Practice-related research

Interaction Between Tobacco Smoke Exposure and Zinc Intake and Its Effect on Periodontitis: Evidence From NHANES

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ABSTRACT

Aim: Tobacco smoke exposure, zinc intake, and periodontitis are closely related. This study intended to assess the relationship between tobacco smoke exposure and zinc intake and its effect on periodontitis.

Materials and methods: This cross-sectional study included 9364 participants from the National Health and Nutrition Examination Survey (NHANES) of USA. A weighted multivariate logistic regression model was used to investigate the independent relationship and interaction effect among tobacco smoke exposure, zinc intake, and periodontitis. Odds ratio (OR) with 95% confidence interval (CI) was calculated. The additive interaction was evaluated using relative excess risk due to interaction (RERI), attributable proportion of interaction (AP), and synergy index (SI).

Results: In all, 56.57% participants had periodontitis. Compared with participants without tobacco smoke exposure, those with tobacco smoke exposure had increased odds of having periodontitis (OR, 1.96; 95% CI, 1.67–2.31). Similarly, patients with adequate zinc intake were found to have decreased odds of having periodontitis than those with inadequate zinc intake (OR, 0.86; 95% CI, 0.76–0.98). Importantly, there was antagonistic interaction effect between zinc intake and tobacco smoke exposure on periodontitis (RERI: OR, −0.432; 95% CI, −0.829 to −0.034; AP: OR, −0.242; 95% CI, −0.470 to −0.014; SI: OR, 0.645; 95% CI, 0.446 to 0.932).

Conclusions: Tobacco smoke exposure and zinc intake were independently correlated with periodontitis risk. Decreasing tobacco smoke exposure and optimizing dietary zinc intake appear to be important measures that could be taken to control periodontitis.

Introduction

Periodontitis is a prevalent, chronic, and multifactorial inflammatory disease that can result in inflammation and progressive destruction of periodontal support tissue.[1,2] Additionally, the disease is influenced by various factors including smoking, obesity, diabetes, and osteoporosis.[2] A systematic review and meta-analysis of epidemiologic studies revealed that 23.6% of the population is affected by severe periodontitis.[3] Tooth loss caused by periodontitis has a detrimental impact on the ability to chew, consequently influencing dietary consumption and compromising overall quality of life.[4] In addition to its impact on oral health, periodontitis is also associated with an increased risk of chronic disease, including cardiovascular disease (CVD),[5] dementia/cognitive impairment,[6] and oral cancer.[7] Therefore, it is crucial to identify modifiable influencing factors for the prevention and control of periodontitis occurrence and development.

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Tobacco smoke is a common environmental exposure factor and has emerged as a global public health concern.[8] Elevation of reactive oxygen species subsequent to exposure to tobacco smoke facilitates the occurrence and progression of periodontitis by promoting an inflammatory response, impairing immune function, and compromising the regenerative capacity of periodontal tissues.[9] Furthermore, smoking may induce degradation of the extracellular matrix in periodontal tissues by locally enhancing the activity of proteolytic enzymes, thereby contributing to the development of periodontitis.[10] Nutrition is widely recognised as a crucial element in the management and prevention of periodontal disease.[11] Zinc plays a crucial role as a micronutrient in maintaining human body functions and possesses both antioxidant and anti-inflammatory properties, making it a widely used dietary antioxidant.[12] Deficiency of zinc may worsen periodontitis.[13] Furthermore, the presence of zinc has the potential to effectively inhibit oral bacterial toxins.[14] Existing evidence suggests that zinc homeostasis can modulate the detrimental effects of tobacco exposure on the body,[15] and supplementation with zinc has been shown to mitigate the inflammatory response induced by tobacco exposure.[16]

A previous study found an interaction between dietary antioxidant intake and tobacco exposure on the risk of metabolic syndrome amongst individuals aged 12 to 19.[17] A study conducted by Yang et al[18] demonstrated that inadequate zinc intake potentiated the impact of tobacco smoke exposure on the risk of metabolic syndrome, indicating a significant association between low zinc intake and tobacco exposure. However, clinical studies examining the interaction between zinc intake and tobacco exposure on periodontitis risk are limited. In this study, we anticipated that tobacco smoke exposure and zinc intake have an interaction on the risk of periodontitis, utilising data from the National Health and Nutrition Examination Survey (NHANES) database of the Centres for Disease Control, USA.

Methods

Data sources

NHANES is a representative cross-sectional survey of all non-institutionalised civilian populations in the US using multi-stage probability-sampling methods.[18] The data collection process in NHANES comprised 2 parts: an in-person interview (including demographic, socioeconomic, dietary, and health-related questions) and a physical examination (including medical, dental and physiologic measurements, and laboratory tests) performed in the mobile examination centre (https://www.cdc.gov/nchs/nhanes/about_nhanes.htm).

We included participants who had complete information about periodontal examinations from the NHANES 2009–2014 (n = 10,701). Participants with incomplete information on zinc intake (n = 617), serum cotinine (n = 388), or key covariates (n = 256) were excluded. We also excluded some pregnant and lactating patients (n = 76). Finally, 9364 participants were included for further analysis.

Figure 1 shows the screening process of participants. Because the data were obtained from NHANES, a publicly accessible database, the Institutional Review Board of College of Pharmacy, Harbin Medical University, waived the requirement for ethical approval. Prior to participating in the study, all individuals provided written informed consent.

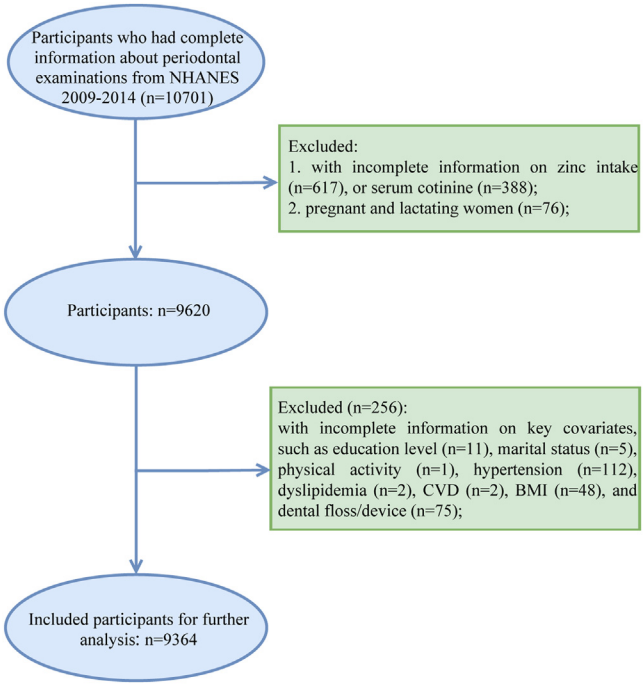

Fig. 1 – Flowchart of study participants from the National Health and Nutrition Examination Survey (NHANES) 2009–2014.

BMI, body mass index; CVD, cardiovascular disease.

Outcome variable

In this study, periodontitis was regarded as the primary outcome variable, with data on periodontitis acquired from oral health/periodontal examination data in NHANES 2009–2014. Dental examiners performed examinations of periodontal and dental status for participants aged ≥30 years in the NHANES database. Similar to previous studies,[19,20] periodontitis diagnosis and staging were conducted in accordance with the Centers for Disease Control and Prevention/American Academy of Periodontology classification/case definition[21,22]: Mild periodontitis was defined as ≥2 interproximal sites with attachment loss (AL) ≥3 mm and ≥2 interproximal sites with pocket depth (PD) ≥4 mm (not on the same tooth) or one site with PD ≥5 mm. Moderate periodontitis was the presence of ≥2 interproximal sites with AL ≥4 mm, not on the same tooth, or the presence of ≥2 interproximal sites with PD ≥5 mm, not on the same tooth. Severe periodontitis was ≥2 interproximal sites with AL ≥6 mm (not on the same tooth) or ≥1 interproximal site with PD ≥5 mm (not on the same tooth). Periodontitis categorised into mild, moderate, or severe periodontitis.

Explanatory variables

Serum cotinine, a primary metabolite of nicotine, serves as a reliable indicator for measuring tobacco smoke exposure. Isotope-dilution high-performance liquid chromatography/atmospheric pressure chemical ionisation tandem mass spectrometry was used to measure serum cotinine level in NHANES participants.[23] Serum cotinine <0.05 ng/mL was considered as no tobacco smoke exposure.

Total zinc intake was the sum of dietary and supplemental intake in this study. In the NHANES database, nutrient intake from foods was assessed using 24-hour diet recalls conducted by trained interviewers. According to recommended dietary allowance, zinc intake ≥8 mg/d for women and ≥11 mg/d for men was considered adequate (https://health.gov/sites/default/files/2019-09/2015-2020_Dietary_Guidelines.pdf).

Covariates

We collected some information of participants: age (years), gender (male/female), race/ethnicity (Mexican American/non-Hispanic Black/non-Hispanic White/other Hispanic/other race), education level (<9th grade/9th−11th grade/high school graduate/, general equivalent diploma or equivalent/some college or Associate of Arts degree/college graduate or above), marital status (married/unmarried), body mass index (BMI; <25 kg/m^2 and ≥25 kg/m^2), poverty-income ratio (PIR; ≤1.85/>1.85), drinking status (nondrinker/drinker/unknown), physical activity (metabolic equivalent [MET], <750 min/wk or ≥750 min/wk], screen time (<4 hours/≥4 hours), hypertension (no/yes), diabetes (no/yes), dyslipidaemia (no/yes), CVD (no/yes), vitamin D intake (<50 nmol/L and ≥50 nmol/L), total energy intake (kcal/d), dental floss/device use (no/yes), last dental visit (>1 year but <5 years ago/>5 years ago, never, or does not know/within last year), nonsteroidal anti-inflammatory agents (no/yes), and anti-infective agents (no/yes). Drinkers were defined as individuals who self-reported consuming a minimum of 12 alcohol drinks per week. Screen time was evaluated using 2 questions: “During the past 30 days, on average how many hours per day did you sit and watched TV or videos?” “During the past 30 days, on average how many hours per day did you use a computer or play computer games outside of work or school?” Hypertension/diabetes/dyslipidaemia/CVD were identified based on self-reported medical history or current use of prescribed medication for these conditions.

Statistical analysis

Three weighted variables—SDMVSTRA, SDMVPSU, and WTMEC2YR—from the NHANES database were utilised to perform weighted analysis on all data. Continuous variables were expressed as mean ± standard error (SE), and group comparisons were analysed via t test. Categorical variables were presented as the number of cases and the composition ratio [n (%)], with intergroup comparisons conducted through either χ^2 test or Fisher exact probability method.

Confounding factors was screened by weighted univariate logistic regression analysis. Weighted logistic regression models were applied to evaluate the associations of tobacco smoke exposure and zinc intake on the risk of periodontitis, respectively. Model 1 was the unadjusted crude model. Model 2 adjusted for all covariates, including age, gender, race/ethnicity, education level, marital status, PIR, screen time, hypertension, diabetes, dyslipidaemia, CVD, vitamin D intake, total energy intake, dental floss/device use, last dental visit, and nonsteroidal anti-inflammatory agents. Odds ratio (OR) and 95% confidence interval (CI) were calculated accordingly. P values <.05 were statistically significant. Importantly, the coexistence effect of tobacco smoke exposure and zinc intake on the risk of periodontitis was assessed via weighted multivariate regression model. To investigate the additive interaction effect between tobacco smoke exposure and zinc intake on the risk of periodontitis, we employed 3 indicators: relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI). The presence of an additive interaction was determined when the 95% CI for RERI or AP did not include 0 or when the 95% CI for SI did not contain 1.[17] Subgroup analysis was performed based on gender, BMI, and diabetes status.

Results

Characteristics of all participants

A total of 9364 participants were included in the study, with 4701 (49.93%) men and 4663 (50.07%) women. The mean age was 51.04 years. Of these participants, 6111 (70.01%) were married and 3253 (29.99%) were unmarried. For the purposes of this study, we also found that 5297 (56.57%) participants had periodontitis. Table 1 shows the comparison of baseline information between the periodontitis and nonperiodontitis groups. The patients with periodontitis were older, had a higher total energy intake and higher proportions of tobacco smoke exposure, and had an inadequate zinc intake compared to those without periodontitis (P < .05). Additionally, significant differences were also shown between the periodontitis and nonperiodontitis patients in gender, race/ethnicity, PIR, education level, marital status, screen time, hypertension, diabetes, dyslipidaemia, CVD, vitamin D intake, dental floss/device use, last dental visit, and nonsteroidal anti-inflammatory agents (P < .05).

Independent association of tobacco smoke exposure and zinc intake with periodontitis risk

Table 2 presents the independent relationship of tobacco smoke exposure and zinc intake with periodontitis risk. In the unadjusted model, serum cotinine ≥0.05 ng/mL was associated with increased odds of periodontitis (model 1: OR, 2.14; 95% CI, 1.87−2.45; P < .001). After adjusting for age, gender, race/ethnicity, education level, marital status, PIR, screen time, hypertension, diabetes, dyslipidaemia, CVD, vitamin D intake, total energy intake, dental floss/device use, last dental visit, and nonsteroidal anti-inflammatory agents, compared with participants with serum cotinine <0.05 ng/mL, those with serum cotinine levels ≥0.05 ng/mL were still linked with an increased odds of having periodontitis (model 2: OR, 1.96; 95% CI, 1.67−2.31; P < .001). These results indicated that

Table 1 – Characteristics of 9364 participants from NHANES 2009–2014 and comparison of characteristics between the periodontitis and nonperiodontitis groups.

Variables	Total (N = 9364)	Nonperiodontitis group (n = 4067)	Periodontitis group (n = 5297)	*P*
Age, mean (SE)	51.04 (0.24)	47.93 (0.31)	54.34 (0.33)	<.001
Gender, No. (%)				<.001
Female	4663 (50.07)	2451 (57.65)	2212 (42.03)	
Male	4701 (49.93)	1616 (42.35)	3085 (57.97)	
Race/ethnicity, No. (%)				<.001
Mexican American	1348 (7.93)	423 (5.58)	925 (10.41)	
Non-Hispanic Black	1882 (10.12)	665 (7.80)	1217 (12.59)	
Non-Hispanic White	4183 (69.98)	2106 (76.01)	2077 (63.58)	
Other Hispanic	931 (5.27)	387 (4.73)	544 (5.85)	
Other race, including multiracial	1020 (6.70)	486 (5.88)	534 (7.57)	
PIR, No. (%)				<.001
≤1.85	3577 (25.99)	1202 (19.23)	2375 (33.18)	
>1.85	5059 (67.68)	2590 (75.08)	2469 (59.81)	
Unknown	728 (6.33)	275 (5.69)	453 (7.01)	
Education level, No. (%)				<.001
<9th grade	875 (4.93)	188 (2.37)	687 (7.65)	
9th–11th grade (including 12th grade with no diploma)	1238 (9.85)	363 (6.51)	875 (13.40)	
High school graduate/GED or equivalent	2047 (21.07)	733 (17.09)	1314 (25.30)	
Some college or AA degree	2669 (30.14)	1253 (30.37)	1416 (29.89)	
≥College graduate	2535 (34.01)	1530 (43.65)	1005 (23.75)	
Marital status, No. (%)				<.001
Married	6111 (70.01)	2782 (74.00)	3329 (65.77)	
Unmarried	3253 (29.99)	1285 (26.00)	1968 (34.23)	
Drink status, No. (%)				.982
Nondrinkers	1158 (9.67)	494 (9.61)	664 (9.73)	
Drinkers	7764 (86.49)	3393 (86.59)	4371 (86.38)	
Unknown	442 (3.84)	180 (3.80)	262 (3.89)	
Physical activity, No. (%)				.086
<750 Met*min/wk	4126 (40.93)	1726 (39.66)	2400 (42.28)	
≥750 Met*min/wk	5238 (59.07)	2341 (60.34)	2897 (57.72)	
Screen time, No. (%)				<.001
<4 h	3366 (38.47)	1684 (43.62)	1682 (33.00)	
≥4 h	2669 (29.74)	1187 (29.75)	1482 (29.73)	
Unknown	3329 (31.79)	1196 (26.63)	2133 (37.27)	
Hypertension, No. (%)				<.001
No	3850 (44.45)	2013 (50.87)	1837 (37.64)	
Yes	5514 (55.55)	2054 (49.13)	3460 (62.36)	
Diabetes, No. (%)				<.001
No	7706 (86.53)	3583 (90.75)	4123 (82.04)	
Yes	1658 (13.47)	484 (9.25)	1174 (17.96)	
Dyslipidaemia, No. (%)				<.001
No	2280 (24.43)	1138 (27.05)	1142 (21.65)	
Yes	7084 (75.57)	2929 (72.95)	4155 (78.35)	
CVD, No. (%)				<.001
No	8572 (92.81)	3862 (95.56)	4710 (89.89)	
Yes	792 (7.19)	205 (4.44)	587 (10.11)	
Serum cotinine, No. (%)				<.001
<0.05 ng/mL	5443 (61.58)	2701 (70.20)	2742 (52.42)	
≥0.05 ng/mL	3921 (38.42)	1366 (29.80)	2555 (47.58)	
BMI, No. (%)				.085
<25 kg/m^2	2452 (26.54)	1122 (27.48)	1330 (25.55)	
≥25 kg/m^2	6912 (73.46)	2945 (72.52)	3967 (74.45)	
Vitamin D, No. (%)				<.001
<50 nmol/L	2785 (22.25)	1024 (18.20)	1761 (26.56)	
≥50 nmol/L	6579 (77.75)	3043 (81.80)	3536 (73.44)	
Zinc intake, No. (%)				<.001
Adequate	5991 (68.22)	2748 (70.56)	3243 (65.74)	
Inadequate	3373 (31.78)	1319 (29.44)	2054 (34.26)	
Total energy intake, kcal/d, mean (SE)	2178.87 (15.54)	2154.94 (15.95)	2204.31 (22.60)	.038
Dental floss/device use, No. (%)				<.001
No	2945 (27.48)	970 (22.10)	1975 (33.20)	
Yes	6419 (72.52)	3097 (77.90)	3322 (66.80)	

(*continued*)

Table 1. (*Continued*)

Variables	Total (N = 9364)	Nonperiodontitis group (n = 4067)	Periodontitis group (n = 5297)	P
Last dental visit, No. (%)				<.001
>1 y but <5 y	1605 (16.10)	670 (15.22)	935 (17.03)	
>5 y, never, or does not know	4167 (39.31)	1393 (30.48)	2774 (48.68)	
Within last year	3592 (44.60)	2004 (54.30)	1588 (34.29)	
Nonsteroidal anti-inflammatory agents, No. (%)				<.001
No	8170 (87.97)	3600 (89.34)	4570 (86.52)	
Yes	1194 (12.03)	467 (10.66)	727 (13.48)	
Anti-infective agents, No. (%)				.578
No	8929 (94.82)	3863 (94.65)	5066 (95.00)	
Yes	435 (5.18)	204 (5.35)	231 (5.00)	

AA, Associate of Arts; BMI, body mass index; CVD, cardiovascular disease; GED, general equivalent diploma; MET, metabolic equivalent; NHANES, National Health and Nutrition Examination Survey; PIR, poverty-income ratio;

tobacco smoke exposure may enhance susceptibility to periodontitis. Similarly, after adjusting for all covariates, patients with adequate zinc intake were found to have decreased odds of having periodontitis than those with inadequate zinc intake (model 2: OR, 0.86; 95% CI, 0.76–0.98; $P = .020$).

Effect on periodontitis risk

We assessed the interaction of tobacco smoke exposure and zinc intake on periodontitis risk in this analysis. The interactive items between serum cotinine and zinc intake were established, including the following: serum cotinine <0.05 ng/mL and inadequate zinc intake, serum cotinine <0.05 ng/mL and adequate zinc intake, serum cotinine ≥0.05 ng/mL and inadequate zinc intake, and serum cotinine ≥0.05 ng/mL and adequate zinc intake. As shown in Table 3, taking "serum cotinine <0.05 ng/mL and inadequate zinc intake" as a reference, the combination of serum cotinine ≥0.05 ng/mL and inadequate zinc intake was associated with an increased odds of having periodontitis after adjusting for covariates (model 2: OR, 2.23; 95% CI, 1.80–2.78). Although we also observed increased odds of having periodontitis amongst patients with serum cotinine ≥0.05 ng/mL and adequate zinc intake (model 2: OR, 1.78; 95% CI, 1.43–2.23), the magnitude of this interaction effect on periodontitis was significantly decreased compared to that of serum cotinine ≥0.05 ng/mL and insufficient zinc intake (OR, 1.78 vs 2.23). In addition, Table 3 displays that RERI with 95% CI was −0.432 (−0.829 to −0.034), AP with 95% CI was −0.242 (−0.470 to −0.014), and SI with 95% CI was 0.645 (0.446–0.932). These results indicated that there was antagonistic interaction effect between zinc intake and tobacco smoke exposure on periodontitis (Figure 2).

Table 2 – Independent association of tobacco smoke exposure and zinc intake with periodontitis risk by weighted logistic regression model.

Variables	Model 1		Model 2	
	OR (95% CI)	P	OR (95% CI)	P
Tobacco smoke exposure				
Serum cotinine <0.05 ng/mL	Ref.		Ref	
Serum cotinine ≥0.05 ng/mL	2.14 (1.87–2.45)	<.001	1.96 (1.67–2.31)	<.001
Zinc intake				
Inadequate	Ref.		Ref.	
Adequate	0.80 (0.72–0.89)	<.001	0.86 (0.76–0.98)	.020

Model 1: Unadjusted crude model.
Model 2: Adjusted for all covariates, including age, gender, race/ethnicity, education level, marital status, poverty-income ratio, screen time, hypertension, diabetes, dyslipidaemia, cardiovascular disease, vitamin D intake, total energy intake, dental floss/device, last dental visit, and nonsteroidal anti-inflammatory agents.
CI, confidence interval; OR, odds ratio.

Subgroup analysis

The independent and joint effect of tobacco smoke exposure and zinc intake on periodontitis risk was analysed in different populations. As shown in Table 4, the relationship of tobacco smoke exposure with the development of periodontitis was still presented in all subgroups. However, in gender-based subgroups and subgroups of patients with BMI <25 kg/m^2 or patients with diabetes, the association of zinc intake and periodontitis risk was not significant ($P > .05$). Furthermore, the joint effect of serum cotinine ≥0.05 ng/mL and inadequate zinc intake was related to increased odds of having periodontitis in all subgroups. The combined effect of serum cotinine ≥0.05 ng/mL and adequate zinc intake on periodontitis was also significant in male, female, BMI<25 kg/m^2, BMI≥25 kg/m^{2}and nondiabetes subgroups.

Discussion

In the current study, we found that tobacco smoke exposure and zinc intake were independently correlated with periodontitis risk. Results of additive interaction analysis showed an antagonistic interaction effect between tobacco smoke exposure and zinc intake on periodontitis development.

Numerous studies have shown that tobacco smoke exposure may expedite the development of atherosclerotic thrombosis by impairing endothelial function, eliciting an

Table 3 – Interaction between tobacco smoke exposure and zinc intake and its effect on periodontitis risk.

Variables	Model 1		Model 2	
	OR (95% CI)	P	OR (95% CI)	P
Serum cotinine <0.05 ng/mL and inadequate zinc intake	Ref.		Ref.	
Serum cotinine <0.05 ng/mL and adequate zinc intake	0.89 (0.79–1.02)	.088	0.98 (0.84–1.14)	.784
Serum cotinine ≥0.05 ng/mL and inadequate zinc intake	2.29 (1.94–2.71)	<.001	2.23 (1.80–2.78)	<.001
Serum cotinine ≥0.05 ng/mL and adequate zinc intake	1.81 (1.53–2.15)	<.001	1.78 (1.43–2.23)	<.001
RERI (95% CI)	−0.372 (−0.714 to −0.030)		−0.432 (−0.829 to −0.034)	
APAB (95% CI)	−0.205 (−0.399 to −0.011)		−0.242 (−0.470 to −0.014)	
SI (95% CI)	0.686 (0.499 to 0.945)		0.645 (0.446 to 0.932)	

Model 1: Unadjusted crude model.
Model 2: Adjusted for all covariates, including age, gender, race/ethnicity, education level, marital status, poverty-income ratio, screen time, hypertension, diabetes, dyslipidaemia, cardiovascular disease, vitamin D intake, total energy intake, dental floss/device, last dental visit, and non-steroidal anti-inflammatory agents.
AP, attributable proportion; CI, confidence interval; OR, odds ratio; RERI, relative excess risk due to interaction; SI, synergy index.

inflammatory response, fostering platelet adhesion, and inducing plaque instability, which poses a potential threat to human health.[24,25] In this analysis, after adjusting age, gender, race/ethnicity, education level, marital status, PIR, screen time, hypertension, diabetes, dyslipidaemia, CVD, vitamin D intake, total energy intake, dental floss/device use, last dental visit, and nonsteroidal anti-inflammatory agents, we observed a significant positive association between tobacco smoke exposure and periodontitis for the total population and different subgroups.

The relationship between tobacco smoke exposure and periodontitis has previously been proposed and investigated.[26,27] A cross-sectional study by Sutton et al[27] found that individuals with any exposure to environmental tobacco smoke exhibited a 28% higher likelihood of experiencing periodontitis compared to those without exposure. Tobacco smoke exposure–related periodontitis is usually attributed to an inflammatory response.[8] It is well known that the dietary antioxidant zinc is extensively utilised and has been shown to be an important factor in the development of numerous diseases.[28] A review highlighted that the disturbance of zinc balance is anticipated to have a negative effect on periodontal well-being and play a role in the advancement and escalation of periodontitis.[29] Zinc plays a significant role in the regulation of immune functions, management of bacterial infection, maintenance of balanced inflammatory responses, and mitigation of oxidative stress. These factors are closely linked to the development and progression of periodontitis.[13] An animal experiment suggested that the dysregulation of zinc homeostasis enhances vulnerability to chronic lung injury following exposure to cigarette smoke.[15]

To the best of our knowledge, the joint effects of tobacco smoke exposure and zinc intake on the development of periodontitis have rarely been studied. Herein, we found that there was an antagonistic interaction effect between tobacco smoke exposure and zinc intake on periodontitis. In other words, the

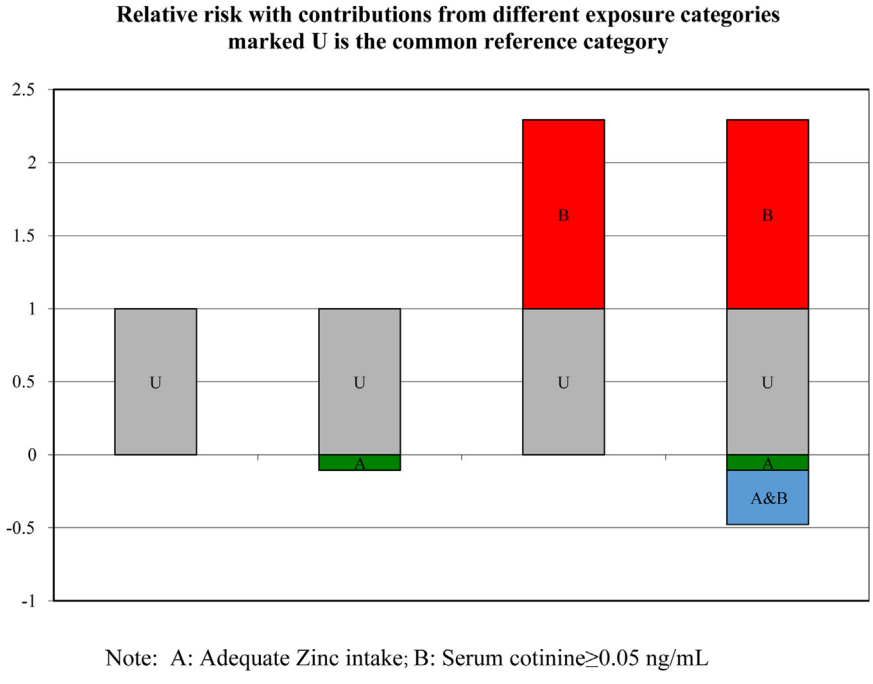

Fig. 2 – Interaction between tobacco smoke exposure and zinc intake and its effect on periodontitis risk.

Table 4 – Subgroup analysis by gender, BMI, and diabetes status.

Subgroup	OR (95% CI)	*P*
Male (n = 4701)		
Serum cotinine <0.05 ng/mL	Ref.	
Serum cotinine ≥0.05 ng/mL	1.93 (1.53–2.43)	<.001
Inadequate zinc intake	Ref.	
Adequate zinc intake	0.85 (0.69–1.04)	.118
Serum cotinine <0.05 ng/mL and inadequate zinc intake	Ref.	
Serum cotinine <0.05 ng/mL and adequate zinc intake	1.08 (0.81–1.43)	.594
Serum cotinine ≥0.05 ng/mL and inadequate zinc intake	2.56 (1.86–3.53)	<.001
Serum cotinine ≥0.05 ng/mL and adequate zinc intake	1.80 (1.22–2.66)	.004
Female (n = 4663)		
Serum cotinine <0.05 ng/mL	Ref.	
Serum cotinine ≥0.05 ng/mL	1.94 (1.54–2.43)	<.001
Inadequate zinc intake	Ref.	
Adequate zinc intake	0.87 (0.74–1.01)	.074
Serum cotinine <0.05 ng/mL and inadequate zinc intake	Ref.	
Serum cotinine <0.05 ng/mL and adequate zinc intake	0.90 (0.73–1.11)	.311
Serum cotinine ≥0.05 ng/mL and inadequate zinc intake	1.93 (1.43–2.60)	<.001
Serum cotinine≥0.05 ng/mL and Adequate Zinc intake	1.73 (1.34–2.23)	<.001
BMI <25 kg/m^2 (n = 5785)		
Serum cotinine <0.05 ng/mL	Ref.	
Serum cotinine ≥0.05 ng/mL	1.94 (1.40–2.70)	<.001
Inadequate zinc intake	Ref.	
Adequate zinc intake	0.97 (0.70–1.34)	.850
Serum cotinine <0.05 ng/mL and inadequate zinc intake	Ref.	
Serum cotinine <0.05 ng/mL and adequate zinc intake	1.20 (0.82–1.75)	.340
Serum cotinine ≥0.05 ng/mL and inadequate zinc intake	2.46 (1.51–4.01)	<.001
Serum cotinine ≥0.05 ng/mL and adequate zinc intake	2.06 (1.22–3.49)	.008
BMI ≥25kg/m^2 (n = 6912)		
Serum cotinine <0.05 ng/mL	Ref.	
Serum cotinine ≥0.05 ng/mL	1.94 (1.62–2.32)	<.001
Inadequate zinc intake	Ref.	
Adequate zinc intake	0.84 (0.74–0.96)	.009
Serum cotinine <0.05 ng/mL and inadequate zinc intake	Ref.	
Serum cotinine <0.05 ng/mL and adequate zinc intake	0.92 (0.78–1.08)	.299
Serum cotinine ≥0.05 ng/mL and inadequate zinc intake	2.09 (1.65–2.67)	<.001
Serum cotinine ≥0.05 ng/mL and adequate zinc intake	1.69 (1.32–2.17)	<.001
Diabetes (n = 1658)		
Serum cotinine <0.05 ng/mL	Ref.	
Serum cotinine ≥0.05 ng/mL	1.99 (1.44–2.74)	<.001
Inadequate zinc intake	Ref.	
Adequate zinc intake	0.80 (0.56–1.13)	.206
Serum cotinine <0.05 ng/mL and inadequate zinc intake	Ref.	
Serum cotinine <0.05 ng/mL and adequate zinc intake	0.88 (0.57–1.35)	.546
Serum cotinine ≥0.05 ng/mL and inadequate zinc intake	2.09 (1.29–3.37)	.003
Serum cotinine ≥0.05 ng/mL and adequate zinc intake	1.67 (0.95–2.93)	.075
Nondiabetes (n = 7706)		
Serum cotinine <0.05 ng/mL	Ref.	
Serum cotinine ≥0.05 ng/mL	1.95 (1.62–2.35)	<.001
Inadequate zinc intake	Ref.	
Adequate zinc intake	0.87 (0.77–0.99)	.045
Serum cotinine <0.05 ng/mL and inadequate zinc intake	Ref.	
Serum cotinine <0.05 ng/mL and adequate zinc intake	0.99 (0.84–1.17)	.935
Serum cotinine ≥0.05 ng/mL and inadequate zinc intake	2.23 (1.75–2.85)	<.001
Serum cotinine ≥0.05 ng/mL and adequate zinc intake	1.80 (1.43–2.26)	<.001

Adjusted for all covariates, including age, gender (not adjusted in male and female subgroup), race/ethnicity, education level, marital status, poverty-income ratio, screen time, hypertension, diabetes (not adjusted in diabetes and nondiabetes subgroup), dyslipidaemia, cardiovascular disease, vitamin D intake, total energy intake, dental floss/device, last dental visit, and nonsteroidal anti-inflammatory agents.
BMI, body mass index; OR, odds ratio; CI, confidence interval.

combined impact of tobacco smoke exposure and zinc intake may mitigate the risk of periodontitis development in comparison to tobacco smoke exposure alone. Some underlying mechanisms may support the antagonistic interaction effect between tobacco smoke exposure and zinc intake on the development of periodontitis. Tobacco smoke exposure may disrupt the redox homeostasis in the body, alter antioxidant levels, and impact periodontal disease activity,[30] whilst zinc

intake can mitigate oxidative stress and preserve inflammatory response equilibrium.[13] More research is needed to further explore the mechanisms of this antagonistic interaction effect.

In addition, we also explored the interaction between zinc intake and smoking status on periodontitis risk. The population was divided into 3 groups based on self-reported smoking status: former smokers (n = 2385), current smokers (n = 1756), and nonsmokers (n = 5223). As shown in Supplementary Table 1, taking "nonsmoking and inadequate zinc intake" as a reference, patients with both current smoking and inadequate zinc intake (OR, 3.17; 95% CI, 2.42–4.14) and patients with both current smoking and adequate zinc intake (OR, 2.27; 95% CI, 1.75–2.94) had increased odds of having periodontitis after adjusting for covariates. We also observed an antagonistic interaction effect of zinc intake and current smoking on the risk of periodontitis (SI, 0.612; 95% CI, 0.392–0.957). However, the relationship of patients with both former smoking and inadequate zinc intake and its effect on periodontitis risk was not statistically significant ($P > .05$).

Overall, this study indicated the potential significance of understanding the antagonistic interaction between tobacco smoke exposure and zinc intake on mitigating the risk of periodontitis. However, we must acknowledge some limitations of this analysis. First, the assessment of zinc intake was based on a self-reported questionnaire using 24-hour dietary recall, which may introduce recall bias. Second, the participants in the NHANES database, whilst utilising a multistage hierarchical probabilistic design approach, are exclusively US citizens and may not be fully representative of individuals residing in other regions globally. Consequently, it is imperative to use caution when interpreting the findings of this study. Third, the Centers for Disease Control and Prevention/American Academy of Periodontology classification/case definition, based on previous NHANES studies, was employed in this study to diagnose and stage periodontitis. The 2018 World Workshop Classification System is also used to classify periodontitis.[31] The utilisation of diverse definition criteria may potentially introduce bias. Therefore, future studies may utilise different criteria for validation purposes. Last, the dataset employed was cross-sectional, and the duration of smoking and the duration of zinc intake cannot be determined; thus, it was not possible to establish a causal relationship among tobacco smoke exposure and zinc intake and any effect on periodontitis. Given these limitations, more prospective, multicentre studies are needed to confirm our findings and explore possible mechanisms of antagonistic interaction effect.

Conclusions

This analysis may provide epidemiological evidence for the antagonistic interaction effect between tobacco smoke exposure and zinc intake on periodontitis development. Decreasing tobacco smoke exposure and optimising dietary zinc intake are important steps toward actively and effectively controlling the occurrence of periodontitis.

Conflict of interest

None disclosed.

Author contributions

BL and XL designed the study. BL wrote the manuscript. LY collected, analysed, and interpreted the data. XL critically reviewed, edited, and approved the manuscript. All authors read and approved the final manuscript.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.identj.2024.04.007.

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