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Association between brominated flame retardants (BFRs) and periodontitis: Results from a large population-based study

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Abstract

Background Brominated flame retardants (BFRs) are widely utilized to mitigate the flammability of various materials. Previous studies have revealed the impact of BFRs exposure on hormonal disruption and bone metabolism which are closely related to periodontitis. However, it remains unknown the potential relationship between BFRs and periodontitis. This study aimed to explore the association between BFRs exposure and periodontitis in US adults.

Methods The data analyzed in this study were obtained from the National Health and Nutrition Examination Survey (NHANES) 2009–2014. Twelve serum BFRs were quantified using isotope dilution gas chromatography high-resolution mass spectrometry. Univariable and multivariable logistic regression was employed to evaluate the association between serum BFRs and periodontitis. Bayesian kernel machine regression (BKMR) analyses were utilized to assess the association between mixtures of BFRs and periodontitis.

Results A total of 3311 eligible participants were included. Serum BFRs (PBDE-47, PBDE-99, and PBDE-154) were significantly associated with periodontitis, and the odds ratios (ORs) and corresponding 95% confidence intervals(*CI*s) were 1.15(1.01,1.29), 1.10(1.01,1.20), and 1.12(1.01,1.25), respectively. Notably, these three BFRs were also significantly associated with the severity of periodontitis. Additionally, the BKMR model revealed a significant association between the mixture of all twelve BFRs and periodontitis.

Conclusions This preliminary study suggests a significant association between specific serum BFRs (PBDE-47, PBDE-99, and PBDE-154) and periodontitis and its severity. Further prospective and experimental studies are warranted to validate our findings.

Keywords Periodontitis, BFRs, PBDEs, Oral health, BKMR

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Introduction

Periodontitis, a multifactorial chronic inflammatory disease, is widely recognized as one of the most prevalent diseases in humans. A microbial infection of a susceptible host is the primary cause of periodontitis, which leads to the reciprocal interaction between a dysbiotic biofilm and the host immune-inflammatory reactions. Its etiology involves a variety of causative factors, such as genetic predisposition, socio-economic status, level of education, and economic environment, as well as uncontrolled diabetes mellitus and lifestyle choices [1–3]. The primary manifestations of this condition encompass the loss of alveolar bone and periodontal tissue support. With a global prevalence ranging from 45 to 50%, periodontitis ranks as the sixth most common human disease [4]. If left untreated, it can lead to tooth loss, impaired masticatory function, compromised nutritional status, and diminished quality of life [3]. Consequently, investigating the risk factors associated with periodontitis is of paramount importance. While recent years have witnessed a surge in research on risk factors related to diet and lifestyle behaviors [5–9], studies exploring the impact of environmental substances in daily life remain scarce [10, 11].

Brominated flame retardants (BFRs), specifically poly brominated diphenyl ethers (PBDEs) and poly brominated biphenyls (PBBs), which account for about 21% of the total production of BFRs [12, 13], are widely used in plastics, electrical equipment, foams, and furniture products to improve their fire resistance [14]. The utilization of flame retardants has witnessed a significant rise due to the implementation of stringent fire safety regulations by numerous countries [15]. Whereas most BFRs lack covalent bonds with the host polymer and readily penetrate into the indoor environment, humans can be widely exposed to BFRs through inhalation of dust and air, dietary intake and dermal contact [16]. Its high solubility in adipose tissue renders it easily assimilated by organisms and progressively accumulated within the food chain. Several studies have shown that BFR has thyrotoxicity, neurotoxicity, and reproductive and developmental toxicity, affecting human health [17–19]. Despite certain flame retardants being banned, the persistent nature of these chemicals in certain consumer goods and their ability to accumulate in biological systems imply that humans worldwide will continue to be exposed to them for several decades [13, 20].

Previous studies have indicated that elevated exposure to PBDEs can adversely affect bone metabolism and mineral density [21]. Given that alveolar bone loss is an important feature of periodontitis, these findings suggest a potential link between PBDE exposure and periodontal health. Moreover, BFRs, including PBDEs, are known endocrine disruptors that can alter the levels of sex hormones such as estradiol and testosterone [22]. Since both bone metabolism disorders and hormonal imbalances have been associated with periodontitis [23–25], it is plausible to hypothesize a correlation between BFRs exposure and periodontitis. Despite this rationale, the relationship between BFRs and periodontitis has not been examined in prior studies. Therefore, the present study seeks to address this research gap by investigating the association between exposure to individual or mixed BFRs and periodontitis in a nationally representative population using data from the National Health and Nutrition Examination Survey (NHANES). This study will contribute valuable insights into the prevention of periodontitis from the perspective of environmental pollutant exposure.

Methods

Study population

NHANES, a program for evaluating the health and nutritional well-being of both adults and children in the United States, includes a series of cross-sectional nationally representative health examination surveys. In this study, we selected publicly accessible data originating from three distinct cycles of NHANES, namely 2009–2010, 2011–2012, and 2013–2014. These particular cycles were chosen due to their inclusion of comprehensive full-mouth periodontal examinations, with the exception of the third molars. The intricate process employed to identify eligible participants is elucidated in Fig. 1. The inclusion criteria for this study were as follows: (1) participants aged 30 years or older with complete periodontal examination data, and (2) participants with complete serum BFRs examination data. 3357 participants with incomplete periodontal examinations and 72 participants with incomplete serum BFRs data were excluded. The final intersection of periodontal examination data and serum BFRs data, 3311 participants, were included in the subsequent analyses.

BFRs detection

The comprehensive protocols for detecting BFRs can be accessed on the official NHANES website. In summary, serum samples were subjected to processing using a Gilson 215 liquid processor. A total of nine serum BFRs, namely 2, 4, 4′-Tribromodiphenyl ether(PBDE-28), 2, 2′, 4, 4′-Tetrabromodiphenyl ether(PBDE-47), 2, 2′, 3, 4, 4′-Tentabromodiphenyl ether (PBDE-85), 2, 2′, 4, 4′, 5-Pentabromodiphenyl ether (PBDE-99), 2, 2′, 4, 4′, 6-Pentabromodiphenyl ether (PBDE-100), 2, 2′, 4, 4′, 5, 5′-Hexabromodiphenyl ether (PBDE-153), 2, 2′, 4, 4′, 5, 6′-Hexabromodiphenyl ether (PBDE-154), Decabromodiphenyl ether (PBDE-209), 2, 2′, 4, 4′, 5, 5′-Hexabromobiphenyl (PBB-153), were quantified utilizing

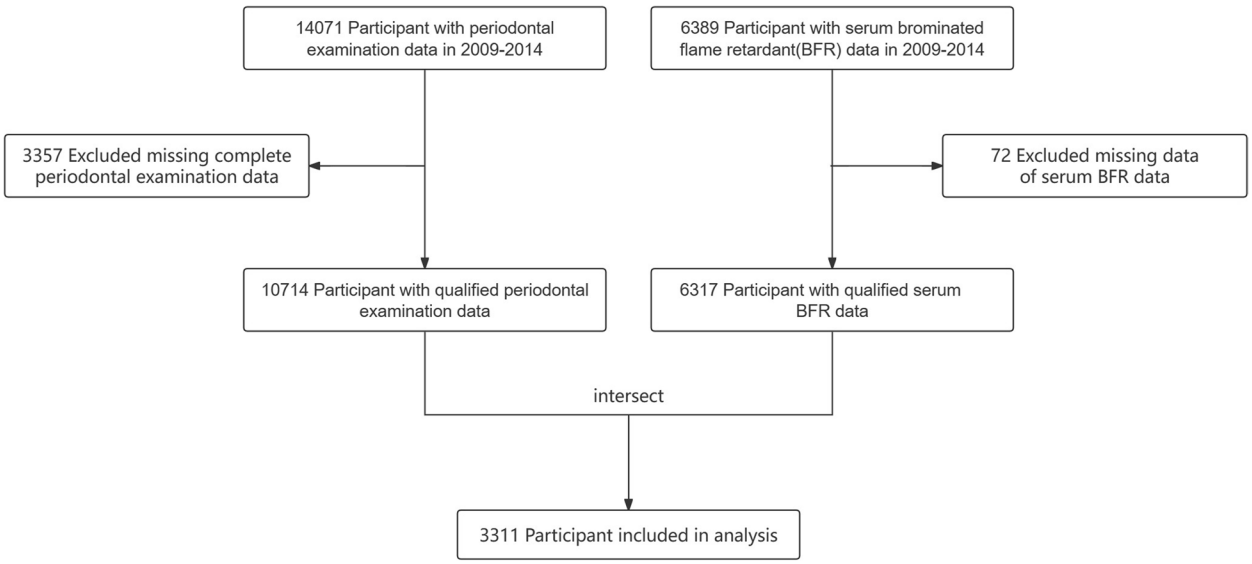

Fig. 1 Flowchart of inclusion exclusion criteria

automated liquid/liquid extraction followed by sample clean-up. Isotope dilution gas chromatography high resolution mass spectrometry (GC/IDHRMS) was subsequently employed to determine the target analytes. The Supplementary Table 1 presents the minimum detection limits for the nine BFRs.

Periodontal examination

The study utilized measurements of probing pocket depth (PPD) and clinical attachment level (CAL) to diagnose periodontitis. Participants were classified into four categories of periodontitis severity based on their PPD and CAL measurements, as well as the CDC/APP definition [26]. Specifically, mild periodontitis was defined as having ≥ 2 interdental sites with AL ≥ 3 mm but < 4 mm, ≥ 2 interdental sites with PD ≥ 4 mm but < 5 mm (not on the same tooth), or one site with PD ≥ 5 mm. Moderate periodontitis was defined as having ≥ 2 interdental sites with AL ≥ 4 mm but < 6 mm, or ≥ 2 interdental sites with PD ≥ 5 mm (not on the same tooth). Severe periodontitis was defined as having ≥ 2 interdental sites with AL ≥ 6 mm (not on the same tooth), and ≥ 1 interdental sites with PD ≥ 5 mm. Participants who did not fall into any of these categories were classified as having no periodontitis [27].

Covariates

The study also took into account potential confounding variables, including age, gender, smoking, daily alcohol consumption, marital status, education, household poverty-to-income ratio (PIR), body mass index (BMI), hypertension, and diabetes. Smoking status was categorized as current smoker, former smoker (participants who do not smoke now but have smoked more than 100 cigarettes in their lifetime), or never smoker, while marital status was categorized as married, never married, or unmarried but with a partner. Educational attainment was grouped into high school and below, college, and college and above. Age, BMI, daily alcohol consumption, and household PIR were analyzed as continuous variables. Hypertension was defined as self-reported use of anti-hypertensive medication or having a measured systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg [28]. Diabetes was defined as self-reported diagnosis or medication use, or having Hemoglobin A1c (HbA1c) ≥ 6.5%, fasting blood glucose ≥ 126 mg/dL, or blood glucose ≥ 200 mg/dL on an oral glucose tolerance test [29].

Data analysis

To account for the intricate survey design employed in the NHANES, appropriate sampling weights were utilized during the analysis of the collected data. Descriptive analyses involved the representation of continuous variables as medians (25th and 75th percentiles) due to their non-normal distribution, while categorical variables were expressed as frequencies (percentages). The general characteristics of participants with and without periodontitis were compared using either the chi-square test (for categorical variables) or the Mann–Whitney U test (for continuous variables). The Mann–Whitney U test was used to compare serum BFRs levels between participants with and without periodontitis, while the Kruskal–Wallis test and the Dunn's post hoc

test from the 'FSA' package were used to compare differences between different severities of periodontitis. Weighted binary logistic regression models were employed to calculate the odds ratios (ORs) and corresponding 95% confidence intervals (*CI*s) in order to assess the potential association between BFRs and periodontitis. Model 1 represented the unadjusted model, while Model 2 accounted for various confounding factors such as age, sex, smoking, alcohol consumption, education, marital status, household PIR, BMI, hypertension, and diabetes status.

To assess the relationship between BFRs mixtures and periodontitis, the Bayesian kernel machine regression model (BKMR) based on the "bkmr" package were used. This approach took into consideration the potential synergistic, non-additive, and non-linear effects that may arise from multiple environmental exposures. The model included ten covariates, namely age, gender, smoking, alcohol consumption, education, marital status, household PIR, BMI, hypertension, and diabetes status. Missing values of the covariates were imputed using the multiple interpolation method implemented in the "mice" package. After fitting the final model using a Markov chain Monte Carlo (MCMC) sampler for 10,000 iterations, the posterior inclusion probability (PIP) was estimated for each chemical, and exposure-outcome function estimates were generated. Furthermore, an overall mixed-effects analysis was conducted.

In addition, a restricted cubic spline (RCS) was plotted using the "RCS" package to explore the non-linear relationship between BFRs and periodontitis. Participants were categorized into four groups based on the severity of periodontitis (no periodontitis, mild, moderate, and severe), and an unordered polynomial logistic regression model was utilized to investigate the correlation between serum BFRs levels and the severity of periodontitis, considering the unsatisfactory results of parallelism testing.

Mediation analyses were further performed using the "mediation" package to explore the potential mediating roles of sex hormones (including estradiol and testosterone) as well as skull bone mineral density in the relationship between BFRs levels and periodontitis. In the sensitivity analyses, we firstly re-analyzed the relationship between BFRs and periodontitis based on the 2018 new periodontal classification [30]. Moreover, considering that the number of teeth may be a confounding factor influencing the classification of periodontal status, we additionally adjusted the number of missing teeth based on the Model 2. In addition, we also excluded the cancer population to further assess the robustness of the results. All statistical analyses were performed with a significance level of 0.05 using R version 4.2.1.

Results

Table 1 presents an overview of the study population, highlighting various characteristics. Notably, age, alcohol consumption, and household poverty income ratio exhibited statistically significant differences ($P<0.05$) between individuals with periodontitis and those without. Conversely, there was no significant difference in BMI between the two groups ($P=0.102$). Moreover, categorical variables such as gender, marital status, race, smoking, hypertension, and diabetes demonstrated significant differences between the periodontitis and non-periodontitis groups. In addition, differences in the characteristics of participants with different severities of periodontitis are presented in Supplementary Table 2.

The distribution of nine BFRs is visually represented in Fig. 2 and Supplementary Table 3. Among these BFRs, the serum levels of eight (PBDE-28, PBDE-47, PBDE-85, PBDE-99, PBDE-100, PBDE-154, PBDE-209, and PBB-153) exhibited statistically significant differences between the periodontitis and non-periodontitis groups. Furthermore, the differences in the concentrations of these BFRs among different severities of periodontitis are presented in Supplementary Table 4.

Univariable logistic analyses were conducted to assess the association between serum concentrations of various BFRs and periodontitis. PBDE-28, PBDE-47, PBDE-85, PBDE-99, PBDE-100, PBDE-154, and PBB-153 displayed significant associations with periodontitis (all $P<0.05$). After adjusting for potential confounders, PBDE-47 (OR = 1.15, 95%*CI*: 1.01–1.29), PBDE-99 (OR = 1.10, 95%*CI*: 1.01–1.20), and PBDE-154 (OR = 1.12, 95%*CI*: 1.01–1.25) maintained significant associations with periodontitis (Table 2). RCS analysis results, as depicted in Fig. 3, demonstrated a non-linear relationship between serum concentrations of PBDE-47, PBDE-99, PBDE-154, and the odds ratio (OR) for periodontitis (P for non-linear <0.05).

Figure 4A illustrates the varying degrees of significant correlation among six BFRs (PBDE-28, PBDE-47, PBDE-85, PBDE-99, PBDE-100, and PBDE-154). Additionally, the BKMR model revealed a significant correlation between the mixtures of all nine BFRs and periodontitis (Fig. 4B). Notably, PBDE-154 emerged as the primary contributor to the overall mixture effect (Fig. 4C). Supplementary Table 5 presents the PIP values, indicating the significance of each BFR's association with periodontitis. A PIP value closer to 1 signifies a stronger association. In this regard, PBDE-154 exhibited the highest significance (PIP = 0.979).

When participants were categorized into four groups based on the severity of periodontitis (no periodontitis, mild periodontitis, moderate periodontitis, and severe periodontitis), unordered polynomial logistic regression

Table 1 Characteristics of the study population, National Health and Nutrition Examination Survey (NHANES) 2009–2014 (*N* = 3311)

Characters	Total *N* = 3311	Non periodontitis *N* = 1589	Periodontitis *N* = 1722	*P* value
Age, year (median (25 and 75 percentile))	49.0 (39.0, 60.0)	46.0 (37.0, 57.0)	54.0 (44.0, 64.0)	< 0.001
Sex, n(%)				< 0.001
Female	1705(51.5)	969(58.6)	736(42.5)	
Male	1606(48.5)	620(41.5)	986(57.5)	
Marital status, n(%)				< 0.001
Married	1949(58.9)	990(67.6)	959(57.6)	
Never married	359(10.9)	194(9.9)	165(9.7)	
Unmarried but have/had partner	1001(30.3)	405(22.5)	596(32.7)	
Drinking, median (25 and 75 percentile)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	< 0.001
PIR, median (25 and 75 percentile)	3.2 (1.7, 5.0)	3.9 (2.2, 5.0)	2.4 (1.3, 4.1)	< 0.001
BMI, median (25 and 75 percentile)	28.0 (24.6, 32.7)	27.75 (24.4, 32.4)	28.29 (24.9, 32.7)	0.102
Education level, n(%)				< 0.001
High school	720(21.8)	286(17.5)	434(26.7)	
Less than High school	791(23.9)	227(8.6)	564(24.3)	
Some collage or above	1797(54.3)	1075(73.9)	722(49.0)	
Smoking status, n(%)				< 0.001
Former	851(25.7)	367(24.2)	484(28.3)	
Never	1871(56.5)	1028(63.6)	843(46.9)	
Current	587(17.7)	194(12.2)	393(24.8)	
Diabetes, n(%)				0.002
No	2804(85.3)	1402(90.4)	1402(85.3)	
Yes	482(14.7)	167(9.6)	315(14.7)	
Hypertension, n(%)				< 0.001
No	1832(55.4)	979(63.1)	853(54.6)	
Yes	1478(44.7)	610(36.9)	868(45.5)	

The chi-square test (for categorical variables) or Mann–Whitney U test (for continuous variables) was used to compare the characteristics of participants with and without periodontitis

PIR Poverty-to-income ratio, *BMI* Body mass index

models revealed significant correlations between three BFRs (PBDE-47, PBDE-99, and PBDE-154) and the severity of periodontitis (Supplementary Table 6). Notably, PBDE-154 exhibited the strongest associations with the severity of periodontitis, with ORs and 95%*CI*s of 1.22 (1.08, 1.38) for mild periodontitis, 1.12 (1.02, 1.22) for moderate periodontitis, and 1.18 (1.07, 1.31) for severe periodontitis.

Furthermore, we observed that sex hormones partially mediated the relationship between BFRs levels and periodontitis. Specifically, testosterone explained 3.17%, 4.38%, and 4.40% of the relationships involving PBDE47, PBDE99, and PBDE154, respectively, with respect to periodontitis, whereas estradiol mediated 4.27%, 6.08%, and 4.17% of the associations, respectively (Supplementary Fig. 1). We also found a significant mediation role of skull bone mineral density in the relationship between BFR levels and periodontitis (Supplementary Fig. 2). Additionally, to further confirm the robustness of the results, we further performed a series of sensitivity analyses by excluding the cancer population, using the 2018 new periodontal classification, or additionally adjusted the number of missing teeth, respectively. Generally consistent results were yielded and are shown in Supplementary Tables 7–9.

Discussion

In this extensive cross-sectional study utilizing a nationally representative sample, our findings have demonstrated a positive correlation between specific BFRs (PBDE-47, PBDE-99, and PBDE-154) and periodontitis. Furthermore, we have observed a significant relationship between these three BFRs and the severity of periodontitis. The application of the BKMR model has also provided support for a significant association between twelve mixtures of BFRs and periodontitis.

Although there is no direct epidemiological or laboratory evidence to explain the observed association between BFRs and periodontitis, several previous studies have indicated that elevated exposure to BFRs can adversely affect

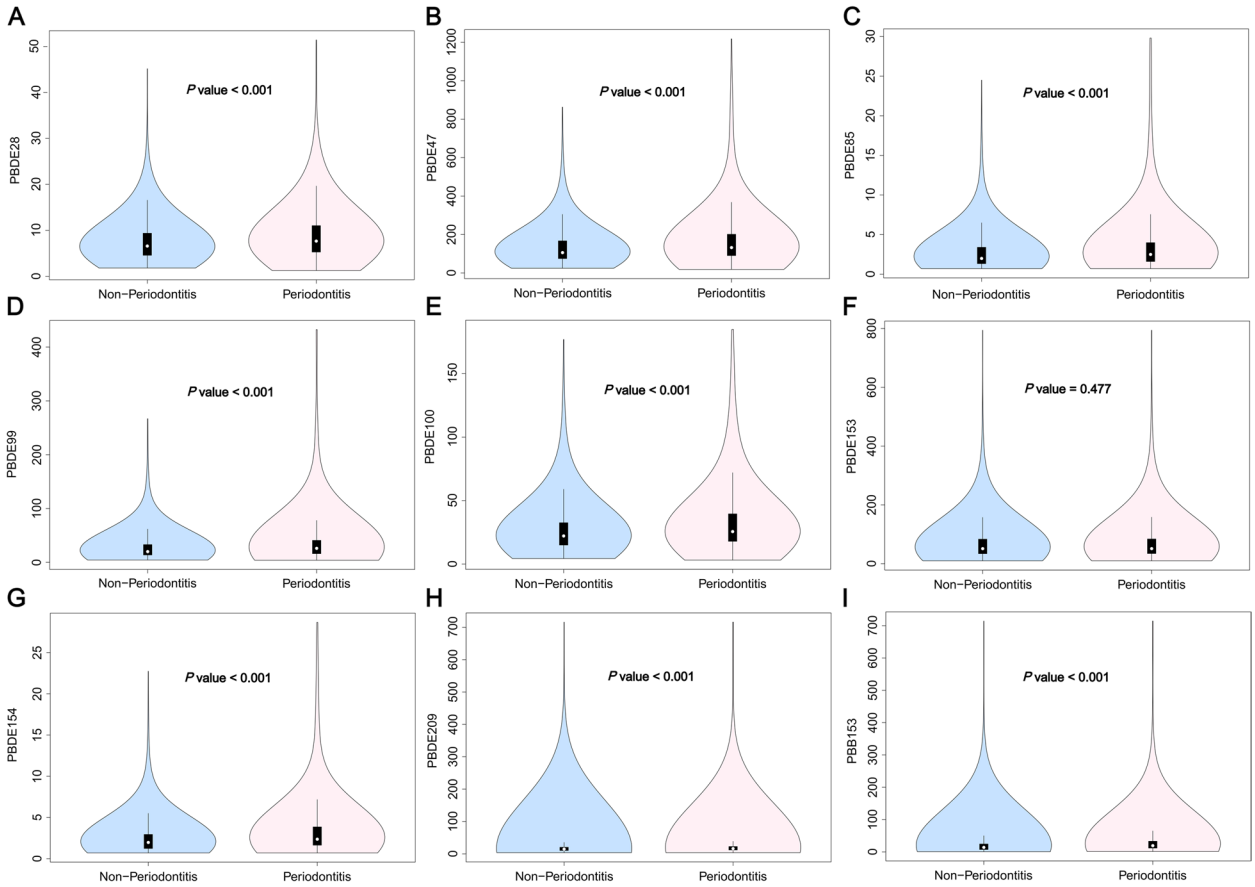

Fig. 2 Comparison of serum levels of BFRs between periodontitis and non-periodontitis groups. Note: *P*-values were derived from the Mann–Whitney U test

Table 2 Univariable and multivariable logistic regression for the association between serum BFRs and periodontitis in NHANES 2009–2014

Variables	Model 1		Model 2	
	OR (95%*CI*)	*P* value	OR (95%*CI*)	*P* value
PBDE-28	1.40 (1.26,1.57)	< 0.001	1.14(0.98,1.32)	0.094
PBDE-47	1.33 (1.20,1.47)	< 0.001	1.15(1.01,1.29)	0.031
PBDE-85	1.24 (1.14,1.34)	< 0.001	1.10(0.99,1.22)	0.067
PBDE-99	1.21 (1.13,1.30)	< 0.001	1.10(1.01,1.20)	0.023
PBDE-100	1.23 (1.13,1.33)	< 0.001	1.07(0.97,1.19)	0.165
PBDE-153	1.06 (0.98,1.15)	0.130	0.96(0.86,1.07)	0.419
PBDE-154	1.30 (1.18,1.42)	< 0.001	1.12(1.01,1.25)	0.036
PBDE-209	1.05 (0.98,1.14)	0.173	1.03(0.97,1.08)	0.316
PBB-153	1.06 (1.01,1.10)	0.016	0.99(0.93,1.05)	0.720

According to their respective interquartile range (IQR) to estimate the odds ratios (ORs) per IQR increase in levels of BFRs. Model 1: unadjusted model; Model 2: adjusted for age, sex, educational level, marital status, PIR, BMI, daily alcohol consumption, smoking status, hypertension, diabetes

bone metabolism and bone density [21, 31]. In the present study, we observed a significant mediating effect of skull density on the relationship between certain BFRs and periodontitis. Since periodontitis involves the destruction of alveolar bone supporting the teeth, it is plausible that BFRs could accelerate this process by disrupting normal bone turnover mechanisms. Additionally, BFRs have the potential to disrupt the levels of sex hormones in the body by affecting the hypothalamic-pituitary–gonadal axis [22, 32]. Given the role of hormones such as estrogen in modulating immune responses and inflammation [33], it is possible that BFRs could influence the progression of periodontitis by dysregulating these hormonal pathways. These findings provided valuable insights for the underlying mechanism of BFRs and periodontitis, but the specific mechanisms remain to be elucidated through subsequent experimental studies.

Furthermore, our findings highlight the importance of considering mixtures of BFRs when assessing their health

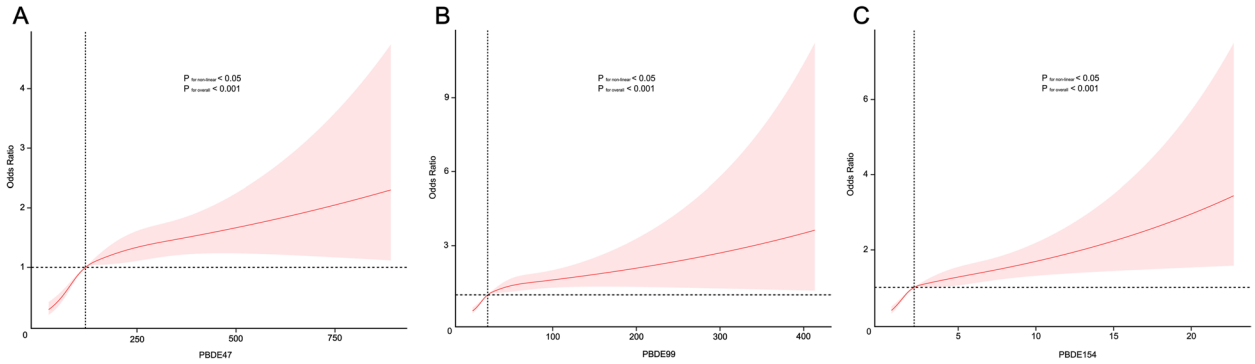

Fig. 3 Restricted cubic spline curves of serum PBDE-47, PBDE-99, PBDE-154 concentrations

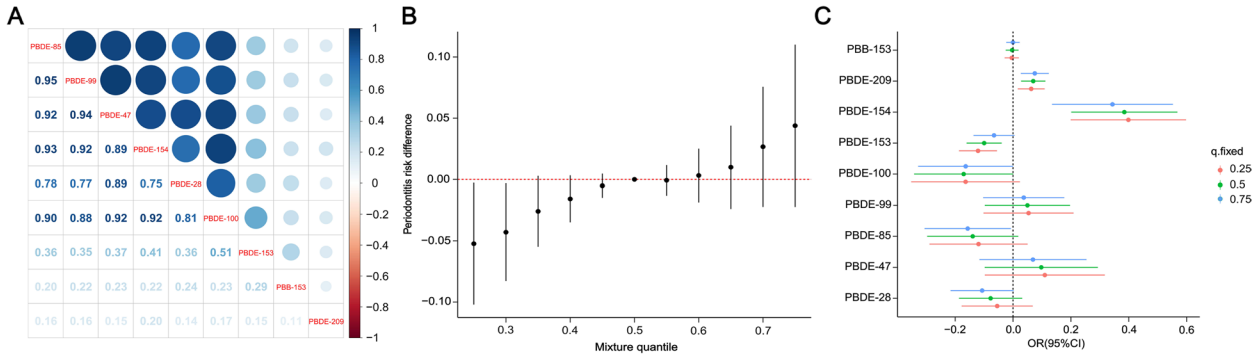

Fig. 4 **A** Spearman rank correlation analysis on serum concentrations of twelve BFRs; (**B**) The overall effect of BFRs mixtures using the BKMR model; (**C**) Single BFRs-exposure effect on periodontitis when other BFRs are fixed at a specific quantile (25th, 50th, and 75th)

impacts. It is important to acknowledge that BFRs are not commonly found in isolation within the environment, and there may exist interactions among them. Employing the BKMR model, this study revealed a positive correlation between mixtures of BFRs and periodontitis. The use of the BKMR model allowed us to explore the combined effects of multiple BFRs on periodontitis risk, providing a more comprehensive understanding of how complex chemical mixtures may interact to influence disease outcomes [34]. This approach is particularly relevant given the ubiquitous presence of multiple BFRs in the environment and their potential for cumulative exposure [35].

The findings from the unordered polynomial logistic regression analysis indicated a positive correlation between BFRs and the severity of periodontitis. Several in vitro studies have provided evidence of BFRs' ability to enhance the production of pro-inflammatory cytokines, including IL-1β, IL-6, and TNF-α [36–38]. These inflammatory factors have been previously associated with the pathogenesis of periodontitis [39, 40]. Therefore, it is plausible to suggest that exposure to BFRs with pro-inflammatory properties may contribute to the development of periodontitis by activating a biologically plausible mechanism.

This study possesses several strengths. Firstly, a comprehensive approach was employed to investigate the correlation between individual and mixed BFRs and periodontitis, utilizing a nationally representative large sample. Secondly, this study is the first epidemiological study to explore the relationship between BFRs and periodontitis. Thirdly, the possible mediating effects of sex hormones and skull density on the relationship between BFRs and periodontitis were further investigated. The findings of this study will provide valuable insights for future prospective and mechanistic studies.

Nonetheless, it is crucial to acknowledge the limitations of this study. Firstly, due to its cross-sectional nature, establishing causality is challenging, and only epidemiological associations can be ascertained. Secondly, the possibility of bias arising from residual and unmeasured confounding factors, as well as measurement errors, cannot be entirely ruled out. Nonetheless, the inclusion of E-values (refer to Supplementary Table 10) provides evidence that the observed

associations are unlikely to be entirely explained by unmeasured confounders.

Conclusion

This study provides preliminary evidence indicating a positive correlation between specific BFRs (PBDE-47, PBDE-99, and PBDE-154) and periodontitis as well as its severity. These findings offer novel perspectives on the prevention of periodontitis through the lens of environmental exposure and contribute to the development of targeted public health policies aimed at reducing environmental risks and improving oral health outcomes. However, future studies should focus on conducting extensive prospective studies on larger scale samples and exploring the underlying mechanisms to confirm and strengthen our observations.

Abbreviations

BFRs	Brominated flame retardants
NHANES	National Health and Nutrition Examination Survey
BKMR	Bayesian kernel machine regression
ORs	Odds ratios
*CI*s	Confidence intervals
PBDEs	Poly brominated diphenyl ethers
PBBs	Poly brominated biphenyls
NCDC	National Centers for Disease Control and Prevention
PBDE-28	2, 4, 4´-Tribromodiphenyl ether
PBDE-47	2, 2´, 4, 4´-Tetrabromodiphenyl ether
PBDE-85	2, 2´, 3, 4, 4´-Tentabromodiphenyl ether
PBDE-99	2, 2´, 4, 4´, 5-Pentabromodiphenyl ether
PBDE-100	2, 2´, 4, 4´, 6-Pentabromodiphenyl ether
PBDE-153	2, 2´, 4, 4´, 5, 5´-Hexabromodiphenyl ether
PBDE-154	2, 2´, 4, 4´, 5, 6´-Hexabromodiphenyl ether
PBDE-209	Decabromodiphenyl ether
PBB-153	2, 2´, 4, 4´, 5, 5´-Hexabromobiphenyl
GC/IDHRMS	Isotope dilution gas chromatography high resolution mass spectrometry
PPD	Probing pocket depth
CAL	Clinical attachment level
CDC/APP	Centers for Disease Control and Prevention/American Academy of Periodontology
PIR	Poverty-to-income ratio
BMI	Body mass index
HbA1c	Hemoglobin A1c
MCMC	Markov chain Monte Carlo
PIP	Posterior inclusion probability
RCS	Restricted cubic spline

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12903-024-04796-4.

Additional file 1: Supplementary Table 1. Common abbreviations for BFRs and minimum detection limits for BFRs in serum.

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Authors' contributions

Fa Chen and Yanfen Li were involved in the conceptualization and design of the study. Yanhong Pan and Qiansi Chen were responsible for drafting the manuscript and making substantial revisions. Yiming Yu and Qiansi Chen were involved in conducting statistical analyses. Zilin Liu, Bingqin Xie, Yu Huang and Han Yang were responsible for creating figures and tables. Baochang He and Fuhua Yan were involved in data collection and interpretation. All authors were involved in the critical revision of the manuscript.

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Availability of data and materials

The data that support the findings of this study are available in NHANES (National Health and Nutrition Examination Survey) at: https://www.cdc.gov/nchs/nhanes/index.htm.

Declarations

Ethics approval and consent to participate

The NCHS Research Ethics Review Board reviewed and approved NHANES, and all participants provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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