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Abstract

Background Environmental exposure to toxic brominated □ame retardants (BFRs) has been con□rmed to have

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selected PBB153 and eight PBDEs with a detection rate above 75% as key exposure variables. In this study, eight PBDEs include 2,4,4´-Tribromodiphenyl ether (PBDE28), 2,2´,4,4´-Tetrabromodiphenyl ether (PBDE47), 2,2´,3,4,4´-Tentabromodiphenyl ether (PBDE85), 2,2´,4,4´,5-Pentabromodiphenyl ether (PBDE99), 2,2´,4,4´,6-Pentabromodiphenyl ether (PBDE100), 2,2´,4,4´,5,5´-Hexabromodiphenyl ether (PBDE153), 2,2´,4,4´,5,6´-Hexabromodiphenyl ether (PBDE154), and Decabromodiphenyl ether (PBDE209). Concentrations of serum BFRs below the lower limit of detection (LLOD) were determined by dividing the LLOD value by the square root of two, following the methods provided in the NHANES dataset [4, 26, 27].

Covariates

To minimize the impact of confounders and provide a more accurate assessment of the relationship between BFRs and hyperlipidemia risk, we included demographic characteristics (gender, age, race, and marital status), socioeconomic characteristics (family poverty income ratio), and health-related factors (body mass index, alcohol use, and serum cotinine) as covariates, based on published research and clinical diagnostic knowledge [2, 4].

e categories for covariates were as follows: gender (male, female), race (mexican american, other hispanic, non-hispanic white, non-hispanic black, other race/ multi-race), marital status (married, living with partner, widowed, divorced, separated, and never married), family poverty income ratio (PIR) (< 1, 1–3,≥3), body mass index (BMI) (< 18.5,18.5–25, ≥ 25), and alcohol use (yes, no). To precisely re ect smoking status and estimate the degree of environmental tobacco smoke exposure, we prefer serum cotinine levels to self-reported survey data regarding smoking [28–31]. All these variables were included to adjust for potential confounders and to examine their

analysis among nine Ln-transformed BFRs. Multivariate logistic regression was implemented to examine the association between individual BFRs and hyperlipidemia. In this analysis, concentrations of nine serum BFRs were input as either ln-transformed variables or categorical variables with four quartiles. e calculation of odds ratios and corresponding 95% con dence intervals were used to explore single serum BFRs's e ect on hyperlipidemia. Model 1 was crude. e second model have modi ed covariates for age, gender, race, marital status, alcohol use, BMI, family PIR, and serum cotinine.

To comprehensively investigate the toxic e ects of mixed serum BFRs on hyperlipidemia risk, we employed various statistical models. Firstly, the WQS model was utilized to quantify the combined e ect of 9 serum BFRs on hyperlipidemia risk. WQS regression is designed for analyzing complex environmental mixtures characterized by high collinearity among their components, as it creates a composite index that captures the cumulative impact of the mixture [25, 32, 33]. To construct this index, we categorized each component into quantiles and utilized a two-step process for weight estimation. Our data was performed with 1000 bootstrap iteration, and split into validation and training sets. Speci cally, 40% of the data were randomly allocated to a training set, while the remaining 60% were assigned into a validation set.

e co-exposure level of serum BFRs was represented by

Association of mixture BFRs exposure with hyperlipidemia risk in WQS regression and QGC analysis

Findings from WQS con rmed that doubling of serum BFRs may elevate the risk of hyperlipidemia (OR: 1.21, 95% CI: 1.09–1.34) while adjusted all covariates. PBDE209 made the most single contribution to hyperlipidemia risk, followed by PBB153 and PBDE100. PBDE99 had lowest weight and had relative low contribution to hyperlipidemia risk (Fig. 3). e qgcomp model analysis found that serum BFRs co-levels were also signi cantly correlated with higher possibility of hyperlipidemia (OR: 1.20, 95%CI: 1.1–1.32) (Figure S1).

BKMR analysis to evaluate the correlations of mixed serum BFRs and hyperlipidemia

According to the results of the combined e ect of BFRs on hyperlipidemia in Fig. 4A, co-exposure to BFRs was positively associated with hyperlipidemia risk. Speci cally, hyperlipidemia risk was signi cantly increased when BFRs mixtures were at the 25th to 35th percentiles in comparison to the 50th percentile. And we also found a positive trend when all BFRs were at above the 60th

Table 2 Associations between single BFRs and hyperlipidemia in the NHANES

Outcomes	Categorical models					Continuous models	
	Q1	Q2	Q3	Q4	*P* trend	OR (95%CI)	*P* value
PBDE28							
Model 1	1.0 (ref.)	1.42 (1.23, 1.63)	1.69 (1.47, 1.96)	2.31 (1.99, 2.69)	< 0.001	1.73 (1.58,1.89)	< 0.001
Model 2	1.0 (ref.)						

percentile, relative to when all BFRs were at their 50th percentile. We further compared the single exposure-response relationship to the 25th percentile while setting the remaining BFRs at the 25th, 50th, or 75th percentile. As shown in Fig. 4B, PBDE28 and PBDE209 exhibited signi cantly positive associations with an increased risk of hyperlipidemia when the levels of the remaining BFRs were at the 25th, 50th, and 75th percentiles. In addition, we explored the interaction relationships among 9 serum BFRs (Figure S2), and a possible interaction between PBB153 and PBDE154, as well as PBB153 and PBDE47 was identi ed. Table S2 presents the PIP within the BKMR model, with PBDE209 (1.00) displaying the highest PIP value, followed by PBDE28 (0.9960) and PBDE85 (0.4458).

Figure 5 displayed the ndings from RCS model. A signi cant dose-response relationship has been observed among PBDE28, PBDE47, PBDE100, PBDE154, PBDE209, and PBB153 and the hyperlipidemia risk (*P* for overall < 0.05). A linear dose-response relationship for these BFRs concentrations with hyperlipidemia risk was established (*P* for nonlinear > 0.05).

Discussion

Our research represents a recent contribution to estimating the association between individual and mixtures of serum BFRs and hyperlipidemia risk in U.S. adults. Logistic regression models con rmed that individual BFRs, such as PBDE 28, PBDE 47, PBDE 85, PBDE 99, PBDE 100, PBDE 154, PBDE 209, and PBB 153, are

de ciency or resistance can result in reduced lipoprotein lipase activity in diabetic patients, subsequently causing dyslipidemia [42].

Furthermore, the ndings demonstrated that PBB153 were positively link to hyperlipidemia risk. e dose of PBB mixture exposure may link to decreased levels in serum triglyceride and cholesterol, thereby in uencing blood lipid levels [43]. PBB153 may contribute to hyperglycemia and dyslipidemia, increasing the risk of hyperlipidemia events. Moreover, exposure to PBB153 was a risk factor for subsequent disorders, such as abdominal obesity, and metabolic syndrome, further increasing the risk of hyperlipidemia [44, 45].

e positive correlations were also observed between PBDE 28, PBDE 47, PBDE 99, and PBDE154 and hyperlipidemia risk. As renowned endocrine disruptors, enduring presence of PBDEs in adipose tissue had the potential to interfere with the regular functions of lipid metabolism, thereby posing a health risk to humans [46, 47]. Evidence suggests that elevated serum levels of PBDEs accumulate in adipose tissue and may appear to interfere with related

positively associated with low HDL and hypertriglyceridemia risk in adults [2]. Additionally, the RCS analysis also revealed the positive linear relationship between serum PBDE28, PBDE47, PBDE100, PBDE154, PBDE209, and PBB153 and hyperlipidemia risk. However, further

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