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Urinary phthalate metabolite and bisphenol A levels in the Korean adult population in association with sociodemographic and behavioral characteristics: Korean National Environmental Health Survey (KoNEHS) 2012–2014

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ABSTRACT

Backdground: Phthalates and bisphenol A (BPA) have been used in a variety of consumer products and are detected widely in both humans and the environment. Demographic and socio-economic characteristics that affect exposure to these chemicals have been investigated among several general populations; however, nationally-representative population-based studies are limited to Canada, Germany, and the USA. Moreover, relatively little is known about the socio-demographic characteristics that influence exposure to these chemicals among nationally representative populations of Asia.

Methods: Data are obtained from the Korean National Environmental Health Survey (2012–2014). In total, 6,478 adults (aged 19 and older) were recruited and sampled for urinary levels of major phthalate metabolites and bisphenol A. In addition, demographic and socio-economic parameters were determined from questionnaire data and the characteristics associated with urinary concentrations of the target chemicals were assessed.

Results: Urinary levels of bis(2-ethylhexyl) phthalate (DEHP) and dibutyl phthalate (DBP) metabolites of Korean adults were generally higher, but those of mono-benzyl phthalate (MBzP) were lower, and BPA were similar or higher than those reported from national biomonitoring programs in the United States and Canada. Similar to other nationally representative populations, females and older adults showed higher creatinine-adjusted phthalate metabolite and BPA levels among the Korean population. Meanwhile, monthly household income and education were negatively associated with urinary phthalate metabolites. Among personal care products, nail polish use was positively associated with both phthalate metabolites and BPA concentrations in urine.

Conclusion: Our observations based on a nationally representative population of Korea show that socio-demographic determinants for these urinary chemicals vary by country, and should be considered for developing appropriate mitigation measures and policies.

1. Introduction

Phthalates and bisphenol A (BPA) have been widely used as plasticizers in polyvinyl chloride (PVC), or as raw materials of polycarbonate and epoxy resin. Many consumer products (e.g., household goods, medical equipment, toys, and cosmetic products) contain phthalates and BPA (Gayathri et al., 2004; Le et al., 2008; Schettler, 2006; Zhou et al., 2011). Due to their widespread use, phthalates and BPA have been frequently detected in the environment, indoor dust, food, consumer products (Geens et al., 2009; Guo et al., 2012), and humans (CDC, 2018; Guo et al., 2011; Health Canada, 2013; Monika et al., 2014).

Several nationwide biomonitoring programs have reported the widespread presence of these chemicals in human urine. The National Health and Nutrition Examination Survey (NHANES) of the United States (US) reported that phthalate metabolites and BPA were detected

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in > 70% and 92% of urine samples collected from the general US population, respectively (Calafat et al., 2008; Silva et al., 2004). Meanwhile, the Canadian Health Measures Survey (CHMS) detected 11 phthalate metabolites and BPA in more than 90% of the general population (Health Canada, 2013). In the Korean National Environmental Health Survey (KoNEHS), conducted from 2009 to 2011, the detection rate of bis(2-ethylhexyl) phthalate (DEHP) and dibutyl phthalate (DBP) metabolites in urine was over 99%, while that of BPA was over 80% among the general adult population (Park et al., 2016).

BPA and phthalates are suspected endocrine-disrupting chemicals, and have been associated with several human diseases, including hormone-related and metabolic disorders, insulin resistance, abnormal liver function, and cardiovascular diseases (Casals-casas and Desvergne, 2011; Grun and Blumberg, 2009; Han and Hong, 2016; Lang et al., 2008; Meeker et al., 2007, 2010). Therefore, efforts have been made to identify the sources and exposure pathways of and to mitigate exposure to these chemicals among general human populations worldwide.

Exposure sources and pathways of phthalates and BPA are thought to be highly diverse (Vandenberg et al., 2007; Wormuth et al., 2006). Humans are exposed to these chemicals via ingestion and, to a lesser extent, via inhalation or dermal contact (Fromme et al., 2007; Sathyanarayana et al., 2008). Phthalates and BPA have been detected in raw and processed foods, including dressings and butter, fish products, and pork products (Bradley et al., 2013; Heinemeyer et al., 2013; Schecter et al., 2013). Therefore, dietary exposures were generally considered as a major source of these chemicals in humans (Colacino et al., 2010; Zota et al., 2016). In addition to dietary exposure, phthalates, especially with lower molecular weight, can also be delivered to humans via inhalation of air-borne dust and dermal contact from the use of personal care products (Braun et al., 2014; Geens et al., 2009, 2012).

In addition to behavioral and lifestyle parameters, several socio-demographic characteristics have been reported to be associated with urinary phthalate metabolites and BPA concentrations (Kobrosly et al., 2012; Zota et al., 2014). For instance, household income along with lifestyle parameters such as the use of housing material, household products, personal care products, and cosmetics have been associated with phthalate exposure (Kobrosly et al., 2012; Schettler, 2006). In addition, socio-demographic characteristics such as education could influence dietary behavior that may be associated with exposure to phthalates and BPA: Higher education group tended to consume significantly more dairy products, fruits, and vegetables than those with lower educational attainment (Deshmukh-Taskar et al., 2007). In another study, a low diet score characterized by low intakes of fruits and vegetables was associated with low educational attainment (Robinson et al., 2004). Because behavioral and lifestyle characteristics vary by time and region, associations between socio-demographic parameters and the levels of phthalates and BPA exposure are often inconsistent by ethnicity, time, or region (Mitro et al., 2018). Therefore, understanding such characteristics that are associated with exposure to these chemicals is relevant for public health.

Given this background, the aim of this study was to determine major socio-demographic characteristics associated with urinary levels of phthalate metabolites and BPA in the adult Korean population. For this purpose, a dataset obtained from a nationally representative adult population of Korea was used. The observations of this study can provide information useful to better identify major sources and pathways of exposure to these chemicals among general adult populations, and eventually help develop appropriate exposure mitigation measures against this important group of chemicals in Korea.

2. Materials and methods

The details of KoNEHS are described elsewhere (Park et al., 2016). Briefly, the second round of the survey was designed to determine levels of 21 environmental chemicals, including metals, phthalates, and volatile organic compounds, among the general adult population of Korea (aged 19 or older). For this purpose, about 6,000 participants were recruited between 2012 and 2014 based on a two-stage, proportionally stratified sampling design by gender, age, and geographic characteristics. Geographical characteristics included urban, rural, and coastal, which were determined based on location of the region and occupation of majority of the residents as of 2010. Spot urine samples were sampled at survey centers situated throughout the country between 7 p.m. and 9 p.m., and participants completed a questionnaire through a face-to-face interview conducted by trained personnel. The questionnaire included questions divided into six categories: demographic and socio-economic information, family history, indoor and outdoor environments, occupational history, dietary habits, and lifestyle related to environmental chemical exposure. This study was approved by the Research Ethics Committee of the National Institute of Environmental Research, Korea.

2.1. Measurement of urinary phthalate metabolites and BPA

Upon collection, spot urine samples were delivered cold (0–4 °C) to the laboratories, and stored frozen (−20 °C) within 24 h of collection until analysis. We did not detect the target analytes in specimen cups, storage vials, handling material, or any analytical reagents used for collection or analysis of the sample. Samples were hydrolyzed with β-glucuronidase/arylsulfatase enzyme (*E. coli*-K12, Roche Biomedical), followed by liquid-liquid extraction with ethyl ether. Urinary chemicals were measured using ultra-performance liquid chromatography mass spectrometry separation, followed by electrospray ionization and tandem mass spectrometry (Xeno TQ-S; Waters, Milford, MA, USA), as described in detail elsewhere (Silva et al., 2007; Völkel et al., 2005). For separation of phthalates, ACQUITY ULPC® BEH Phenyl column was used, and for BPA, ACQUITY ULPC® BEH C18 column was used.

The measured phthalate metabolites included secondary oxidized metabolites of DEHP (i.e., mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP)), hydrolytic metabolites of benzyl butyl phthalate (i.e., mono-benzyl phthalate (MBzP)), and DBP (i.e., mono-*n*-butyl phthalate (MnBP)). The limits of detection for MEHHP, MEOHP, MECPP, MBzP, MnBP, and BPA were 0.28, 0.26, 0.34, 0.27, 0.44, and 0.15 μg/L, respectively.

Quality control procedures for all analytes were followed according to the protocols recommended by the National Institute of Environmental Research. In addition, the analytical laboratory successfully participated in the quality control programs run by the Korea Association of Quality Assurance for Clinical Laboratory and German External Quality Assessment Scheme for Analysis of Organic Chemicals in Biological Materials twice per year.

2.2. Statistical analysis

KoNEHS uses a two-stage, proportionally stratified sampling design. For design-based analysis, sample weights were required to reflect the differential probability of selection and for non-response, and were post-stratified to the 2010 National Population and Housing Census of Korea. Information on strata (based on administrative districts and socioeconomic status) and cluster (sampling unit) were used in regression model.

For the descriptive statistics, geometric means (GM) with 95% confidence intervals (CIs) and percentiles for urinary phthalate metabolites and BPA were calculated to determine the creatinine-adjusted concentrations. All the urinary creatinine concentrations were above the method detection limit (LOD: 0.015 g/L, Range: 0.05–4.98 g/L), we did not exclude data based on creatinine concentrations. Analytical results below the method detection limit (MDL) were substituted with a value of the respective MDL divided by the square root of 2. The sum of MEHHP, MEOHP, and MECPP concentrations was designated as the

total DEHP metabolites (i.e., **Σ**DEHP). When one or two of the DEHP metabolites were non-detected, the MDL divided by the square root of 2 was substituted to calculate **Σ**DEHP. Because phthalate metabolites and total BPA concentrations were right-skewed lognormal distribution, the data were ln-transformed for analysis. The correlations among phthalate metabolite and BPA were estimated using Spearman correlation analysis.

To evaluate the influences of socio-demographic characteristics on urinary chemical concentrations, multiple linear regression models were developed with selected socio-economic and behavioral characteristics as predictors and phthalate metabolites and BPA as dependent variables. The predictor variables were selected only when a variable was significantly associated ($p < 0.05$) with phthalate metabolites or BPA in the univariate regression model with covariates of gender and age (Supplementary Table S1). The reports of previous studies were also considered (Kobrosly et al., 2012; Schettler, 2006). For urinary phthalate and BPA concentrations, both unadjusted (measured) and creatinine-adjusted concentrations were applied to the statistical analysis (Barr et al., 2005; LaKind et al., 2014). Unless otherwise mentioned, the description and interpretation of the results are based on creatinine-adjusted chemical concentrations, throughout this study.

Proportional change of the arithmetic mean associated with each predictor level, relative to the reference level, was calculated by adjusting other predictors in the model, and was presented as the adjusted proportional change, following the method outlined in Mckelvey et al. (2007). Predictor variables obtained from the questionnaire, including gender, age group (categorized in 10-year intervals), monthly household income (by quartiles), highest education attained (under middle school, middle to high school, or over high school), house type (detached, row/town house, or apartment), personal care product use such as perfume, body cleanser, and nail polish (used once or more in the last month or never used), and residential area (rural or urban/coastal area), were added to the multiple regression model as dichotomous or nominal variables. Monthly household income was categorized based on the income criteria established by Statistics Korea. Data analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

Among the 10,438 subjects who were initially contacted for participation, a total of 6,478 adults (2,774 males and 3,704 females) completed the questionnaire and provided at least one biological sample, i.e., urine or blood specimen (response rate: 62.1%). The demographic characteristics of the participants, including age, gender, education, monthly household income, and house type, are presented in Table 1. Among the 6,478 subjects, 8 persons failed to submit a urine sample. Therefore, the target population in the present study was 6,470 adults.

3.1. Occurrence of phthalate metabolites and bisphenol A in urine

The ΣDEHP metabolites (i.e., sum of MEHHP, MEOHP, and MECPP), MBzP, and BPA were detected in > 98%, 93%, and 87% of urine samples, respectively. BPA was moderately correlated with all phthalate metabolites ($0.35 < r < 0.45$, $p < 0.001$, Supplementary Table S2). The GM (95% CI) of the concentration of ΣDEHP metabolites, MBzP, MnBP, and BPA were 70.3 (68.3–72.3), 3.82 (3.59–4.08), 32.5 (31.0–34.2), and 1.49 (1.42–1.57) μg/g-creatinine, respectively (Table 2). The unadjusted GMs of urinary ΣDEHP metabolites, MBzP, MnBP, and BPA were 50.5 (48.5–52.5), 2.81 (2.62–3.02), 23.6 (22.3–25.1), and 1.09 (1.02–1.16) μg/L, respectively (Supplementary Table S3).

3.2. Urinary chemical levels by gender, age, and residential area

Urinary levels of creatinine-adjusted DEHP metabolites, MBzP, and MnBP were higher among females and in older participants (Table 3). The GM of urinary ΣDEHP metabolites was 58.6 μg/g-creatinine in males and 83.9 μg/g-creatinine in females. ΣDEHP metabolite levels increased with age, with the lowest concentrations were found in participants aged 19–29 (55.6 μg/g-creatinine), while the highest were in those aged 70 years and older (104 μg/g-creatinine). Similar directions of age dependence were observed for creatinine-adjusted MBzP and MnBP. There was no statistical significance in levels of phthalate metabolites according to residential area (Table 3). For creatinine-adjusted BPA levels, females showed significantly higher levels than males. Unlike phthalate metabolites, residents from rural/coastal areas showed significantly lower levels of BPA concentrations than those from urban areas. Creatinine-adjusted BPA levels did not differ by age, except for those in their 50s. Meanwhile, for unadjusted (measured) BPA concentrations, gender and age showed different patterns of association, but residential area showed the same directions of association.

Table 1
Demographic and socio-economic characteristics of participants in KoNEHS, 2012–2014.

	N	Weighted percent
Total	6,478	100
Gender		
Male	2,774	49.2
Female	3,704	50.8
Age (years)		
19-29	537	17.7
30-39	1,056	19.7
40-49	1,226	21.4
50-59	1,439	19.4
60-69	1,335	11.0
70 +	885	10.6
Education		
< Middle school	1,420	14.0
Middle-High school	2,822	40.0
> High school	2,236	46.0
Monthly Household Income (US$/month)		
Low (< 1,300)	1,797	19.5
Mid-Low (1,300–2,600)	1,626	23.6
Mid-High (2,600–3,600)	1,090	19.8
High (≥3,600)	1,941	37.1
House Type		
Detached house	2,280	25.3
Row/Town house	1,075	20.5
Apartment	3,123	54.2
Residence area		
Urban	5,765	93.1
Rural/Coastal	713	6.9

3.3. Urinary levels by population characteristics

Most phthalate metabolite levels were significantly lower among those with higher monthly household incomes or higher education levels (Table 3). In addition, people living in apartments showed lower urinary phthalate metabolite levels, including metabolites of DEHP and BBzP, than those living in detached houses. Regarding BPA, unlike phthalate metabolites, those with higher education exhibited marginally higher urinary levels. In addition, people using nail polish at least once a month showed higher levels of urinary phthalate metabolites and BPA concentrations. Use of body cleanser was also positively associated with creatinine-adjusted BPA level. On the other hand, uses of perfume and body cleanser were negatively associated with creatinine-adjusted ΣDEHP levels.

4. Discussion

Based on KoNEHS 2012–2014, urinary levels of phthalate metabolites and BPA of the general Korean population were generally higher

Table 2
Weighted geometric means and selected percentiles of phthalate metabolites and BPA by sociodemographic characteristics of the adult Korean population. (μg/g creatinine).

	DEHP				BBzP	DnBP	BPA
	ΣDEHP	MEHHP	MEOHP	MECPP	MBzP	MnBP	BPA
Total	70.3 (68.3–72.3)	24.3 (23.5–25.1)	16.8 (16.2–17.3)	28.0 (27.2–28.8)	3.82 (3.59–4.08)	32.5 (31.0–34.2)	1.49 (1.42–1.57)
25th	46.3 (45.1–47.5)	15.9 (15.2–16.5)	10.8 (10.5–11.2)	18.5 (17.9–19.0)	2.02 (1.88–2.17)	21.0 (20.0–22.0)	0.77 (0.72–0.81)
50th	68.6 (66.1–71.2)	23.9 (23.0–24.7)	16.6 (16.1–17.2)	27.4 (26.4–28.4)	3.63 (3.41–3.87)	31.6 (29.9–33.3)	1.49 (1.39–1.59)
75th	103 (99.0–106)	36.5 (35.2–37.9)	25.7 (24.6–26.8)	41.4 (40.0–42.8)	7.00 (6.54–7.50)	49.2 (46.3–52.2)	2.95 (2.76–3.15)
95th	192 (183–202)	70.7 (67.3–74.3)	49.0 (46.7–51.4)	77.2 (73.2–81.3)	20.6 (18.6–22.7)	105 (96.5–115)	8.70 (7.72–9.80)
% < LOD	1.04	1.13	1.36	1.04	6.06	1.99	13.0
Gender							
Males	58.6 (56.6–60.7)	20.7 (19.9–21.6)	13.7 (13.2–14.3)	23.2 (22.4–24.0)	3.38 (3.14–3.63)	27.5 (26.0–29.1)	1.27 (1.19–135)
Females	83.9 (81.4–86.4)	28.4 (27.4–29.4)	20.3 (19.6–21.1)	33.7 (32.6–34.7)	4.32 (4.02–4.62)	38.2 (36.4–40.1)	1.75 (1.65–1.85)
Age Group							
19-29	55.6 (51.5–60.0)	18.8 (17.3–20.4)	13.0 (11.9–14.2)	22.9 (21.2–24.6)	3.31 (29.2–3.75)	26.7 (24.5–29.1)	1.48 (1.32–1.65)
30-39	58.5 (56.0–61.1)	20.3 (19.3–21.3)	14.0 (13.3–14.7)	23.4 (22.5–24.4)	3.33 (3.06–3.63)	28.0 (26.1–30.0)	1.50 (1.37–1.65)
40-49	68.3 (65.1–71.6)	23.7 (22.5–25.1)	16.4 (15.6–17.3)	27.1 (25.9–28.3)	3.70 (3.36–4.09)	33.0 (30.8–35.4)	1.57 (1.43–1.72)
50-59	77.6 (74.4–81.0)	27.6 (26.3–28.9)	18.5 (17.7–19.3)	30.0 (28.7–31.4)	3.88 (3.52–4.27)	33.6 (31.5–35.7)	1.62 (1.48–1.77)
60-69	87.2 (83.1–91.5)	29.9 (28.4–31.4)	20.7 (19.6–21.9)	34.8 (33.1–36.6)	4.59 (4.24–4.96)	41.0 (38.0–44.2)	1.42 (1.31–1.54)
≥70	104 (97.9–110)	35.4 (33.1–37.8)	25.5 (24.0–27.1)	41.5 (39.3–43.7)	5.43 (4.91–6.00)	43.3 (39.7–47.1)	1.24 (1.14–1.35)
Monthly Household Income (US$)							
< 1,300	92.7 (87.4–98.3)	32.1 (30.1–34.2)	22.1 (20.8–23.6)	36.9 (34.8–39.0)	5.26 (4.74–5.83)	41.3 (37.8–56.0)	1.38 (1.27–1.50)
1,300–2,600	70.7 (67.6–73.9)	24.2 (23.0–25.4)	17.1 (16.3–17.9)	28.1 (26.9–29.4)	3.85 (3.55–4.19)	32.0 (30.0–34.1)	1.47 (1.35–1.60)
2,600–3,600	66.5 (63.4–79.8)	23.3 (22.1–24.6)	15.9 (15.0–16.8)	26.4 (25.1–27.7)	3.80 (3.41–4.22)	30.9 (28.8–33.3)	1.52 (1.36–1.69)
≥3,600	62.5 (59.9–65.1)	21.6 (20.6–22.6)	14.8 (14.1–15.5)	25.0 (24.0–26.1)	3.24 (2.91–3.61)	29.9 (28.0–31.9)	1.56 (1.44–1.68)
Educational Level							
< Middle	105 (99.7–110)	36.1 (34.1–38.2)	25.1 (23.8–26.5)	41.7 (39.8–43.6)	5.48 (4.98–6.03)	44.4 (41.2–47.9)	1.34 (1.24–1.46)
Mid-High	75.1 (73.0–77.2)	26.3 (25.5–27.2)	18.0 (17.5–18.6)	29.5 (28.6–30.4)	4.05 (3.79–4.33)	33.2 (31.3–35.2)	1.57 (1.47–1.67)
> High	58.8 (56.5–61.2)	20.1 (19.3–21.0)	13.9 (13.3–14.6)	23.8 (22.8–24.7)	3.26 (2.99–3.56)	29.1 (27.5–31.9)	1.48 (1.38–1.59)
House Type							
Detached	81.9 (78.1–85.8)	28.2 (26.8–39.7)	19.5 (18.5–20.5)	32.7 (31.2–24.2)	4.56 (4.21–4.95)	36.0 (33.2–39.1)	1.43 (1.32–1.56)
Row house	70.3 (65.9–74.9)	24.5 (22.7–26.4)	16.9 (15.8–18.2)	27.9 (26.2–29.6)	3.90 (3.48–4.37)	32.1 (28.3–36.5)	1.67 (1.47–1.90)
Apartment	65.5 (63.0–68.1)	22.6 (21.7–23.6)	15.6 (14.9–16.3)	26.1 (25.1–27.2)	3.49 (3.16–3.86)	31.2 (29.3–33.1)	1.46 (1.36–1.56)
Residential Area							
Urban	69.5 (67.5–71.6)	24.0 (23.2–24.8)	16.6 (16.0–17.2)	27.8 (27.0–28.6)	3.80 (3.55–4.06)	32.4 (30.8–34.1)	1.52 (1.44–1.61)
Rural/Coastal	81.4 (73.1–90.5)	28.9 (25.9–32.2)	19.6 (17.8–21.5)	31.6 (28.1–35.5)	4.22 (3.60–4.94)	34.6 (29.2–40.9)	1.18 (1.04–1.33)

Total DEHP (ΣDEHP) was derived from sum of MEHHP, MEOHP, and MECPP.

than those reported from the US (NHANES) and Canada (CHMS), while those of BBzP metabolites and BPA were lower (Table 4). The average urinary MBzP concentration was 2.81 μg/L, which was lower than those from the US (5.6 μg/L) and Canada (7.5 μg/L). Meanwhile, the average urinary BPA concentration was 1.09 μg/L, which was also lower than that in Canada (1.79 μg/L), but similar to the US levels (1.2 μg/L). These dissimilarities can be explained by differences in lifestyles and dietary habits, as well as physiological characteristics, e.g., body fat distribution (Koo et al., 2002; Martina et al., 2012; Schettler, 2006). In Korea, phthalates such as DEHP, BBP, and DBP have recently been restricted for use in consumer products and toys (The Chemicals Control Act; Korean Ministry of Government Legislation, 2010), cosmetics (The Cosmetics Act; Korean Ministry of Government Legislation, 2013), and prohibited in food storage products (The Food Sanitation Act; Korean Ministry of Government Legislation, 2011). Urinary levels of DEHP and DBP metabolites, and BPA in KoNEHS 2012–2014 were generally lower than those of KoNEHS 2009–2011 (Table 4), perhaps corresponding to such restrictions.

Socio-demographic characteristics such as gender, age, monthly household income, and education levels were associated with the urinary phthalate metabolite and BPA concentrations. Similar to the results of the general adult populations of the US and Canada (CDC, 2018; Health Canada, 2013; Lakind and Naiman, 2015), urinary phthalate metabolite and BPA levels were higher in females than males. One possible explanation for this gender difference can be found from the different use of personal care products and dietary consumption patterns by gender (CDC, 2018; Varshavsky et al., 2016). The age-dependent increases in creatinine-adjusted phthalate metabolites among the Korean population were similar to those observed in the general US population, where the median urinary concentrations of MEOHP, MBzP, and MnBP in the US adult males increased with age in NHANES 2011–2012 (Meeker and Ferguson, 2014). The association between age group and urinary BPA levels observed in the present study were also very similar to that reported in the US population. In NHANES 2003–2012, unadjusted urinary BPA level was negatively associated with age, but the direction and significance of the relationship disappeared after creatinine adjustment (Lakind and Naiman, 2015). The different patterns of age dependence between urinary phthalate metabolites and BPA suggest that these compounds may have different sources of exposure among the general population. Another possible explanation was differences of physiological metabolism with age, e.g., cytochrome P450 system including UDP-glucuronyl transferase and clearance of creatinine (Barr et al., 2005; Cotreau et al., 2005; Yaghjyan et al., 2016).

By creatinine-adjustment, the direction of associations between gender and urinary chemical concentrations was changed, while other predictors did not show such gender-dependent difference. Creatinine-adjustment has been one of most frequently used and widely accepted methods of correction for urinary dilution (O'Brien et al., 2017). As males excrete more creatinine, a metabolite of creatine, than females, creatinine-adjusted chemical concentration often becomes greater among females when the unadjusted concentrations of the urinary chemical are similar. For this reason, in the US population (NHANES, 2011–2012), male participants showed greater unadjusted urinary BPA level, but lesser creatinine-adjusted BPA level compared to female (Lakind and Naiman, 2015). For this general US population, the urinary creatinine concentrations of males were 1.47 times greater than those of females, while the urinary BPA concentrations of males were only 1.1

Table 3
Adjusted proportional changes in creatinine-adjusted (μg/g-creatinine) and measured (μg/L) phthalate metabolites and bisphenol A by socio-demographic characteristics of the adult Korean population.

	ΣDEHP[a]		MBzP		MnBP		BPA	
Dependent Variable Conc.	Creatinine Adjusted Conc.	Measured Conc.	Creatinine. Adjusted Conc.	Measured Conc.	Creatinine. Adjusted Conc.	Measured Conc.	Creatinine. Adjusted Conc.	Measured Conc.
Gender								
Males	ref.							
Females	1.38 (1.32, 1.44)**	0.91 (0.86, 0.97)**	1.18 (1.10, 1.27)**	0.78 (0.71, 0.85)**	1.32 (1.25, 1.38)**	0.86 (0.81, 0.92)**	1.31 (1.21, 1.42)**	0.88 (0.80, 0.96)**
Age group								
19-29	ref.							
30-39	1.04 (0.96, 1.13)	0.98 (0.87, 1.10)	1.02 (0.89, 1.17)	0.95 (0.82, 1.11)	1.07 (0.98, 1.17)	1.00 (0.89, 1.14)	1.05 (0.91, 1.20)	0.98 (0.82, 1.18)
40-49	1.17 (1.08, 1.28)**	1.03 (0.91, 1.17)	1.11 (0.95, 1.29)	0.95 (0.81, 1.12)	1.26 (1.16, 1.38)**	1.10 (0.96, 1.26)	1.09 (0.95, 1.26)	0.96 (0.81, 1.15)
50-59	1.25 (1.14, 1.38)**	1.01 (0.88, 1.15)	1.08 (0.94, 1.23)	0.87 (0.74, 1.02)*	1.26 (1.14, 1.38)**	1.00 (0.87, 1.15)	1.15 (0.99, 1.33)*	0.93 (0.78, 1.11)
60-69	1.29 (1.18, 1.43)**	0.99 (0.86, 1.14)	1.12 (0.96, 1.31)	0.86 (0.72, 1.03)	1.44 (1.29, 1.62)**	1.10 (0.93, 1.30)	1.05 (0.90, 1.22)	0.80 (0.66, 0.97)**
≥70	1.43 (1.29, 1.59)**	1.04 (0.89, 1.20)	1.22 (1.01, 1.46)**	0.89 (0.73, 1.08)	1.42 (1.26, 1.62)**	1.02 (0.86, 1.21)	0.92 (0.78, 1.08)	0.67 (0.55, 0.82)**
Residential area								
Urban	ref.							
Rural/Coastal	1.03 (0.94, 1.14)	1.01 (0.91, 1.13)	0.96 (0.82, 1.12)	0.93 (0.78, 1.12)	0.97 (0.82, 1.14)	0.95 (0.77, 1.16)	0.81 (0.70, 0.93)**	0.78 (0.68, 0.90)**
Monthly household income (US$)								
< 1,300	ref.							
1,300–2,600	0.93 (0.86, 1.00)*	0.97 (0.88, 1.07)	0.85 (0.73, 0.97)**	0.89 (0.76, 1.03)	0.90 (0.85,0.99)**	0.94 (0.83, 1.05)	1.00 (0.90, 1.12)	1.05 (0.92, 1.19)
2,600–3,600	0.93 (0.85, 1.00)*	0.90 (0.81, 1.00)**	0.87 (0.74, 1.01)*	0.85 (0.71, 1.01)*	0.90 (0.81, 1.00)**	0.87 (0.76, 0.99)**	1.04 (0.91, 1.18)	1.01 (0.87, 1.16)
≥3,600	0.89 (0.83, 0.97)**	0.90 (0.81, 0.99)**	0.76 (0.65, 0.88)**	0.78 (0.67, 0.91)**	0.87 (0.78, 0.98)**	0.88 (0.76, 1.01)*	1.07 (0.95, 1.21)	1.08 (0.93, 1.24)
Education levels								
< Middle	ref.							
Mid-High	0.93 (0.88, 0.98)**	0.94 (0.86, 1.03)	0.92 (0.83, 1.01)*	0.93 (0.82, 1.05)	0.93 (0.86, 1.01)*	0.99 (0.88, 1.10)	1.10 (0.98, 1.23)	1.13 (0.98, 1.29)*
> High	0.85 (0.79, 0.91)**	0.90 (0.81, 1.00)**	0.83 (0.73, 0.94)**	0.87 (0.75, 1.01)*	0.94 (0.85, 1.05)	1.08 (0.94, 1.23)	1.06 (0.93, 1.20)	1.13 (0.97, 1.31)
House type								
Detached	ref.							
Row house	0.97 (0.91, 1.04)	0.98 (0.88, 1.09)	0.93 (0.82, 1.05)	0.94 (0.80, 1.10)	0.97 (0.85, 1.11)	0.94 (0.84, 1.05)	1.08 (0.94, 1.25)	1.08 (0.90, 1.30)
Apartment	0.94 (0.89, 1.00)**	0.91 (0.83, 0.99)**	0.89 (0.78, 1.01)*	0.86 (0.74, 1.00)**	0.97 (0.87, 1.08)	0.98 (0.85, 1.13)	0.93 (0.82, 1.04)	0.89 (0.78, 1.02)
Personal Care Products								
Perfume								
Never	ref.							
More than once a month	0.94 (0.90, 0.98)**	0.97 (0.90, 1.04)	0.94 (0.86, 1.02)	0.97 (0.88, 1.08)	0.98 (0.93, 1.02)	1.00 (0.92, 1.09)	0.95 (0.87, 1.03)	0.98 (0.89, 1.08)
Hair spray								
Never	ref.							
More than once a month	1.01 (0.97, 1.05)	1.01 (0.95, 1.07)	0.98 (0.92, 1.04)	0.97 (0.90, 1.05)	0.99 (0.95, 1.03)	0.94 (0.87, 1.02)	1.00 (0.93, 1.08)	1.00 (0.91, 1.10)
Body cleanser								
Never	ref.							
More than once a month	0.96 (0.91, 1.00)*	0.98 (0.91, 1.05)	1.03 (0.95, 1.12)	1.07 (0.97, 1.18)	1.03 (0.98, 1.09)	1.04 (0.95, 1.14)	1.10 (0.99, 1.21)*	1.12 (1.00, 1.26)**
Nail polish								
Never	ref.							
More than once a month	1.07 (1.01, 1.14)**	1.11 (1.02, 1.21)**	1.13 (1.03, 1.25)**	1.18 (1.05, 1.33)**	1.08 (1.02, 1.14)**	1.18 (1.07, 1.29)**	1.12 (1.00, 1.26)**	1.15 (1.01, 1.30)**

*p < 0.10, **p < 0.05.
[a] Molar concentration (nmol/g-creatinine, nmol/L).

Table 4
Comparison of geometric mean (95% percentile concentrations) of urinary phthalate metabolites and BPA with those reported from other national biomonitoring programs. (ug/L).

	DEHP			BBzP	DBP	BPA
	MEHHP	MEOHP	MECPP	MBzP	MnBP	
Korea [a]						
2009–2011	20.6 (77.3)	15.5 (57.8)	–	–	44.7 (208)	1.76 (5.87)
2012–2014	17.5 (71.5)	12.1 (47.9)	20.1 (70.2)	2.81 (19.3)	23.6 (106)	1.09 (8.18)
USA [b]	12.4 (104)	7.59 (54.9)	19.4 (126)	5.61 (39.6)	13.5 (68.9)	1.79 (9.60)
Canada [c]	13 (59)	7.4 (34)	–	7.5 (57)	20 (87)	1.2 (6.7)

[a] KoNEHS, aged 19 years and over (Park et al., 2016; Choi et al., 2017).
[b] NHANES. 2009–2010, aged 20 years and over (CDC, 2018).
[c] CHMS, 2009–2011, aged between 3 and 79 years of age (Health Canada, 2013).

times greater than those of females. Similar to the US general population, the urinary creatinine levels of Korean males were 1.5 times greater than those of females in the present Korean population.

Among the Korean population, residential area was identified as a determinant of urinary concentrations of BPA, but not phthalate metabolites. Type of residence location (i.e., urban vs. rural) has long been considered as an important factor affecting exposure to these chemicals among humans (Blount et al., 2000; Calafat et al., 2005; Colacino et al., 2011). This can be explained by different dietary patterns and consumer product use by region (Braun et al., 2014; Geens et al., 2012; Varshavsky et al., 2016). However, the direction of the association for residential area has not always been consistent among populations. For instance, rural females showed higher MBzP levels than urban females in a US reference population, while no association was observed between other urinary phthalate metabolites and residential area (Blount et al., 2000). Meanwhile, in more recent studies, urban residents showed higher levels of DEHP, DBP, and MBzP than rural residents in Egypt and India (Colacino et al., 2011; Pant et al., 2008). However, for BPA, the association with residential area (i.e., higher BPA levels in urban residents of Korea) was the same as that reported in the US population (NHANES III), where urinary BPA levels were significantly higher among the urban population (Calafat et al., 2005).

Unlike the general US population, in the Korean population, socioeconomic characteristics such as monthly household income and highest education attained were negatively associated with urinary phthalate metabolite levels, but not with BPA. Among women of childbearing age in NHANES 2001–2008, higher economic status and education level were related to lower BBzP and DBP exposure (Kobrosly et al., 2012). However, in the general US population in NHANES 2005–2014, higher income and education level were associated with higher cumulative phthalates levels (Varshavsky et al., 2018). Regarding BPA, inverse associations were observed in both NHANES 2003–2004 (Calafat et al., 2008) and NHANES 2003–2012 (Lakind and Naiman, 2015). People with higher economic and education levels have been suggested to be more concerned with dietary behavior, including healthy diet and food-related health problems (Cullen et al., 2007; Deshmukh-Taskar et al., 2007; Robinson et al., 2004; Shea, 2003; Yoo et al., 2006), which may influence the extent of contact with food containers that may contain PVC or personal care products that may contain phthalates or BPA. The effects of such precautionary behaviors appear to be more evident for phthalates than BPA among Koreans, possibly due to the more diverse sources of BPA exposure compared to phthalates among Koreans.

Among the personal care products considered, the use of nail polish was positively associated with urinary phthalate metabolite or BPA concentrations. In addition, the use of body cleanser was positively associated with urinary BPA levels. This observation confirmed the importance of these cosmetic or consumer products, and possibly other related products that may be applied together with these products, in terms of BPA and phthalate exposure. While food processing and packaging are considered to be major sources of exposure to phthalates and BPA among the general population (Fromme et al., 2007; Rudel et al., 2011), cosmetics, perfumes, and personal care products have also been suggested as possible sources of exposure (Braun et al., 2014; Harley et al., 2016; Meeker et al., 2013). Interestingly, use of perfume and body cleanser was negatively associated with creatinine adjusted ΣDEHP metabolites. The reason for this observation is unclear, but it could be due to other factors that are associated with the use of these personal care products. Ingestion has been suggested as one of major exposure pathways for DEHP, while dermal contact and inhalation are those for low-molecular-weight phthalates such as DEP and DBP (Erythropel et al., 2014; Heudorf et al., 2007). Indeed, DEP has been used in perfume, hair product, and deodorant, and DBP in nail polish, however, DEHP has been detected at extremely low concentrations in perfume and nail polish, compared to low-molecular-weight phthalates (Koo and Lee, 2004).

As a cross-sectional study, our study has the intrinsic limitation that it cannot reveal the causal relationship between chemical exposure and socio-demographic or behavioral characteristics. In addition, this study did not consider dietary characteristics and the use of phthalate-containing products, e.g., PVC flooring materials and food packaging, that might affect phthalate and BPA exposure among the general population. Fasting time before urine collection, which is an important factor in interpreting the measurements of urinary phthalate metabolites and BPA (Alyward et al., 2011), was not considered in the spot urine sampling design. However, this study has a unique advantage in that the results are based on a nationally representative population with the highest ever sample size, enabling the generalization of the findings to the general Korean population. Thus, the results of this study can be applied in follow-up studies to identify major sources and pathways of this important group of compounds.

5. Conclusion

Among the adult Korean population, urinary concentrations of biomarkers of exposure to DEHP and DBP were generally higher than those reported in national biomonitoring programs in the US and Canada, while those of BBzP and BPA were similar or lower. Several socio-demographic and behavioral characteristics, i.e., gender, age, household income, education level, and nail polish use, were associated with phthalate or BPA exposure. Similar to other nationally representative populations, females and older participants tended to show higher urinary concentrations of creatinine-adjusted phthalate metabolites or BPA. Unlike the general US population, higher income or education was related with lower urinary phthalate metabolites among the Korean population. However, higher education was positively related with urinary BPA levels among the Korean population. The observations of this study provide information useful to better identify major sources and pathways of exposure to these chemicals among general adult populations, and eventually help develop appropriate

exposure mitigation measures.

Conflicts of interest

The authors have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2019.02.003.

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