



## Concentrations of polybrominated diphenyl ethers in breast milk correlated to maternal age, education level, and occupational exposure

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### ABSTRACT

The aim of the present study is to determine whether levels of polybrominated diphenyl ethers in breast milk in the general population are associated with demographic parameters, socioeconomic status, lifestyle factors, and occupational exposure. Forty-six participants are randomly selected from healthy women recruited between April 2007 and April 2008 from local hospitals in southern Taiwan. Thirty PBDE isomers in breast milk are analyzed using a gas chromatograph with a high resolution mass spectrometer. The mean  $\pm$  standard deviation of  $\sum$ PBDEs in breast milk is  $3.59 \pm 1.07$  ng/g lipid. Our current value of  $\sum$ PBDEs in breast milk is 0.7-fold lower compared to the past value in our previous study between 2000 and 2001. Higher levels of  $\sum$ PBDEs might be significantly associated with older maternal age and maternal age of the present study is between 22 and 42 years old. Levels of  $\sum$ PBDEs and certain PBDEs in breast milk are not correlated with maternal pre-pregnant BMI (Body mass index), parity, and lipid contents of breast milk. The  $\sum$ PBDEs level in breast milk is lower in more educated women after controlling for age and pre-pregnancy BMI in our subjects. The main factors associated with  $\sum$ PBDEs in breast milk are age and education level among the binary variables of demographic, socioeconomic, and lifestyle characteristics in this report. The exploratory relationships are found between PBDEs in breast milk and age, education level, or occupational exposure due to small sampling size.

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### 1. Introduction

Polybrominated diphenyl ethers (PBDEs) are fire retardants commonly used in consumer products including cables, textiles, conveyances, synthetic building materials, carpet liners, and electronic circuit boards and cases [1]. They are persistent and ubiquitous in the environment and biota [1,2]. Congeners of PBDEs have

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been shown to cause reproductive disorders, neurotoxic effects, developmental effects, endocrine disruption, and thyroid gland dysfunction in animal models [3,4]. A few epidemiological studies in the general population are strengthened on the basis of whether PBDEs exposure can induce adverse health effects [5–12]. There were no significant correlations between PBDE levels and thyroid hormones in cord blood probably due to the small sampling size ( $n = 18$ ) [9].  $\sum$ PBDEs were positively related to levels of thyroxine and reverse triiodothyronine in blood samples from adult male sport fish consumers [7]. There was a non-significant association of  $\sum$ PBDEs with diabetes in two studies [5,8], while Lim et al. revealed that BDE-153 showed an inverted U-shaped association with metabolic syndrome [5]. Prenatal PBDE exposures were significantly related to decreased total and free thyroxine levels [11]. A study found significantly higher  $\sum$ PBDEs concentrations in the

breast milk of nursing mothers of boys with cryptorchidism than in the nursing mothers of boys not affected by the disorder [10]. Main et al. [10] also found that  $\sum$ PBDEs in breast milk associated positively with the serum of luteinizing hormone. Our previous study showed that background-level PBDEs in 20 breast milk samples had a possible association with low birth weight and short birth length [12]. No large-scale epidemiological studies have been conducted on the association of PBDEs exposure with health; therefore, the harmful effects of PBDEs on human health are still unknown [13].

Fish, meat, and dairy consumption as well as dust ingestion may be the major routes of exposure to PBDEs, with air inhalation usually playing a small additional role [10,13–16]. Owing to high lipid contents of breast milk, PBDE congeners of breast milk are easily detected by current analytical technologies. Breast milk is also a non-invasive specimen convenient for continuous biomonitoring of PBDEs in the general population. It is possible that a breastfed infant is postnatally exposed to PBDEs via breastfeeding. An assessment study indicated that infant consumption of PBDEs from breast milk was the largest contributor to lifetime exposure [17]. However, several reports indicate the opposite. For example, Fangstrom et al. concluded that PBDEs in children were most probably derived from environmental sources rather than maternal transfer [18]. A recent study of family members with non-occupational exposure to PBDEs suggested that toddlers and children had a higher risk of PBDEs exposure and faced higher risks of PBDE-related health effects than their parents [19].

The use of most PBDEs, like pentaBDEs and octaBDEs, has been banned in Europe and voluntarily withdrawn from developing countries, including Taiwan. Temporal trends or changes of PBDEs in breast milk were evaluated in a few studies after the ban or restriction of PBDEs use [20–23], but no reports were evaluated in Taiwan. PBDEs environmental monitoring and biomonitoring data are limited in Taiwan. In our previous study [12], levels of  $\sum$ PBDEs in breast milk collected between 2000 and 2001 in central Taiwan were comparable to levels in breast milk collected during the same period in Europe or East-Asian countries, but 10–20 times lower than that measured in the United States. We also found that the ratios of PCB153/BDE-47, PCB153/BDE-153, and PCB153/ $\sum$ PBDEs were significantly correlated with frequent consumption of fish and shellfish, but not of meat or other food-stuffs [24]. In the present study, we determine the current levels of PBDEs in Taiwanese breast milk to calculate differences in PBDEs between the present survey and the past data investigated from 2000 to 2001. It is examined whether PBDEs in breast milk are associated with demographic characteristics (e.g., age), socioeconomic status (e.g., education level), and lifestyle factors (e.g., occupational exposure). The main influences of PBDEs exposure among the factors of demographic characteristics, socioeconomic status, and lifestyle were also determined in the present study.

## 2. Materials and methods

### 2.1. Recruitment of study participants

Breast milk was collected from women who delivered at local hospitals in southern Taiwan between 5 April 2007 and 30 April 2008. We obtained approval from the Department of Gynecology and Obstetrics in four local hospitals and the Institutional Review Board (IRB) of the Human Research Ethics Committee at Pingtung Christian Hospital, Taiwan, in 2007. All participants gave informed consent after receiving detailed explanations of the study and potential consequences prior to enrollment.

Our participants were healthy pregnant women recruited from four local hospitals in southern Taiwan. A well-trained researcher

interviewed participants during routine prenatal health check-ups in an obstetrics clinic. The following criteria were required for inclusion: residence time of at least three years in southern Taiwan, a supply of more than 120-mL breast milk, and willingness to strictly follow our protocol of collecting milk samples. Of the more than 250 pregnant women invited, 146 agreed to join our study. After 146 subjects delivered their newborns, five subjects were excluded mainly due to the fact that the obstetricians considered the safety of mothers and newborns without collection of cord blood. Thirty-eight mothers were further excluded because they did not give us the sufficient breast milk. One hundred three participants were enrolled into our study after voluntary donations of cord blood and breast milk. Forty-six samples were randomly selected from 103 breast milk samples for further chemical analysis. The participants immediately answered the questionnaire with the assistance of our researcher when they agreed to join this study in an obstetrics clinic. Height, pre-pregnancy weight, and systolic and diastolic blood pressure were measured during routine prenatal examination in the obstetrics clinic. Age, ethnicity, socioeconomic status (e.g., annual household income, education level, occupation, and position), smoking and dietary habits, occupational and non-occupational exposure to PBDEs, frequency of computer use, alcohol consumption, reproductive history, medical history, and menstruation history were determined by our questionnaire. Occupational exposure was defined as participating in occupations involving the manufacturing or processing of fabrics, plastic, or foam in the past three years for more than six months and 20 or more hours per week.

### 2.2. Sample collection

The detailed procedure used for collecting breast milk is described elsewhere in this study [25]. In brief, breast milk was collected manually during breastfeeding at home from two to four weeks after childbirth. The time period of sampling was between May 2007 and June 2008. Participants collected their milk samples in three chemical-free glass-bottles with Teflon seals and froze them at home ( $-4^{\circ}\text{C}$ ). When the amount of milk stored was approximately 90–120 mL, the participants telephoned us and we came to their home to collect the samples. These were immediately transported to a laboratory at National Pingtung University of Science and Technology and stored at  $-20^{\circ}\text{C}$ . Twenty-five millilitre samples in chemical-free containers were sent to Supermicro Mass Research and Technology Center at Cheng Shiu University in southern Taiwan for chemical analysis.

### 2.3. Chemical analysis

Thirty native PBDE standards (BDE-7, -15, -17, -28, -47, -49, -66, -71, -77, -85, -99, -100, -119, -126, -138, -139, -140, -153, -154, -156, -183, -184, -191, -196, -197, -203, -206, -207, -208, and -209) were purchased from Cambridge Isotope Laboratories (Andover, MA, United States). The  $^{13}\text{C}_{12}$ -labeled standards of the 10 PBDEs were obtained from Wellington Laboratories (Guelph, Canada). High purity sodium sulfate, alumina oxide, potassium oxalate, and silica gel were obtained from Merck (Darmstadt, Germany).

The method used to analyze PBDEs in breast milk was modified to change parts of procedures described in previous studies [24,26,27]. Briefly,  $^{13}\text{C}_{12}$ -labeled PBDE congeners of BDE-15, -28, -47, and -99 (100 ng/mL), and -153, -154, -183, and -197 (200 ng/mL), and -207 and -209 (500 ng/mL) were added into breast-milk samples before the extraction. A mixture of 45 mL of acetone and 15 mL of milk sample was extracted with 15 mL of *n*-hexane, sonicated for 20 min, and centrifuged for 15 min (2000 rpm,  $20^{\circ}\text{C}$ ). This step was repeated at least three times. The extract was pooled and then washed with distilled water and dried over

anhydrous sodium sulfate. The lipid content of the breast milk was determined gravimetrically.

The extract was cleaned up as follows. The first cleanup involved treatment with concentrated sulfuric acid. The next cleanup procedure involved a multi-layered silica column packed sequentially with a plug of glass wool, 0.3 mL of activated silica gel, 0.5 mL of silver nitrate (AgNO<sub>3</sub>) silica gel (10%, w/w), 0.3 mL of activated silica gel, 0.5 mL of basic silica gel, 0.3 mL of activated silica gel, 6.2 mL of acid silica gel, and 2.0 mL of anhydrous granular sodium sulfate. The sample extract, dissolved in 5 mL of *n*-hexane, was added to the multi-layered silica column with two additional 5-mL rinses. The absorbed material on the column was eluted with 30 mL of dichloromethane/hexane (10/90, v/v) and the entire eluate was collected, concentrated to a volume of about 1 mL using a rotary evaporator, transferred to the top of an acid alumina column, and eluted with 15 mL of hexane followed by 20 mL dichloromethane/hexane (4/96, v/v). The eluate was discarded and the adsorbed material on the column was eluted again with 30 mL dichloromethane/hexane (40/60, v/v), collected, concentrated to near dryness by using a nitrogen stream, and then transferred to a vial. 50 µL of <sup>13</sup>C-labeled BDE-139 was added in a vial containing the eluate as an internal standard after the clean up prior to injection. The final extract was reduced in volume to 1 mL under a stream of nitrogen.

The 30 PBDEs were assayed using a high resolution gas chromatograph (Hewlett-Packard 6970, Palo Alto, United States) and a high resolution mass spectrometer (Micromass Autospec Ultima, Manchester, UK) with a DB-5HT column (*L* = 15 m, i.d. = 0.25 mm, film thickness = 0.1 µm) (J&W Scientific, Folsom, CA) with splitless injection. The two most abundant isotope masses were measured for each congener. Quantification was performed using internal/external standard mixtures via the isotope dilution method.

Solvents and reagents were tested before each procedure. All glassware was washed with HPLC ultra-grade hexane or acetone (Merck, Darmstadt, Germany) before use. The blank tests of solvents and glassware were regularly checked. Recovery measured for 10 <sup>13</sup>C<sub>12</sub>-labeled PBDE internal standards was added in breast milk before the extraction to ensure recovery in the whole process of chemical analysis. The recovery rates were calculated to be between 70% and 130%. The limits of detection (LODs) of 29 PBDEs were 0.8–16 pg/g lipid. For BDE-209, the LOD was 110 pg/g lipid. For quality control, a laboratory blank and a QC pooled breast milk sample were included in each batch of approximately 10 samples. The result of a Shewhart control chart for QC pooled breast milk samples fully obeyed the control limit of mean ± 3SD and the warning limits of mean ± 2SD, respectively.

#### 2.4. Statistical analysis

Analytical measurements lower than the LODs were set to half of the LODs for subsequent statistical analysis. Only four PBDE-209 values were found to be below LODs. Levels of PBDEs were shown to be normally distributed using the Kolmogorov–Smirnov method after logarithmic transformation. Spearman's rank correlation coefficients were initially used to assess the relationships between PBDE levels and the demographic characteristics (e.g., pre-pregnancy BMI) or associated lifestyle factors (e.g., frequency of using a computer per day, h/day). Student's *t*-tests were used to compare geometric means in two different groups (e.g., smokers and passive smokers). Univariate analysis of covariance (ANCOVA) tests were used to evaluate differences in two groups (e.g., education level) after age and pre-pregnancy BMI were adjusted. The log-transformed PBDE levels were predicted by the binary variables including age, pre-pregnancy BMI, parity, ethnicity, household income, smokers, passive smokers, computer use, and occupational exposure using the multiple stepwise linear regression models.

**Table 1**

Descriptive statistics and characteristics of study subjects (*n* = 46).

	Mean ± SD	Range
Mothers		
Age (years)	30.1 ± 4.3	22–41
Pre-pregnant BMI (kg/m <sup>2</sup> )	21.9 ± 4.1	15.4–32.8
Parity <sup>a</sup>	1.9 ± 0.9	1–4
Milk lipid content (%)	3.4 ± 1.0	1.93–7.5
	Frequency (no. of persons)	Percent
Smokers	5	7
Passive smokers	24	52
Ethnic <sup>b</sup>		
Early inhabitants	34	74
Southern Min	26	57
Hakkanese	7	15
Mainlander	1	2
Original inhabitants or Aborigine	6	13
New inhabitants or non-native born	6	13
Education level		
Junior high school or lower	6	13
Senior high school	16	34
Junior college	12	26
University	9	20
Graduate school	3	7
Annual household income (US dollars)		
<\$10,000	5	11
\$10,000–20,000	18	39
\$20,000–33,400	17	37
\$33,400–50,000	5	11
>\$50,000	1	2
Computer users <sup>c</sup>	22	48
Occupational exposure <sup>d</sup>	6	13

<sup>a</sup> Uniparas: 19 people; biparas: 17; triparas: 8; quadriparas: 2.

<sup>b</sup> Ethnic groups are classified into original, early, and new inhabitants based on the recommendation from Taiwanese government. Non-native born women were 2 from China, 3 from Vietnam, and 1 from the Philippines. Early inhabitants are considered Chinese because their ancestors immigrated to Taiwan at different times.

<sup>c</sup> Use a computer more than 2 h/day.

<sup>d</sup> Subject works in a factory that manufactures plastics, foam, fiber, or silica gel.

Analyses were carried out using the Statistical Package for Social Science (SPSS) version 12.0.

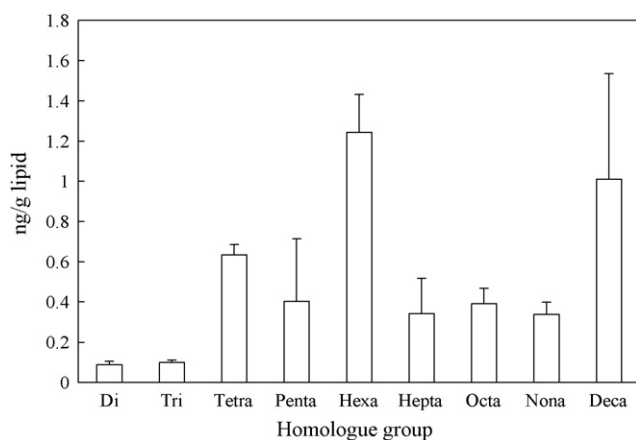
### 3. Results

The descriptive statistics of our participants are shown in Table 1. The mean and median  $\sum$ PBDEs are 3.59 and 3.01 ng/g lipid, respectively, and the concentrations of each of the 30 PBDEs are listed in Table 2. The dominant PBDE congeners are BDE-47 (15.9%), BDE-153 (26.5%), and BDE-209 (13.1%). The three main PBDEs (hexaBDEs, tetraBDEs, and decaBDE) represent 60.3% of  $\sum$ PBDEs (Fig. 1). BDE-197 and BDE-207 account for 6.9% and 4.6%, respectively, of  $\sum$ PBDEs. The toxicity and adverse effects of BDE-197 and BDE-207 are still unknown. Levels of PBDEs in breast milk from various countries in years since 2003 are shown in Table 3 [28–35]. Levels of  $\sum$ PBDEs in breast milk from Taiwan (the present report) are comparable to those from Korea [30], China [32,33], and Poland [35] (Table 3), slightly lower than those from Russia [28], and slightly higher than those from Japan [31]. The highest  $\sum$ PBDEs levels (17–148 times higher than those in other countries; Table 3) are in the United States [34].

Women's age is significantly correlated with  $\sum$ PBDE levels in breast milk using Spearman's rho correlation coefficients ( $r = 0.308$ ,  $p = 0.037$ ), but there is not a significantly linear correlation with  $\sum$ PBDEs (Pearson correlation  $r = 0.259$ ,  $p = 0.082$ ) (data not shown). Milk levels of  $\sum$ PBDEs (geometric mean) are significantly higher in women >30 years of age than in women ≤30 years of age (Table 4).

**Table 2**  
Levels of 30 PBDE homologues in breast milk from southern Taiwan (ng/g lipid).

PBDEs (bromine number)	N < LOD <sup>a</sup> (%)	MDL <sup>b</sup>	Mean ± SD	Median
BDE-7 (2 Br)	41 (89)	0.001	0.001 ± 0.001	0.001
BDE-15 (2 Br)	0 (0)	0.001	0.084 ± 0.113	0.052
BDE-17 (3 Br)	41 (89)	0.004	0.007 ± 0.003	0.006
BDE-28 (3 Br)	0 (0)	0.003	0.085 ± 0.062	0.066
BDE-47 (4 Br)	0 (0)	0.016	0.571 ± 0.264	0.539
BDE-49 (4 Br)	1 (2)	0.004	0.031 ± 0.016	0.032
BDE-66 (4 Br)	2 (4)	0.003	0.015 ± 0.007	0.013
BDE-71 (4 Br)	46 (100)	0.004	0.005 ± 0.003	0.005
BDE-77 (4 Br)	32 (70)	0.001	0.001 ± 0.001	0.001
BDE-85 (5 Br)	10 (22)	0.001	0.009 ± 0.007	0.009
BDE-99 (5 Br)	0 (0)	0.011	0.178 ± 0.096	0.144
BDE-100 (5 Br)	0 (0)	0.003	0.194 ± 0.093	0.173
BDE-119 (5 Br)	24 (52)	0.002	0.012 ± 0.015	0.005
BDE-126 (5 Br)	37 (80)	0.001	0.004 ± 0.023	0.001
BDE-138 (6 Br)	13 (28)	0.002	0.008 ± 0.005	0.007
BDE-139 (6 Br)	11 (24)	0.002	0.010 ± 0.008	0.009
BDE-140 (6 Br)	11 (24)	0.002	0.011 ± 0.007	0.009
BDE-153 (6 Br)	0 (0)	0.007	0.952 ± 0.426	0.855
BDE-154 (6 Br)	0 (0)	0.001	0.089 ± 0.058	0.071
BDE-156 (6 Br)	46 (100)	0.001	0.001 ± 0.001	0.001
BDE-183 (7 Br)	1 (2)	0.005	0.167 ± 0.200	0.098
BDE-184 (7 Br)	32 (70)	0.003	0.006 ± 0.006	0.004
BDE-191 (7 Br)	44 (96)	0.006	0.007 ± 0.003	0.007
BDE-196 (8 Br)	2 (4)	0.006	0.037 ± 0.042	0.025
BDE-197 (8 Br)	0 (0)	0.003	0.249 ± 0.230	0.158
BDE-203 (8 Br)	1 (2)	0.007	0.076 ± 0.070	0.056
BDE-206 (9 Br)	11 (24)	0.017	0.067 ± 0.057	0.052
BDE-207 (9 Br)	0 (0)	0.015	0.165 ± 0.170	0.106
BDE-208 (9 Br)	2 (4)	0.011	0.066 ± 0.052	0.046
BDE-209 (10 Br)	4 (9)	0.110	0.471 ± 0.425	0.346
∑PBDEs	–	–	3.59 ± 1.70	3.01

<sup>a</sup> Number of samples below the limit of detection (LOD).<sup>b</sup> Method detection limit.**Fig. 1.** The distribution of PBDE homologue levels in breast milk (mean ± SE).

Older women seem to have significantly higher levels of triBDEs, tetraBDEs, hexaBDEs, and heptaBDEs than younger women do in this study. No significant associations of pre-pregnant BMI with levels of ∑PBDEs and PBDEs from diBDEs to decabDE are performed. Women with low pre-pregnancy BMI ( $\leq 21$  kg/m<sup>2</sup>) are exposed to more ∑PBDEs compared to women with higher BMI, although this correlation is not significant. A borderline-significant association of education level with the level of ∑PBDEs exposure is shown before controlling the confounders. Levels of ∑PBDEs, hexaBDEs, octaBDEs, nonaBDEs, and decabDE are higher in women with less education than in women with more education, after adjustment for age and pre-pregnancy BMI. There are no significant differences in ∑PBDEs and PBDEs from diBDEs to decabDE in the binary variables of parity, ethnicity, and household income after age and pre-pregnancy BMI is adjusted. We only find that the breast-milk levels of hexaBDEs are significantly lower in non-native born women than in native-born ones before or after age and pre-pregnancy BMI is controlled.

**Table 3**  
Current levels of PBDEs in breast milk from various countries (ng/g lipid).

Country	N	Sampling year	BDE-28	BDE-47	BDE-85	BDE-99	BDE-100	BDE-153	BDE-154	BDE-183	Reference
Russia	10	2003–2004	–	0.140	–	ND	0.043	0.32	–	–	Tsydenova et al. [28]
Spain	30	2003–2004	<0.01	0.22	0.12	0.38	0.46	0.10	<0.01	0.28	Gómara et al. [29]
Korea	9	2004	–	0.810	–	0.200	0.340	0.79	–	–	Sudaryanto et al. [30]
Japan	105	2004	0.070	1.24	–	1.07	1.12	0.54	0.270	–	Eslami et al. [31]
China <sup>a</sup>	19	2004	–	0.490	–	0.120	0.150	0.74	–	–	Sudaryanto et al. [32]
China <sup>b</sup>	205	2005	–	0.51	–	0.11	0.08	0.33	0.05	0.12	Li et al. [33]
America	38	2004	1.8	40.7	1.02	11.8	6.91	5.15	0.630	6.22	Johnson-Restrepo et al. [34]
Poland	22	2004	0.070	1.03	–	0.470	0.150	0.530	–	0.080	Jaraczewska et al. [35]
Taiwan <sup>c</sup>	46	2007–2008	0.085	0.571	0.009	0.178	0.194	0.952	0.089	0.167	The present study

<sup>a</sup> Human milk was collected in the vicinity of Nankang in central China.<sup>b</sup> Human milk was collected from Beijing in northern China.<sup>c</sup> The profiles of PBDEs in breast milk from Taiwan were the same as those in breast milk from central China.

**Table 4**  
Associations between PBDEs in breast milk and demographic parameters and socioeconomic status (ng/g lipid).

	DiBDEs	TriBDEs	TetraBDEs	PentaBDEs	HexaBDEs	HeptaBDEs	OctaBDEs	NonaBDEs	DecaBDE	∑PBDEs
<b>Maternal age</b>										
≤30 years (n = 23)	0.057 <sup>a</sup>	0.062	0.481	0.331	0.810	0.102	0.255	0.210	0.346	2.84
>30 years (n = 23)	0.060	0.096	0.665	0.402	1.12	0.163	0.322	0.261	0.402	3.77
p value <sup>b</sup>	0.865	0.013*	0.014*	0.114	0.001**	0.035*	0.220	0.251	0.430	0.021*
<b>Pre-pregnancy BMI</b>										
≤21 kg/m <sup>2</sup> (n = 24)	0.056	0.072	0.561	0.378	0.991	0.124	0.291	0.278	0.427	3.38
>21 kg/m <sup>2</sup> (n = 22)	0.061	0.084	0.571	0.352	0.976	0.135	0.283	0.211	0.321	3.16
p value <sup>b</sup>	0.721	0.366	0.900	0.570	0.906	0.693	0.883	0.298	0.129	0.579
<b>Parity</b>										
Primipara (n = 19)	0.052	0.072	0.586	0.393	0.962	0.132	0.276	0.240	0.427	3.32
Multipara (n = 27)	0.063	0.081	0.551	0.346	1.00	0.127	0.294	0.230	0.338	3.24
p value <sup>b</sup> (p <sup>c</sup> )	0.428 (0.628)	0.537 (0.625)	0.655 (0.287)	0.311 (0.190)	0.755 (0.540)	0.855 (0.594)	0.749 (0.802)	0.828 (0.884)	0.224 (0.279)	0.856 (0.541)
<b>Ethnicity</b>										
Native born (n = 40)	0.058 a	0.078	0.576	0.369	1.05	0.131	0.28	0.237	0.388	3.37
Non-native born (n = 6)	0.058	0.072	0.498	0.343	0.645	0.12	0.334	0.212	0.286	2.7
p value <sup>b</sup> (p <sup>c</sup> )	0.996 (0.811)	0.762 (0.580)	0.470 (0.768)	0.694 (0.848)	0.006** (0.024*)	0.808 (0.930)	0.531 (0.390)	0.4702 (0.753)	0.278 (0.220)	0.227 (0.386)
<b>Education level</b>										
≤High school (n = 22)	0.057	0.08	0.578	0.374	1.01	0.139	0.331	0.262	0.406	3.48
≥Junior college (n = 24)	0.063	0.071	0.533	0.341	0.923	0.104	0.191	0.169	0.293	2.75
p value <sup>b</sup> (p <sup>c</sup> )	0.587 (0.064)	0.549 (0.108)	0.601 (0.875)	0.513 (0.253)	0.538 (0.191)	0.258 (0.143)	0.001** (0.001**)	0.006** (0.002**)	0.128 (0.053)	0.09 (0.016*)
<b>Annual household income</b>										
≤\$20,000 (n = 23)	0.066	0.075	0.537	0.350	0.864	0.119	0.273	0.219	0.340	3.06
>\$20,000 (n = 23)	0.052	0.080	0.596	0.380	1.12	0.141	0.301	0.249	0.408	3.50
p value <sup>b</sup> (p <sup>c</sup> )	0.317 (0.153)	0.730 (0.329)	0.442 (0.995)	0.511 (0.839)	0.030* (0.386)	0.449 (0.954)	0.607 (0.980)	0.508 (0.906)	0.336 (0.519)	0.281 (0.883)

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001.

<sup>a</sup> Geometric mean.

<sup>b</sup> p value in Student's t-test.

<sup>c</sup> p value in an univariate analysis of covariance after adjustment for maternal age and pre-pregnancy BMI.

**Table 5**  
Correlations between PBDEs exposure and smoking habit, passive smokers, computer users, and occupational exposure (ng/g lipid).

	DIBDEs	TriBDEs	TetraBDEs	PentaBDEs	HexaBDEs	HeptaBDEs	OctaBDEs	NonaBDEs	DecaBDE	$\sum$ PBDEs
<b>Smoking habits</b>										
Nonsmokers ( <i>n</i> = 41)	0.057 <sup>a</sup>	0.077	0.567	0.363	0.985	0.132	0.291	0.238	0.382	3.28
Smokers ( <i>n</i> = 5)	0.068	0.081	0.551	0.382	0.977	0.106	0.256	0.201	0.302	3.21
<i>p</i> value <sup>b</sup> ( <i>pf</i> )	0.642 (0.527)	0.852 (0.331)	0.896 (0.721)	0.797 (0.558)	0.967 (0.325)	0.547 (0.874)	0.366 (0.947)	0.583 (0.862)	0.441 (0.611)	0.907 (0.590)
<b>Passive smokers</b>										
Never ( <i>n</i> = 22)	0.054	0.071	0.553	0.356	0.949	0.120	0.262	0.205	0.331	3.06
Experienced ( <i>n</i> = 24)	0.062	0.083	0.577	0.374	1.02	0.138	0.312	0.264	0.415	3.48
<i>p</i> value <sup>b</sup> ( <i>pf</i> )	0.558 (0.587)	0.380 (0.286)	0.763 (0.619)	0.69 (0.543)	0.577 (0.267)	0.551 (0.366)	0.358 (0.211)	0.195 (0.065)	0.235 (0.078)	0.310 (0.127)
<b>Computer users</b>										
Less than 2 h/day ( <i>n</i> = 24)	0.061	0.082	0.567	0.361	1.02	0.147	0.297	0.237	0.354	3.38
More than 2 h/day ( <i>n</i> = 22)	0.055	0.072	0.564	0.369	0.944	0.112	0.276	0.23	0.394	3.16
<i>p</i> value <sup>b</sup> ( <i>pf</i> )	0.673 (0.676)	0.453 (0.618)	0.972 (0.793)	0.864 (0.661)	0.518 (0.970)	0.234 (0.395)	0.690 (0.956)	0.881 (0.737)	0.576 (0.273)	0.593 (0.982)
<b>Occupational exposure</b>										
Never ( <i>n</i> = 40)	0.058	0.078	0.572	0.358	0.959	0.116	0.264	0.220	0.355	3.16
Experienced ( <i>n</i> = 6)	0.059	0.07	0.523	0.417	1.17	0.261	0.500	0.352	0.513	4.10
<i>p</i> value <sup>b</sup> ( <i>pf</i> )	0.967 (0.827)	0.664 (0.869)	0.659 (0.654)	0.401 (0.468)	0.271 (0.258)	0.013* (0.015*)	0.019* (0.031*)	0.097 (0.201)	0.188 (0.408)	0.159 (0.220)

\**p* < 0.05, \*\**p* < 0.01, \*\*\**p* < 0.001.<sup>a</sup> Geometric mean.<sup>b</sup> *p* value in Student's *t*-test.<sup>c</sup> *p* value in an univariate analysis of covariance after adjustment for age and pre-pregnancy BMI.

In Table 5,  $\sum$  PBDE levels are not differed in the binary groups of smoking habits, passive smokers, computer use, and occupational exposure. Levels of heptaBDEs and octaBDEs are significantly higher in women with occupational exposure than in the other women after controlling for age and pre-pregnancy BMI. No significant differences in concentrations of diBDEs to decaBDE are found between the binary groups of smoking habits, passive smoking, and computer use.

The binary variables from Tables 4 and 5 are used to predict levels of  $\sum$  PBDEs and PBDEs from diBDEs to decaBDE in Table 6. Log  $\sum$  PBDEs in breast milk are significantly predicted by the binary variables of age and education level using a multiple stepwise linear regression, but this relationship only explains 23.9% of the total variances. Log nonaBDEs and log triBDEs could be slightly explained by two binary variables (age and education level). Log octaBDEs and log hexaBDEs are slightly correlated with three binary variables including age, education level, and occupational exposure. Log hexaBDEs and log tetraBDEs have significant associations with one binary variable (age) and three binary variables (age, ethnicity, and education level), respectively. Log decaBDE and log diBDEs are not significantly related to the binary variables described in Tables 4 and 5.

#### 4. Discussion

In our present study, a mean level of BDE-153 has the highest concentration among 30 PBDE congeners. The dominant PBDE congener was BDE-47 in most studies [12,36,37] and BDE-153 in some others [28,30,38]. The notable variation of PBDE levels in breast milk from different countries or regions is shown in Table 3. The differences in PBDE distribution are probably due to differences in dietary habits and PBDE contamination in the environment. PBDE concentrations in breast milk from northern China [33] were found to differ significantly from those in central China [32] and southern Taiwan [12]. A probable cause is that the dietary habits and levels of industrialization are different in these three geographic regions. The current sum of 12 PBDE congeners in breast milk (BDE-17, -28, -47, -66, -85, -99, -100, -138, -153, -154, -183, and -209), whose mean is 2.75 ng/g lipid, is lower than the previous value (3.93 ng/g lipid) in breast milk collected in 2000–2001 [24]. Our value in the current study is 0.7-fold lower than the past value in our previous report conducted in 2000–2002.

Few reports show that increased  $\sum$  PBDEs in breast milk are significantly associated with increased age. In our report, higher age is correlated with higher levels of  $\sum$  PBDEs (*p* = 0.021) (Table 4). A positive age-dependency for  $\sum$  PBDEs in the present study is shown for an exploratory relationship and the occurrence of this relation is still unknown. The mother's age was not significantly related to  $\sum$  PBDEs in human specimens from most previous studies [11,12,24,36,39–42]. In several studies, the absence of the age-dependency of  $\sum$  PBDEs was probably due to recent exposure; notably, steady-state concentrations are never achieved in human tissues, and accumulation in the environment is over a short time span [39,43]. In a recent breast-milk study from Japan [23], age-dependency was observed for BDE-153, which was positively correlated to maternal age in Sendai (*n* = 20) and was negatively associated with age of mothers in Kyoto (*n* = 20). Although PBDEs in breast milk are significantly correlated with maternal age in a Japanese report [23] and the present study, the existence of PBDE-age-dependency is still uncertain due to the small sampling sizes, the narrow age of subjects, and the inconsistent results of the two studies.

No significant differences in  $\sum$  PBDEs are found between groups separated on the basis of pre-pregnancy BMI and parity (Table 4). This finding indicating no correlation of PBDEs exposure with maternal BMI and parity is consistent with those in Herbstman's

**Table 6**  
Significant predictors of PBDE level by stepwise linear regression analysis<sup>a</sup>.

PBDEs	Variables	$\beta$	R <sup>2</sup> change	p	Adjusted R <sup>2</sup>
Log $\sum$ PBDEs	Age	0.175	0.116	0.001**	0.239
	Education level	-0.152	0.157	0.004	
Log DecaBDE <sup>b</sup>	-	-	-	-	-
Log NonaBDEs	Education level	-0.265	0.128	0.002**	0.193
	Age	0.188	0.101	0.022*	
Log OctaBDEs	Education level	-0.282	0.158	<0.001***	0.344
	Age	0.198	0.118	0.007**	
	Occupational exposure	0.271	0.112	0.008**	
Log HeptaBDEs	Occupational exposure	0.346	0.113	0.008**	0.258
	Age	0.268	0.097	0.004**	
	Education level	-0.192	0.077	0.036*	
Log HexaBDEs	Age	0.182	0.227	<0.001***	0.420
	Ethnicity	-0.235	0.083	0.001**	
	Education level	-0.156	0.149	0.001**	
Log PentaBDEs <sup>b</sup>	-	-	-	-	-
Log TetraBDEs	Age	0.141	0.130	0.014*	0.110
Log TriBDEs	Age	0.245	0.133	0.001**	0.199
	Education level	-0.173	0.102	0.021*	
Log DiBDEs <sup>b</sup>	-	-	-	-	-

<sup>a</sup> Using two groups divided on the basis of women's age, pre-pregnancy BMI, parity, smoker, passive smoker, ethnicity, education level, annual household income, computer user, and occupational exposure as the predictors.

<sup>b</sup> There were no significant results using a multiple stepwise linear regression.

\*  $p < 0.05$ .

\*\*  $p < 0.01$ .

\*\*\*  $p < 0.001$ .

report and our previous study [11,24]. Recently, a large-scale study ( $n = 1367$ ) showed that only BDE-153 in human blood had a significantly inverse correlation with BMI (Means of age and BMI were 49.7 years and 28.3 kg/m<sup>2</sup>, respectively), but their correlation coefficient was only -0.16 using a Spearman's rank correlation coefficient test [5]. In our study, non-significant differences are found in  $\sum$  PBDE levels of breast milk between the samples from new inhabitants (non-native-born women) and native-born women; whereas the hexaBDEs level of breast milk is lower in new inhabitants compared to in native-born ones. Herbstman [11] found that PBDE levels in mothers' blood were lower in Asian than in Caucasian samples possibly due to differences in exposure routes, pathway, and immigration patterns. Furthermore, there were no significant differences in  $\sum$  PBDEs level among ethnic groups of native-born Taiwanese ( $p = 0.796$ ) (data not shown) and between native-born and new-inhabitant subjects, probably because all subjects in the present study were Eastern Asians.

After adjustment for age and pre-pregnancy BMI, more educated women (a degree of junior college level or higher) are significantly associated with lower  $\sum$  PBDEs exposure. A significantly negative association of  $\sum$  PBDEs with education level still appears in our study after age, pre-pregnancy BMI, parity, ethnicity, annual household income, smokers, passive smokers, computer use, and occupational exposure are adjusted. This correlation does not recommend a causal relationship—there is no hypothesis that can be offered to examine or explain why highly educated women are exposed to more PBDEs. Owing to the small number of our subjects, the elaborate interpretation of the correlation between PBDEs exposure and education level is risky. In our previous study in Taiwan [24], PBDEs level in breast milk from three groups separated on the basis of education level (high school, college, and university)

differed significantly before but not after adjustment for age, pre-pregnancy BMI, and parity. In a study conducted in Baltimore [11],  $\geq 5$  years of post-high school education was significantly correlated with higher level of BDE-47 exposure. It is not concluded whether PBDEs exposure has a non-significant, positive, or negative correlation with higher education level. Further studies are encouraged in the future.

Table 5 shows that levels of PBDEs in breast milk are not related to habitual smoking, passive smoking, and computer use. Occupational exposure is not associated with  $\sum$  PBDEs in breast milk, but it has significant correlations with higher levels of heptaBDEs and octaBDEs. Few studies have reported correlation with occupational exposure. In two Swedish studies [44,45], serum levels of hexaBDEs to nonaBDEs and  $\sum$  PBDEs were higher in workers within the electronic-dismantling industry than in control workers without occupational exposure. Sjödin et al. [45] also indicated that serum levels of BDE-153, -154, and -183 were significantly higher in computer operators than in hospital cleaners. A report from Korea showed similar PBDE levels and congener profiles in incinerator workers and the general population [41]. A Japanese study showing the difference in age-dependency for BDE-153 between Kyoto and Sendai was probably influenced by their occupation (85% housewives in Kyoto and 85% workers in Sendai) [23]. Probably due to small sampling size, the present study only shows an exploratory relationship between occupational exposure and certain PBDEs.

Table 6 shows the significant predictors of  $\sum$  PBDEs and certain PBDEs using the binary variables. The main factors that influenced  $\sum$  PBDEs and certain PBDEs in breast milk are age and education levels in this population. Occupational exposure is also related to women exposed to heptaBDEs and octaBDEs, while these organobromine compounds are associated with the binary vari-

ables of age and education level. The existence of higher  $\Sigma$ PBDE levels in relation to lower education level and order maternal age in the present study is thoroughly considered because small sample size limits the statistical power of our observations. Although our study's primary concern was young mothers and their offspring, PBDEs exposure impacts all human health, particularly aberrations in hormone secretion and neurobehavioural development. Larger studies on the associations between the PBDEs exposure and demographic parameters, socioeconomic status, neurotoxicity, and hormone secretions should be conducted in the future.

Unlike other persistent organic pollutants (POPs), such as polychlorinated-*p*-dioxins and furans (PCDD/Fs), polychlorinated biphenyls (PCBs), and organochlorine pesticides (OCs), PBDEs are not restricted or banned for use in most countries. Most studies had found that higher levels of PCDD/Fs, PCBs, and OCs were strongly correlated with increased maternal age and primiparity, but only weakly correlated with decreased maternal BMI and education level [11,46–49]. The difference in associations between PBDEs and chlorinated POPs may reflect different exposure pathways, toxicokinetics, or the effects of restrictions and bans, and differences in bioavailability, bioaccumulation, biotransformation, and half-lives in biota. Future studies conducted to the associations between PBDEs exposure and influenced factors are needed.

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