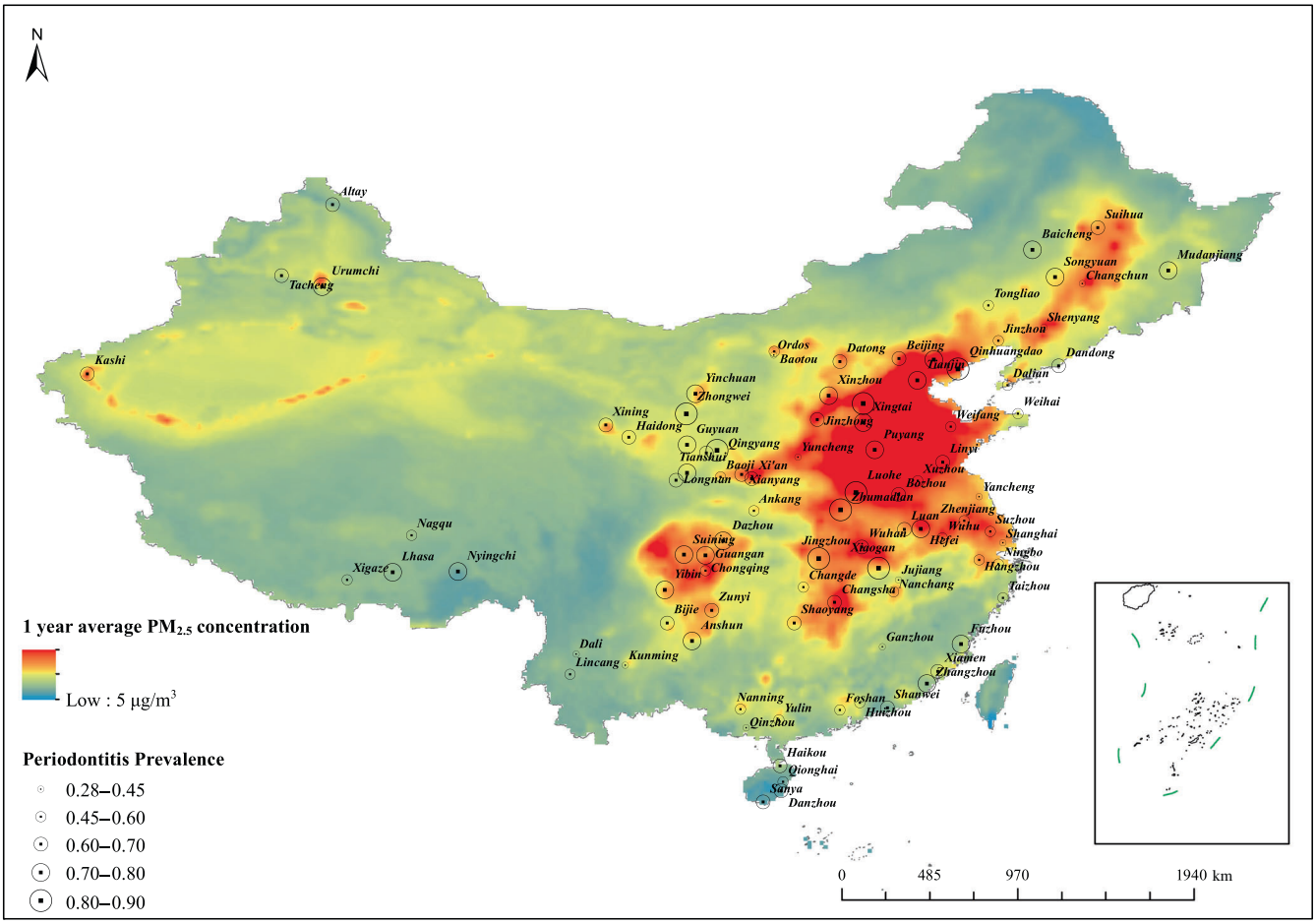

FIGURE 1 Annual mean concentrations of $PM_{2.5}$ across China during 2014–2015, and proportion of individuals diagnosed with periodontitis during the Fourth National Oral Health Survey of China.

TABLE 2 Associations of 1-, 3- and 5-year exposure to $PM_{2.5}$ with periodontitis based on the fourth national oral survey.

	1-year exposure		3-year exposure		5-year exposure	
Periodontitis classification	**OR (95% CI)**	***p* value**	**OR (95% CI)**	***p* value**	**OR (95% CI)**	***p* value**
Total periodontitis ($N = 8391$)						
Crude model	1.08 (1.05, 1.10)	<.01	1.06 (1.04, 1.08)	<.01	1.05 (1.03, 1.07)	<.01
Adjusted model	1.09 (1.06, 1.12)	<.01	1.08 (1.06, 1.11)	<.01	1.07 (1.05, 1.10)	<.01
Mild periodontitis ($N = 2081$)						
Crude model	1.09 (1.06, 1.12)	<.01	1.08 (1.06, 1.11)	<.01	1.08 (1.05, 1.11)	<.01
Adjusted model	1.08 (1.05, 1.12)	<.01	1.08 (1.04, 1.11)	<.01	1.07 (1.04, 1.10)	<.01
Moderate periodontitis ($N = 2196$)						
Crude model	1.00 (0.97, 1.03)	.98	0.99 (0.97, 1.02)	.53	0.99 (0.97, 1.02)	.47
Adjusted model	1.05 (1.01, 1.08)	<.01	1.04 (1.01, 1.07)	.01	1.03 (1.01, 1.06)	.02
Severe periodontitis ($N = 4114$)						
Crude model	1.02 (1.00, 1.04)	.10	1.01 (0.99, 1.04)	.22	1.01 (0.99, 1.03)	.58
Adjusted model	1.01 (0.98, 1.04)	.47	1.01 (0.98, 1.04)	.49	1.00 (0.98, 1.03)	.78

Note: Crude model: no adjustment. Adjusted model: crude model + age, sex, ethnicity, education, urban or rural areas, geographical region, current smoking status, current alcohol consumption status, frequency of dessert consumption, frequency of sweetened beverage consumption, frequency of tooth brushing, frequency of toothpick use, dental cleaning in the past 12 months, medical history of stroke, diabetes, hypertension, heart diseases and COPD.

frequency of dessert consumption, frequency of beverage consumption, education attainment and medical history (stroke, diabetes, hypertension, heart disease and COPD) (Table 3).

The concentration–response relationships for long-term $PM_{2.5}$ exposure and periodontitis are shown in Figure 2. We observed a strong linear relationship when the 1-, 3- and 5-year annual mean concentration of $PM_{2.5}$ exceeded 42, 60 and 62 μg/m^3, respectively. A downward trajectory was found for the 1-, 3- and 5-year exposure concentrations of $PM_{2.5}$ below 28 and 30 μg/m^3, but no statistically significant inverse association was observed at any point.

For the overall teeth, 1-year exposure to $PM_{2.5}$ was significantly associated with the increased risk of periodontal pockets (OR 1.08, 95% CI: 1.05–1.11) but not with increased risks of attachment loss (OR 0.97, 95% CI: 0.95–1.00), calculus (OR 1.05, 95% CI: 0.99–1.11) or bleeding gums (OR 1.01, 95% CI: 0.98–1.05). However, in the analysis by groups of tooth quadrants, the associations for these clinical manifestations in different quadrant were inconsistent with that for the overall teeth, and the magnitude of association varied by different quadrants. Specifically, for the periodontal pockets, we observed an OR of 1.10 (95% CI: 1.07, 1.14) in the UA quadrant and an OR of 1.09 (95% CI: 1.06, 1.11) in the UP quadrant per 10 μg/m^3 increase in 1-year annual $PM_{2.5}$ concentrations. A slightly elevated association was observed in the LA quadrant (OR 1.16, 95% CI: 1.12–1.19) and LP quadrant (OR 1.15, 95% CI: 1.12–1.18), respectively. This finding can also be seen in the spline analysis in the right column. For calculus, the association was mostly pronounced in the LP quadrant (OR 1.09, 95% CI: 1.06–1.13) followed by UA quadrant (OR 1.08, 95% CI: 1.06–1.11) and UP quadrant (OR 1.08, 95% CI: 1.05–1.11). For bleeding gums, we found stronger associations in the LP quadrant (OR 1.07, 95% CI: 1.04–1.09). However, for attachment loss, we did not observe a statistically significant association in any quadrants. The exposure–response curves supported these findings for the relationship between $PM_{2.5}$ and the number of symptomatic teeth, which showed slightly steeper slopes with lower PM exposure concentration and the line farther from the *x*-axis at the fixed exposure levels (Figure 3, Table S2). Sensitivity analyses adjusting for multi-pollutants individually or in combination yielded consistent results (Table S4), which reinforces the robustness of our model and the reliability of our estimated association.

4 | DISCUSSION

In this nationally representative sample, we observed a significant association between long-term exposure to ambient $PM_{2.5}$ and an increased risk of periodontitis. The association was more pronounced for mild periodontitis than moderate and severe periodontitis. As periodontitis is chronic and progressive, this finding suggests a critical role of long-term $PM_{2.5}$ exposure in the early stage of periodontitis. In addition, we found more potent effects of $PM_{2.5}$ on the increased risk of periodontal pockets in the LA and LP teeth and a substantial effect on bleeding gums in the UA and LP teeth, which indicates susceptible tooth quadrants to adverse periodontal effects caused by ambient $PM_{2.5}$ exposure. Given the rising prevalence, substantial effects of periodontal disease and considerable costs of dental treatment for both the individual and the wider the healthcare system, as well as the ubiquitous nature and proven hazard of $PM_{2.5}$, our findings may contribute to reducing the global burden of periodontitis by indicating consideration of $PM_{2.5}$ exposure in periodontal disease prevention and intervention.

Few previous studies have investigated the association between long-term exposure to ambient $PM_{2.5}$ and periodontitis. Our findings

TABLE 3 Associations between 1-year exposure to $PM_{2.5}$ air pollution and periodontitis by different characteristics of participants in the fourth national oral survey.

Subgroup	OR (95% CI)	*p* for trend
Sex		.67
Male	1.07 (1.04, 1.11)	
Female	1.08 (1.05, 1.12)	
Age		.25
35–44	1.06 (1.03, 1.10)	
45–64	1.09 (1.05, 1.14)	
65–74	1.11 (1.07, 1.15)	
Ethnicity		.13
Han	1.08 (1.06, 1.11)	
Other	1.03 (0.96, 1.10)	
Types of living area		.89
Urban	1.08 (1.05, 1.12)	
Rural	1.08 (1.05, 1.11)	
Frequency of dessert consumption		.78
Seldom	1.09 (1.06, 1.12)	
Sometime	1.07 (1.02, 1.12)	
Frequent	1.07 (1.00, 1.16)	
Frequency of sweetened beverage consumption		.78
Seldom	1.08 (1.06, 1.11)	
Sometime	1.06 (0.99, 1.13)	
Frequent	1.10 (0.98, 1.24)	
Smoking status		.33
Never	1.07 (1.04, 1.10)	
Current	1.11 (1.06, 1.16)	
Former	1.05 (0.97, 1.13)	
Educational level		.30
Illiteracy	1.09 (1.03, 1.16)	
Middle school	1.10 (1.07, 1.14)	
High school	1.05 (1.00, 1.11)	
College	1.05 (0.99, 1.11)	
Frequency of alcohol consumption		.66
Never	1.07 (1.04, 1.10)	
Seldom	1.08 (1.03, 1.13)	
Frequent	1.11 (1.04, 1.19)	
Former	1.11 (1.01, 1.23)	
Geographical region		<.001
Northwest China	0.96 (0.89, 1.02)	
Southwest China	1.06 (1.01, 1.12)	
Northeast China	0.67 (0.58, 0.77)	
North China	1.22 (1.14, 1.31)	
East China	1.17 (1.12, 1.22)	
South China	1.04 (0.96, 1.13)	

Note: Models were adjusted for age, sex, ethnicity, education, living in urban or rural areas, geographical region, current smoking status, current alcohol consumption status, frequency of dessert consumption, frequency of sweetened beverage consumption, frequency of tooth brushing, frequency of toothpick use, dental cleaning in the past 12 months, medical history of stroke, diabetes, hypertension, heart diseases and COPD.
Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio; PM, particulate matter.

regarding the associations between $PM_{2.5}$ and periodontitis and tendency in exposure–response relationship are consistent with one previous research, which is the only study linking ambient air pollution to periodontitis available to date. This retrospective study conducted in Taiwan demonstrated the risk of long-term exposure to air pollution on periodontitis using health insurance data, and reported that the hazard ratio of periodontitis for residents with higher exposure levels could increase by more than fourfold compared with those with low exposure levels of $PM_{2.5}$ (<17.5 μg/m^3) (Lin et al., 2022). However, the periodontitis in this study was ascertained only by diagnostic codes formatted according to different revisions of the International Classification of Diseases (ICD) rather than a valid diagnostic method. This may induce substantial bias due to miscoding and misclassification of the ICD. In addition, failure to adjust for critical oral-related covariates such as dietary habits and family history of oral diseases may have led to biased estimates of the effects of fine particulate matter air pollution. By comparison, the periodontitis endpoint in this study was diagnosed through standard periodontal examination and ascertained by a licensed dentist. Our results with full adjustment for behavioural factors related to oral hygiene will provide new reliable evidence on the association between ambient $PM_{2.5}$ and periodontitis in a general population. Though evidence remains scarce for the health effect of long-term exposure to ambient $PM_{2.5}$ on periodontitis, existing evidence has demonstrated a positive association between periodontitis prevalence and cigarette smoke and environmental tobacco smoke (ETS) (Akinkugbe et al., 2016; Javed et al., 2014; Sutton et al., 2017), both of which are substantial sources of $PM_{2.5}$ (Loffredo et al., 2016; Ni et al., 2020). Our findings on $PM_{2.5}$ exposure and increased risk of periodontitis are consistent with these research studies in terms of direction.

This study observed a decreased risk of moderate compared with mild periodontitis and a lack of association of $PM_{2.5}$ with severe periodontitis. In the progression of mild periodontitis to severe periodontitis, other risk factors such as chronic diseases, autoimmune status and oral hygiene may play a major and more critical role compared with air pollution exposure. Moreover, in conjunction with the existing mechanisms of health hazards caused by $PM_{2.5}$, we initially made the research hypothesis that $PM_{2.5}$ may play a deleterious role in the early stages of periodontitis. Therefore, $PM_{2.5}$ exposure associated with mild periodontitis but not with moderate and severe periodontitis was consistent with our hypothesis. However, due to the limitations of the study design, we were unable to identify the specific role of air pollution in the development of periodontitis, which needs to be explored in depth by optimizing epidemiological study design or animal studies. Additionally, our previous study showed that the prevalence of severe periodontitis was higher in smokers and the elderly, which suggested that smoking and old age may contribute more to moderate and severe periodontitis and play a stronger role in the progression of periodontitis than air pollution (Jiao et al., 2021).

We further observed a significant geographical difference in the association between $PM_{2.5}$ and periodontitis, with a more evident association in North, East and Southwest China. This heterogeneity in the effects of $PM_{2.5}$ among regions is comparable to that in previous multi-city studies on particulate matter pollutants and adverse health

outcomes. R. Chen et al. (2017) observed greater effects of $PM_{2.5}$ on mortality risk in Southwest, middle South, North and East China, whereas weak or non-significant effects in Northeast and Northwest China. H. Liu et al. (2017) found stronger associations of particulate matter with stroke hospitalization in northern China than in southern China. Diverse in constituents and sources of particulate matter, levels of air pollutants, climatic characteristics and population adaptation were proposed to be plausible underlying reasons for the spatial heterogeneity (R. Chen et al., 2017; T. Liu et al., 2022; Tian et al., 2019). For instance, the non-significant effects in Northwest regions might be explained in such a way that higher proportions of crustal materials and elements relevant to biomass burning contributed to relatively weaker toxicity of $PM_{2.5}$ in Northwest regions than in other regions (R. Chen et al., 2017; Thurston George et al., 2016; F. Yang et al., 2011). A previous study showed that the proportions of secondary inorganic aerosols (SIAs) in ambient $PM_{2.5}$ in South, East and North China were higher than in West China (Tian et al., 2019). In addition, we found an association between $PM_{2.5}$ exposure and decreased risks of periodontitis in Northeast regions. The inverse association may be due to smaller number of participants than in other regions and should be interpreted with caution.

However, the exact biological mechanisms for the associations between ambient $PM_{2.5}$ and periodontitis remain to be explored. Combined with the pathogenesis of periodontal diseases, where plaque bacteria initiate systemic and local inflammatory response, there are excessive levels of pro-inflammatory mediators and enzymes, which leads to the destruction of periodontal tissues (Genco & Williams, 2010). The pathway underlying the connection between air pollution and other systemic effects might also be the main plausible biological mechanism by which long-term $PM_{2.5}$ exposure increases the risk of periodontitis. A previous study suggested that adults with chronic periodontal infections were more susceptible to increases in particulate matter-induced high-sensitivity C-reactive protein, a biomarker of systemic inflammation, compared with periodontally healthy individuals (T.-H. Yang et al., 2015). Reactive oxygen species-mediated oxidative stress plays a vital role in the pathogenesis of periodontitis (Sacks et al., 2018). $PM_{2.5}$ can reach the mouth through inhalation and be deposited in the mouth (Manojkumar et al., 2019). Experimental data showed that increased exposure to $PM_{2.5}$ was associated with increased micronuclei frequency (considered a biomarker of DNA damage) in oral epithelial cells (Ceretti et al., 2014; Sisenando et al., 2012). The carbon components of $PM_{2.5}$, including elemental and organic carbon, can produce reactive oxygen species (ROS). The former releases a high concentration of ROS in the process of being engulfed by macrophages. The latter also produces a large amount of ROS through its metabolic processes, and the excess ROS induces oxidative stress (Dahiya et al., 2013). Pyroptosis has been proposed to be an essential pathogenesis of periodontitis in recent years, and $PM_{2.5}$ has been shown to induce tissue damage through NLRP3 inflammasome-mediated pyroptosis. Therefore, we postulated that $PM_{2.5}$ might also increase the risk of periodontitis by mediating the pathophysiological pathway of pyroptosis. Furthermore, there is a common chemical component called humic-like substances (HULIS) in both particulate matter and tobacco smoke. Previous studies indicated that inhalation of HULIS to the lung would induce phagocytosis and accumulation of intracellular iron giving rise to iron sequestration and subsequent deficiency of cellular metals, which would cause a series of responses to functional metal deficiency including oxidative stress, activation of cell signalling and transcription factors, release of pro-inflammatory mediators, and apoptosis. Tissue inflammation and

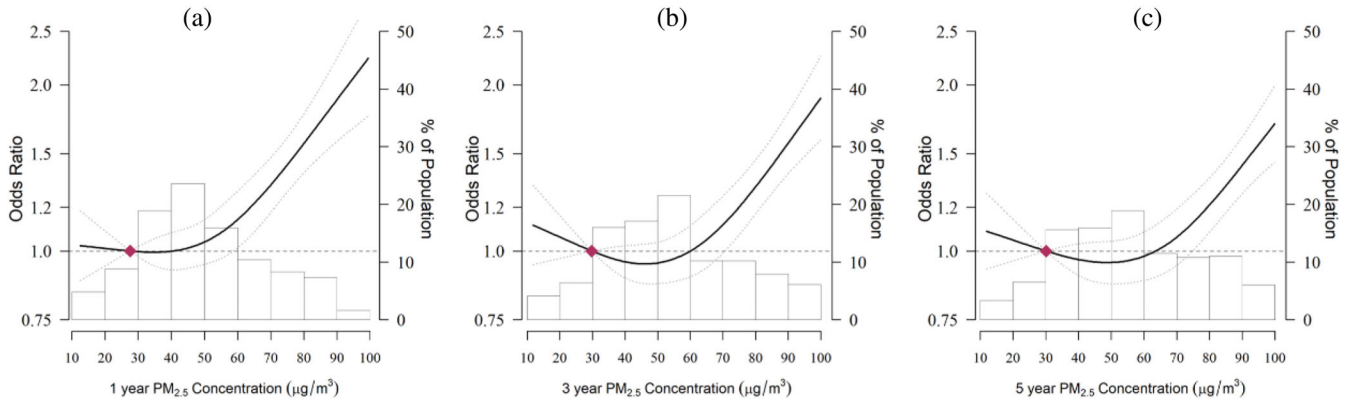

FIGURE 2 The exposure–response relationship between long-term exposure to $PM_{2.5}$ and the risk of periodontitis. The exposure–response curve was calculated using restricted cubic splines with a df of 4 and knots at the 10th, 50th and 90th percentiles of the distribution of 1-year $PM_{2.5}$ concentrations. The reference exposure level was set at the 10th percentile of the distribution of 1-year $PM_{2.5}$ concentrations (27.6 μg/m^3), 3-year $PM_{2.5}$ concentrations (29.8 μg/m^3) and 5-year $PM_{2.5}$ concentrations (30.1 μg/m^3). ORs were adjusted for age, sex, ethnicity, education, living in urban or rural areas, geographical region, current smoking status, current alcohol consumption status, frequency of dessert consumption, frequency of sweetened beverage consumption, frequency of tooth brushing, frequency of toothpick use, dental cleaning in the past 12 months, medical history of stroke, diabetes, hypertension, heart diseases and COPD. The solid line indicates estimated odds ratio values, and the dashed lines indicate their 95% confidence intervals. The bars are histograms (dependent on the right *y*-axis) and indicate the distribution of the $PM_{2.5}$ concentration data. The red dot indicates an odds ratio of 1 when the $PM_{2.5}$ concentration is the reference exposure level. COPD, chronic obstructive pulmonary disease; $PM_{2.5}$, particle matter with a median aerodynamic diameter ≤2.5 μm.

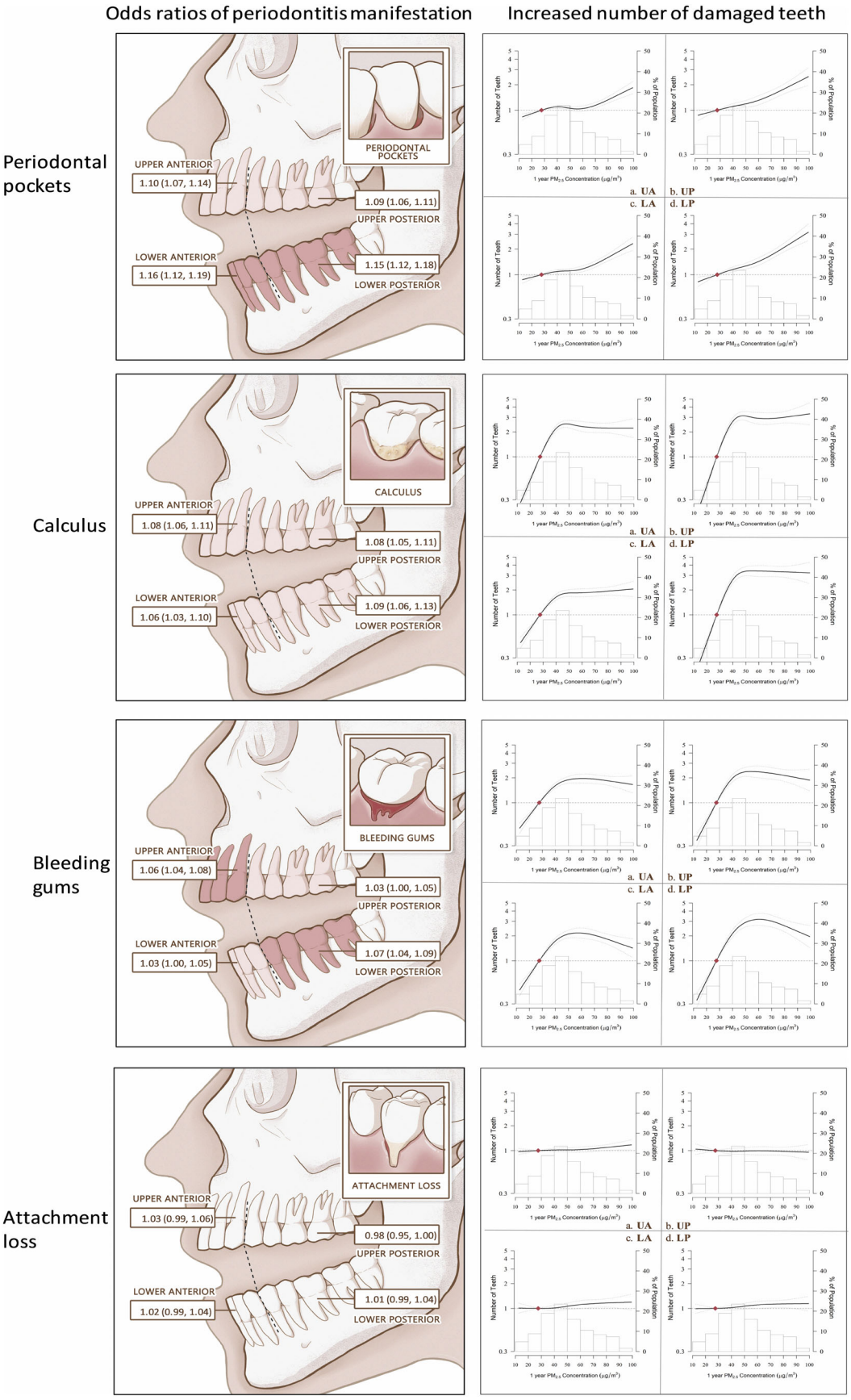

FIGURE 3 Legend on next page.

fibrosis would be further facilitated by these reactions (Ghio et al., 1994; Y. Liu et al., 2014; W. Zhang et al., 2014). In addition, the influence of particulate matter on gut microbiota may also be the potential mechanism by which $PM_{2.5}$ exposure increases the risk of periodontitis (Luo et al., 2023; Qin & Wang, 2023). On the one hand, particulate matter entering the intestinal tract can destroy the intestinal mucosal barrier by affecting gut microbiota. It would cause metabolic disorders and disrupt the immune system (Y. Liu et al., 2021), which increases susceptibility to the hazardous effect of $PM_{2.5}$. On the other hand, the compositional and functional change in gut microbiota induced by particulate matter may strengthen the causal role of gut microbiota in enhancing the risk of periodontitis. However, studies on environmental $PM_{2.5}$ exposure and the occurrence of periodontitis are minimal, and the underlying mechanisms need to be further elucidated.

Furthermore, we observed the associations between long-term $PM_{2.5}$ exposure and three clinical manifestations of periodontitis except for attachment loss. These findings further supported our previous hypothesis that $PM_{2.5}$ increased the risk of periodontitis and may be more strongly associated with clinical manifestations in early progression. For both periodontal pocket and gingival bleeding, higher estimates for the effect of $PM_{2.5}$ exposure were observed in LP teeth, suggesting that teeth in the LP quadrant may be more susceptible to long-term $PM_{2.5}$ exposure. We speculated that the following explanations might be responsible for this susceptibility to LP teeth. First, the teeth in the LP quadrant are close to the pharynx, which divides into the nasopharynx, oropharynx and laryngopharynx. When airborne $PM_{2.5}$ enters the body from the nasal cavity with breathing, the pharynx is the part that must pass through, and the lower back teeth near the oropharynx are more likely to be exposed to $PM_{2.5}$. Second, the months with higher concentrations of air pollution in China are also the seasons with a high incidence of influenza (Song et al., 2021), which causes inflammation and swelling of the tonsils and then nasal congestion (due to the ring-shaped arrangement of the tonsils in the pharynx, which is called the pharynx Waldeyer's ring). People compensate by breathing more frequently through their mouths, and the chances of air entering the body from the mouth increase, and as air enters the mouth and travels towards the pharynx, it is also more likely to affect the lower back teeth near the pharynx. Finally, particulate pollutants and bacteria in saliva can mix to form microbial aerosols and thus cause harm to the teeth in the LP quadrant. These teeth are located at the bottom of the mouth where the salivary pool is located (all the saliva produced by the glands collects at the bottom of the mouth, forming a pool of salivary). Thus, the teeth in LP quadrant are more likely to deposit microbial aerosol and are more vulnerable.

This study possessed a few strengths. First, the current findings were based on data from a national oral health survey with a rigorous periodontal examination, ensuring high accuracy and credibility of diagnosis. Besides, the study was conducted in a country with high levels of ambient air pollutants, wide exposure level ranges and with exposure variability. The application of these data on nationally representative sample guaranteed the feasibility to extrapolate our findings to population in countries with similar air pollution levels as Mainland China. These findings can also provide clinical guiding value that clinicians should consider air pollution exposure as a risk factor when assessing the risk of periodontitis for individuals residing in places with comparable air pollution levels with China. A further strength of this study is the full adjustment for multiple covariates and individual-level risk factors, enhancing the credibility of the results. Several limitations in this study should also be noted. The primary limitation was that the cross-sectional design inherently limited us to establish a causal relationship between $PM_{2.5}$ exposure and periodontitis due to the unknown onset dates of periodontitis and the inability to determine a temporal relationship. We cannot obtain the onset date of periodontitis because periodontal condition was examined at a single time point. Further investigations with an improved study design are needed to confirm these findings. Second, though patients may be exposed to multiple air pollutants simultaneously, we were not able to apply multi-pollutant models in the analyses because of high correlations among air pollutants (B.-Y. Yang et al., 2019). The potential interactive effects of pollutants on periodontitis were unexplored. Third, the $PM_{2.5}$ concentration assessment was based on a comprehensive satellite-based model and individual exposure was assigned only to the residence addresses without taking into account time–activity patterns. Such exposure misclassification may cause residual confounding and underestimate the effect size. It is crucial to highlight that this form of misclassification is non-differential and uniformly affects all study participants, irrespective of the outcome or the level of pollution exposure they experienced. Such a scenario is more likely

FIGURE 3 Associations of long-term exposure to $PM_{2.5}$ with four clinical manifestations of periodontitis (a, c, e, g) and the exposure–response relationship between long-term exposure to $PM_{2.5}$ and the number of damaged teeth (b, d, f, h) by group of tooth quadrants. Odds ratios were adjusted for age, sex, ethnicity, education, living in urban or rural areas, geographical region, current smoking status, current alcohol consumption status, frequency of dessert consumption, frequency of sweetened beverage consumption, frequency of tooth brushing, frequency of toothpick use, dental cleaning in the past 12 months and medical history of stroke, diabetes, hypertension, heart diseases and COPD. The exposure–response curve was calculated using restricted cubic splines with a df of 4 and knots at the 10th, 50th and 90th percentiles of the distribution of 1-year $PM_{2.5}$ concentrations. The reference exposure level was set at the 10th percentile of the distribution of 1-year $PM_{2.5}$ concentrations. The solid line indicates the estimated number of damaged teeth with each clinical manifestation, and the dashed lines indicate their 95% confidence intervals. The bars are histograms (dependent on the right *y*-axis) and indicate the distribution of the $PM_{2.5}$ concentration data. The red dot indicates the odds ratio of 1.00 when the $PM_{2.5}$ concentration is the reference exposure level. COPD, chronic obstructive pulmonary disease; LA, lower anterior; LP, lower posterior; $PM_{2.5}$, particle matter with a median aerodynamic diameter ≤2.5 μm; UA, upper anterior; UP, upper posterior.

to yield attenuated effect estimates (Lin et al., 2016). Fourth, it is noteworthy that we found a modest association due to the distal pathway between ambient air pollution exposure and their potential pathologic effects. However, given the ubiquitous characteristic of ambient air pollutants, small effects have the potential to substantially affect public health. Our study provides supportive evidence that reducing population-level exposures to ambient $PM_{2.5}$ pollution may potentially improve oral health. Finally, previous studies have shown the association of $PM_{2.5}$ exposure with elevated levels of inflammatory factors (white blood cell, C-reactive protein, etc.) (J.-C. Chen & Schwartz, 2008; Dabass et al., 2018; Dubowsky Sara et al., 2006), indicating that systematic inflammation is one of the mechanisms by which $PM_{2.5}$ causes chronic diseases such as cardiovascular disease. Regrettably, blood samples were not collected during the National Oral Health Survey, resulting in the absence of biomarker data. Further studies are warranted to explore the role of inflammatory factors in the relationship between $PM_{2.5}$ and periodontitis.

5 | CONCLUSIONS

In conclusion, this study indicated that long-term exposure to ambient $PM_{2.5}$ was significantly associated with increased risk of periodontitis. Our findings added to the limited evidence on the deleterious effects of long-term exposure to ambient $PM_{2.5}$ on periodontal disease and further provided evidence that there is potential for air pollution mitigation in contributing to prevention of periodontal disease. In view of the worsening health burden of periodontal disease, it might be necessary for healthcare providers to be more concerned about ambient air pollution and integrate it into oral health improvement strategies.

AUTHOR CONTRIBUTIONS

HM and ZZ contributed to conceptualization of the study and supervised the whole project. NL and ZL prepared dataset and conducted formal analysis. XH and NL contributed to the visualization. SS and ZZ contributed to the methodology and validation of the results. WL and NL wrote and revised the original draft. YS, XW, XF, BT, DH, HL, BW, CW, SZ, XL, WR and WW coordinated the design process and contributed to the field implementation of the national survey on behalf of the study steering group. All authors reviewed the article, read the final manuscript and approved the submission. HM and ZZ had full access to all the data in the study and had final responsibility for the decision to submit for publication.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

All authors have completed the Unified Competing Interest form and declare no support from any organization for the submitted work, no financial relationships with any organizations that might have had an interest in the submitted work in the previous 3 years, and no other relationships or activities that could appear to have influenced the submitted work.

DATA AVAILABILITY STATEMENT

Deidentified patient-level data and the full dataset with low risk of identification are available on reasonable request from the corresponding author after approval by the trial steering committee and the ethics committee of the coordinating center.

ETHICS STATEMENT

The ethics committee of the Chinese Stomatological Association approved this study (approval no. 2014-003).

ORCID

Wenjing Li https://orcid.org/0000-0002-9905-3836
Huanxing Meng https://orcid.org/0000-0002-2954-818X

REFERENCES

Akinkugbe, A. A., Slade, G. D., Divaris, K., & Poole, C. (2016). Systematic review and meta-analysis of the association between exposure to environmental tobacco smoke and periodontitis endpoints among nonsmokers. *Nicotine & Tobacco Research*, *18*(11), 2047–2056.

Alexeeff, S. E., Liao, N. S., Liu, X., Van Den Eeden, S. K., & Sidney, S. (2021). Long-term PM2.5 exposure and risks of ischemic heart disease and stroke events: Review and meta-analysis. *Journal of the American Heart Association*, *10*(1), e016890.

Benzian, H., Hobdell, M., Holmgren, C., Yee, R., Monse, B., Barnard, J. T., & Van Palenstein Helderman, W. (2011). Political priority of global oral health: An analysis of reasons for international neglect. *International Dental Journal*, *61*(3), 124–130.

Block, M. L., & Calderón-Garcidueñas, L. (2009). Air pollution: Mechanisms of neuroinflammation and CNS disease. *Trends in Neurosciences*, *32*(9), 506–516.

Brunekreef, B., & Holgate, S. T. (2002). Air pollution and health. *The Lancet*, *360*(9341), 1233–1242.

Ceretti, E., Feretti, D., Viola, G. C., Zerbini, I., Limina, R. M., Zani, C., Capelli, M., Lamera, R., Donato, F., & Gelatti, U. (2014). DNA damage in buccal mucosa cells of pre-school children exposed to high levels of urban air pollutants. *PLoS One*, *9*(5), e96524.

Chapple, I. L. (2014). Time to take periodontitis seriously. *BMJ*, *348*, g2645.

Chen, J.-C., & Schwartz, J. (2008). Metabolic syndrome and inflammatory responses to long-term particulate air pollutants. *Environmental Health Perspectives*, *116*(5), 612–617.

Chen, R., Yin, P., Meng, X., Liu, C., Wang, L., Xu, X., Ross, J. A., Tse, L. A., Zhao, Z., Kan, H., & Zhou, M. (2017). Fine particulate air pollution and daily mortality. A nationwide analysis in 272 Chinese cities. *American Journal of Respiratory and Critical Care Medicine*, *196*(1), 73–81.

Dabass, A., Talbott, E. O., Rager, J. R., Marsh, G. M., Venkat, A., Holguin, F., & Sharma, R. K. (2018). Systemic inflammatory markers associated with cardiovascular disease and acute and chronic exposure to fine particulate matter air pollution (PM2.5) among US NHANES adults with metabolic syndrome. *Environmental Research*, *161*, 485–491.

Dahiya, P., Kamal, R., Gupta, R., Bhardwaj, R., Chaudhary, K., & Kaur, S. (2013). Reactive oxygen species in periodontitis. *Journal of Indian Society of Periodontology*, *17*(4), 411–416.

Dubowsky Sara, D., Suh, H., Schwartz, J., Coull Brent, A., & Gold, D. R. (2006). Diabetes, obesity, and hypertension may enhance associations

between air pollution and markers of systemic inflammation. *Environmental Health Perspectives*, *114*(7), 992–998.

Dye, B. A. (2012). Global periodontal disease epidemiology. *Periodontology 2000*, *58*(1), 10–25.

Genco, R. J., & Borgnakke, W. S. (2013). Risk factors for periodontal disease. *Periodontology 2000*, *62*(1), 59–94.

Genco, R. J., & Williams, R. C. (Eds.). (2010). *Periodontal disease and overall health: A Clinician's guide*. Professional Audience Communications, Inc.

Ghio, A. J., Stonehuerner, J., & Quigley, D. R. (1994). Humic-like substances in cigarette smoke condensate and lung tissue of smokers. *American Journal of Physiology-Lung Cellular and Molecular Physiology*, *266*(4), L382–L388.

Graetz, C., Mann, L., Krois, J., Sälzer, S., Kahl, M., Springer, C., & Schwendicke, F. (2019). Comparison of periodontitis patients' classification in the 2018 versus 1999 classification. *Journal of Clinical Periodontology*, *46*(9), 908–917.

Hajishengallis, G., & Chavakis, T. (2021). Local and systemic mechanisms linking periodontal disease and inflammatory comorbidities. *Nature Reviews. Immunology*, *21*(7), 426–440.

Hamanaka, R. B., & Mutlu, G. M. (2018). Particulate matter air pollution: Effects on the cardiovascular system. *Frontiers in Endocrinology*, *9*. https://www.frontiersin.org/articles/10.3389/fendo.2018.00680

Javed, F., Bashir Ahmed, H., & Romanos, G. E. (2014). Association between environmental tobacco smoke and periodontal disease: A systematic review. *Environmental Research*, *133*, 117–122.

Jiao, J., Jing, W., Si, Y., Feng, X., Tai, B., Hu, D., Lin, H., Wang, B., Wang, C., Zheng, S., Liu, X., Rong, W., Wang, W., Li, W., Meng, H., & Wang, X. (2021). The prevalence and severity of periodontal disease in mainland China: Data from the Fourth National Oral Health Survey (2015-2016). *Journal of Clinical Periodontology*, *48*(2), 168–179.

Keiser-Nielsen, S. (1971). Federation Dentaire Internationale. Two-digit system of designating teeth. *Dental Practice (Ewell)*, *3*(4), 6 passim.

Lin, H., Liu, T., Xiao, J., Zeng, W., Li, X., Guo, L., Zhang, Y., Xu, Y., Tao, J., Xian, H., Syberg, K. M., Qian, Z. (. M.)., & Ma, W. (2016). Mortality burden of ambient fine particulate air pollution in six Chinese cities: Results from the Pearl River Delta study. *Environment International*, *96*, 91–97.

Lin, H., Tsai, S., Lin, F., Hsu, Y. C., Chen, S. W., Chou, R. H., Lin, C. L., Hsu, C. Y., & Chang, K. H. (2022). Prolonged exposure to air pollution increases periodontal disease risk: A nationwide, population-based, cohort study. *Atmosphere (Basel)*, *12*(12), 1668.

Liu, H., Tian, Y., Xu, Y., & Zhang, J. (2017). Ambient particulate matter concentrations and hospitalization for stroke in 26 Chinese cities. *Stroke*, *48*(8), 2052–2059.

Liu, T., Jiang, Y., Hu, J., Li, Z., Guo, Y., Li, X., Xiao, J., Yuan, L., He, G., Zeng, W., Kan, H., Rong, Z., Chen, G., Yang, J., Wang, Y., & Ma, W. (2022). Association of ambient PM1 with hospital admission and recurrence of stroke in China. *Science of the Total Environment*, *828*, 154131.

Liu, Y., Cui, Y., Shi, M., Zhang, Q., Wang, Q., & Chen, X. (2014). Deferoxamine promotes MDA-MB-231 cell migration and invasion through increased ROS-dependent HIF-1α accumulation. *Cellular Physiology and Biochemistry*, *33*(4), 1036–1046.

Liu, Y., Wang, C., Zhao, X., Wu, F., Bai, Y., Teng, M., Wang, X., & Shi, D. (2021). Environmental toxicology of gut microbiota: Status and perspective. *Research of Environmental Sciences*, *34*(8), 1991–2000.

Loffredo, C. A., Tang, Y., Momen, M., Makambi, K., Radwan, G. N., & Aboul-Foutoh, A. (2016). PM2.5 as a marker of exposure to tobacco smoke and other sources of particulate matter in Cairo, Egypt. *The International Journal of Tuberculosis and Lung Disease*, *20*(3), 417–422.

Luo, S., Li, W., Li, Q., Zhang, M., Wang, X., Wu, S., & Li, Y. (2023). Causal effects of gut microbiota on the risk of periodontitis: A two-sample Mendelian randomization study. *Frontiers in Cellular and Infection Microbiology*, *13*, 1160993.

Manojkumar, N., Srimuruganandam, B., & Shiva Nagendra, S. M. (2019). Application of multiple-path particle dosimetry model for quantifying age specified deposition of particulate matter in human airway. *Ecotoxicology and Environmental Safety*, *168*, 241–248.

Møller, P., Danielsen, P. H., Karottki, D. G., Jantzen, K., Roursgaard, M., Klingberg, H., Jensen, D. M., Christophersen, D. V., Hemmingsen, J. G., Cao, Y., & Loft, S. (2014). Oxidative stress and inflammation generated DNA damage by exposure to air pollution particles. *Mutation Research – Reviews in Mutation Research*, *762*, 133–166.

Monsarrat, P., Blaizot, A., Kémoun, P., Ravaud, P., Nabet, C., Sixou, M., & Vergnes, J. N. (2016). Clinical research activity in periodontal medicine: A systematic mapping of trial registers. *Journal of Clinical Periodontology*, *43*(5), 390–400.

Munzel, T., Sorensen, M., Gori, T., Schmidt, F. P., Rao, X., Brook, F. R., Chen, L. C., Brook, R. D., & Rajagopalan, S. (2017). Environmental stressors and cardio-metabolic disease: Part II-mechanistic insights. *European Heart Journal*, *38*(8), 557–564.

Nääv, Å., Erlandsson, L., Isaxon, C., Åsander Frostner, E., Ehinger, J., Sporre, M. K., Krais, A. M., Strandberg, B., Lundh, T., Elmér, E., Malmqvist, E., & Hansson, S. R. (2020). Urban PM2.5 induces cellular toxicity, hormone dysregulation, oxidative damage, inflammation, and mitochondrial interference in the HRT8 trophoblast cell line. *Frontiers in Endocrinology (Lausanne)*, *11*, 75.

Nazir, M. A. (2017). Prevalence of periodontal disease, its association with systemic diseases and prevention. *International Journal of Health Sciences (Qassim)*, *11*(2), 72–80.

Ni, Y., Shi, G., & Qu, J. (2020). Indoor PM2.5, tobacco smoking and chronic lung diseases: A narrative review. *Environmental Research*, *181*, 108910.

Peres, M. A., Macpherson, L. M. D., Weyant, R. J., Daly, B., Venturelli, R., Mathur, M. R., Listl, S., Celeste, R. K., Guarnizo-Herreño, C. C., Kearns, C., Benzian, H., Allison, P., & Watt, R. G. (2019). Oral diseases: A global public health challenge. *The Lancet*, *394*(10194), 249–260.

Petersen, P. E., & Baehni, P. C. (2012). Periodontal health and global public health. *Periodontology 2000*, *60*(1), 7–14.

Pihlstrom, B. L., Michalowicz, B. S., & Johnson, N. W. (2005). Periodontal diseases. *The Lancet*, *366*(9499), 1809–1820.

Qin, J., & Wang, J. (2023). Research progress on the effects of gut microbiome on lung damage induced by particulate matter exposure. *Environmental Research*, *233*, 116162.

Rajagopalan, S., & Landrigan, P. J. (2021). Pollution and the heart. *New England Journal of Medicine*, *385*(20), 1881–1892.

Sacks, D., Baxter, B., Campbell, B. C. V., Carpenter, J. S., Cognard, C., Dippel, D., Eesa, M., Fischer, U., Hausegger, K., & Hirsch, J. A. (2018). Multisociety consensus quality improvement revised consensus statement for endovascular therapy of acute ischemic stroke. *International Journal of Stroke*, *13*(6), 612–632.

Sisenando, H. A., Batistuzzo de Medeiros, S. R., Artaxo, P., Saldiva, P. H., & Hacon, S. S. (2012). Micronucleus frequency in children exposed to biomass burning in the Brazilian Legal Amazon region: A control case study. *BMC Oral Health*, *12*, 6.

Song, Y., Zhang, Y., Wang, T., Qian, S., & Wang, S. (2021). Spatio-temporal differentiation in the incidence of influenza and its relationship with air pollution in China from 2004 to 2017. *Chinese Geographical Science*, *31*(5), 815–828.

Sutton, J. D., Salas Martinez, M. L., & Gerkovich, M. M. (2017). Environmental tobacco smoke and periodontitis in United States nonsmokers, 2009 to 2012. *Journal of Periodontology*, *88*(6), 565–574.

Thurston George, D., Burnett Richard, T., Turner Michelle, C., Shi, Y., Krewski, D., Lall, R., Ito, K., Jerrett, M., Gapstur, S. M., Diver, W. R., & Pope, C. A., III. (2016). Ischemic heart disease mortality and long-term exposure to source-related components of U.S. fine particle air pollution. *Environmental Health Perspectives*, *124*(6), 785–794.

Tian, Y., Liu, H., Wu, Y., Si, Y., Song, J., Cao, Y., Li, M., Wu, Y., Wang, X., Chen, L., Wei, C., Gao, P., & Hu, Y. (2019). Association between ambient fine particulate pollution and hospital admissions for cause specific cardiovascular disease: Time series study in 184 major Chinese cities. *BMJ*, *367*, l6572.

Watt, R. G., Daly, B., Allison, P., Macpherson, L. M. D., Venturelli, R., Listl, S., Weyant, R. J., Mathur, M. R., Guarnizo-Herreño, C. C., Celeste, R. K., Peres, M. A., Kearns, C., & Benzian, H. (2019). Ending the neglect of global oral health: Time for radical action. *The Lancet*, *394*(10194), 261–272.

World Health Organization. (2022). *Global Oral Health Status Report: Towards Universal Health Coverage for Oral Health by 2030*. World Health Organization.

Wu, H., Dong, C., Xiao, W., Wei, H., Shao, Y., Chen, T., & Xia, Y. (2022). Associations between PM2.5 exposure and infant growth: A mediation analysis of oral microbiota. *Science of the Total Environment*, *823*, 153688.

Xing, Y. F., Xu, Y. H., Shi, M. H., & Lian, Y. X. (2016). The impact of PM2.5 on the human respiratory system. *Journal of Thoracic Disease*, *8*(1), E69–E74.

Yang, B.-Y., Guo, Y., Markevych, I., Qian, Z. M., Bloom, M. S., Heinrich, J., Dharmage, S. C., Rolling, C. A., Jordan, S. S., Komppula, M., Leskinen, A., Bowatte, G., Li, S., Chen, G., Liu, K. K., Zeng, X. W., Hu, L. W., & Dong, G. H. (2019). Association of long-term exposure to ambient air pollutants with risk factors for cardiovascular disease in China. *JAMA Network Open*, *2*(3), e190318.

Yang, F., Tan, J., Zhao, Q., du, Z., He, K., Ma, Y., Duan, F., Chen, G., & Zhao, Q. (2011). Characteristics of PM 2.5 speciation in representative megacities and across China. *Atmospheric Chemistry and Physics*, *11*(11), 5207–5219.

Yang, T.-H., Masumi, S.-I., Weng, S.-P., Chen, H.-W., Chuang, H.-C., & Chuang, K.-J. (2015). Personal exposure to particulate matter and inflammation among patients with periodontal disease. *Science of the Total Environment*, *502*, 585–589.

Zhang, W., Wu, Y., Yan, Q., Ma, F., Shi, X., Zhao, Y., Peng, Y., Wang, J., & Jiang, B. (2014). Deferoxamine enhances cell migration and invasion through promotion of HIF-1α expression and epithelial-mesenchymal transition in colorectal cancer. *Oncology Reports*, *31*(1), 111–116.

Zhang, Y., Ji, X., Ku, T., & Sang, N. (2016). Inflammatory response and endothelial dysfunction in the hearts of mice co-exposed to SO_2, NO_2, and PM2.5. *Environmental Toxicology*, *31*(12), 1996–2005.

Zhang, Z., Wang, J., Hart, J. E., Laden, F., Zhao, C., Li, T., Zheng, P., Li, D., Ye, Z., & Chen, K. (2018). National scale spatiotemporal land-use regression model for PM2.5, PM10 and NO_2 concentration in China. *Atmospheric Environment*, *192*, 48–54.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Li, W., Li, N., Liang, Z., Hou, X., Si, Y., Wang, X., Feng, X., Tai, B., Hu, D., Lin, H., Wang, B., Wang, C., Zheng, S., Liu, X., Rong, W., Wang, W., Sun, S., Meng, H., & Zhang, Z. (2024). Long-term exposure to ambient fine particulate matter and periodontitis: An observational study using nationally representative survey data. *Journal of Clinical Periodontology*, 1–14. https://doi.org/10.1111/jcpe.13950