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Urinary Bisphenol A Concentrations and Their Implications for Human Exposure in Several Asian Countries

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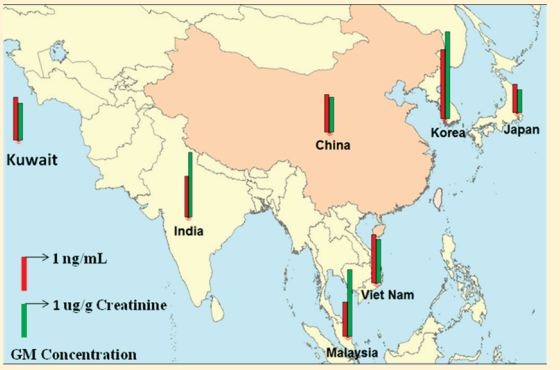
Supporting Information

ABSTRACT: Bisphenol A (BPA) is an industrial chemical used in the manufacture of polycarbonate plastics and epoxy resins. Due to the potential of this compound to disrupt normal endocrinal functions, concerns over human exposure to BPA have been raised. Although several studies have reported human exposure to BPA in Western nations, little is known about exposure in Asian countries. In this study, we determined total urinary BPA concentrations (free plus conjugated) in 296 urine samples (male/female: 153/143) collected from the general population in seven Asian countries, China, India, Japan, Korea, Kuwait, Malaysia, and Vietnam, using high-performance liquid chromatography (HPLC) tandem mass spectrometry (MS/MS). On the basis of urinary BPA concentrations, we estimated the total daily intake. The results indicated that BPA was detected in 94.3% of the samples analyzed, at concentrations ranging from <0.1 to 30.1 ng/mL. The geometric mean concentration of BPA for the entire sample set from seven countries was 1.20 ng/mL. The highest concentration of BPA was found in samples from Kuwait (median: 3.05 ng/mL, 2.45 μg/g creatinine), followed by Korea (2.17 ng/mL, 2.40 μg/g), India (1.71 ng/mL, 2.09 μg/g), Vietnam (1.18 ng/mL, 1.15 μg/g), China (1.10 ng/mL, 1.38 μg/g), Malaysia (1.06 ng/mL, 2.31 μg/g), and Japan (0.95 ng/mL, 0.58 μg/g). Among the five age groups studied (≤19, 20−29, 30−39, 40−49, and ≥50 years), the highest median concentration of BPA was found in urine samples from the age group of ≤19 years. There was no significant difference in BPA concentrations between genders (male and female) or domicile of residence (rural and urban). The estimated median daily intakes of BPA for the populations in Kuwait, Korea, India, China, Vietnam, Malaysia, and Japan were 5.19, 3.69, 2.90, 2.13, 2.01, 1.80, and 1.61 μg/day, respectively. The estimated daily intake of BPA in the seven Asian countries was significantly lower than the tolerable daily intake recommended by the U.S. Environmental Protection Agency. This is the first study to document the occurrence of and human exposure to BPA in several Asian countries.



INTRODUCTION

Bisphenol A (BPA) is primarily used in the production of polycarbonate plastics and epoxy resins, which are widely used in applications such as baby feeding bottles, toys, epoxy food-can linings, medical equipment and tubing, and consumer electronics. BPA is one of the highest production volume chemicals, with three million tons produced each year worldwide.[1] Exposure of humans to BPA occurs predominantly through the diet.[2,46,47] BPA levels have been measured in human fluids and tissues (plasma, serum, placenta, breast milk, semen, and urine) in some industrialized countries around the world.[3−9] The National Health and Nutrition Examination Survey (NHANES) of the United States, conducted in 2003−2004, showed that 93% of 2517 urinary specimens contained detectable levels of BPA.[8]

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BPA can act as a weak estrogen and has been implicated in reproductive and developmental anomalies in laboratory animal studies.[10,11] In addition, BPA has been reported to elicit thyroid hormone disruption, altered pancreatic β-cell function, and obesity-promoting effects.[12−14] A few epidemiological studies have found an association between BPA exposures in humans and ovarian dysfunction, endometrial hyperplasia, and recurrent miscarriage.[15−18,48]

Due to the potential for human exposure and resulting adverse health effects, information regarding body burdens and sources of BPA is needed as a means to develop strategies to mitigate exposures. Little is known on human exposure to and body burdens of BPA in Asian countries.

In the present study, we measured total urinary BPA concentrations (free plus conjugated) in 296 urine samples collected from the general population in seven Asian countries, China, India, Japan, Korea, Kuwait, Malaysia, and Vietnam, with the aim of establishing baseline values of concentrations, geographic patterns and profiles, and daily intakes of BPA.

MATERIALS AND METHODS

Sample Collection. Urine samples (2−10 mL) were collected from seven Asian countries, China (number of samples: $n = 116$), India (21), Japan (36), Korea (32), Kuwait (32), Malaysia (29), and Vietnam (30), from May to July 2010. Urine samples from Korea were collected during 2006−2007. The samples from China, India, Japan, Korea, Kuwait, Malaysia, and Vietnam originated from the cities of Guangzhou/Shanghai/Harbin, Mettupalayam, Ehime/Kumamoto, Seoul/Busan/Yeosu, Al-Asma/Al-Jahra governorates, Kuala Lumpur, and Hanoi, respectively. Spot urine samples were collected in 15 mL polypropylene tubes from healthy volunteers. The age of the donors from the seven countries ranged from 2 to 84 years. All of the collected urine specimens were kept at −20 °C until analysis. Institutional Review Board approvals were obtained from the New York State Department of Health (NYSDOH) for the analysis of human specimens.

Chemicals and Reagents. BPA (purity ≥99%), $^{13}C_{12}$-labeled BPA (purity ≥98%), β-glucuronidase from *Helix pomatia* (145700 units/mL β-glucuronidase; 887 units/mL sulfatase), creatinine (purity ≥99%), acetic acid, and ammonium acetate were purchased from Sigma-Aldrich (St. Louis, MO). Creatinine-d_3 (purity ≥99%) was purchased from CDN Isotopes (Pointe-Claire, Quebec, Canada). The organic solvents used in this study were analytical grade (Mallinckrodt Baker; Phillipsburg, NJ). Water for chromatographic purposes was purified by a Milli-Q system (Millipore; Billerica, MA).

Analysis of BPA. The concentrations of BPA in urine samples were analyzed by enzymatic deconjugation, followed by solid phase extraction (SPE), and high-performance liquid chromatography (HPLC)-isotope dilution-tandem mass spectrometry (MS/MS), as described earlier.[19,20] Briefly, an aliquot (0.5 mL) of urine was spiked with 50 μL of $^{13}C_{12}$-labeled BPA (100 ng/mL); after 1 h of equilibration, the sample was buffered with 300 μL of 1.0 M ammonium acetate containing 22 units of β-glucuronidase (pH 5.0; 7.7 g of ammonium acetate dissolved in 100 mL of Milli-Q water and 6 mL of acetic acid with 50 μL of β-glucuronidase), followed by incubation at 37 °C for 6 h. After digestion, 0.5 mL of 1.0 M formic acid (3.93 mL of formic acid dissolved in 100 mL of Milli-Q water) was added to stop the enzyme activity, and then 0.7 mL of Milli-Q water was added. A RapidTrace SPE Workstation (Caliper Life Sciences, Hopkinton, MA) was used for extraction. A C18 SPE cartridge (200 mg/3 cm^3; Waters, Milford, MA) was prepared by conditioning with 2 mL of methanol, followed by 2 mL of Milli-Q water at a flow rate of 1 mL/min. Then, the urine sample was loaded onto the cartridge at a flow rate of 0.5 mL/min, and the cartridge was rinsed with 2 mL of 10% methanol in Milli-Q water (v:v) at a flow rate of 0.5 mL/min and then dried under a gentle stream of N_2 for 20 min. The analytes were eluted with 5 mL of 15% methanol in ethyl acetate at a flow rate of 0.5 mL/min. The eluate was concentrated by a gentle stream of N_2 to 1 mL for analysis with LC-MS/MS. Creatinine was analyzed with LC-MS/MS after diluting urine samples (5 μL) to approximately 320-fold and adding 800 ng of creatinine-d_3.

Instrumental Analysis. An Applied Biosystems API 2000 electrospray triple quadrupole mass spectrometer (ESI-MS/MS; Applied Biosystems, Foster City, CA), equipped with an Agilent 1100 Series HPLC system (Agilent Technologies Inc., Santa Clara, CA), consisting of a binary pump and an automatic sampler, was used for the measurement of BPA and creatinine. Ten microliters of samples were injected onto a Thermo Betasil C18 (100 mm length ×2.1 mm internal diameter, 5 μm particle diameter) chromatographic column serially connected with a guard column (20 × 2.1 mm, 5 μm; Thermo Electron Co., Bellefonte, PA), at a flow rate of 300 μL/min. BPA was separated by gradient elution (methanol as solvent A and Milli-Q water as solvent B), starting with 15% methanol at 0 min, held for 2 min, and increased to 99% A from 2 to 5 min, held for 11 min, and decreased to 25% A at 15 to 17 min, held for 3 min, with a total run time of 20 min. The negative ion multiple reaction monitoring (MRM) mode was used, and the MRM transitions monitored were 227 > 212 for BPA and 239 > 224 for $^{13}C_{12}$-labeled BPA. Nitrogen was used as both a curtain and collision gas. The collision energy (CE) was −22 eV, the interface temperature (TEM) was 400 °C, and the ionspray voltage (IS) was −4500 V. For the analysis of creatinine, the isocratic mobile phase, containing 50% methanol in Milli-Q water and 0.1% formic acid, was used; the total run time was 5 min. The positive ion MRM transitions monitored were 114 > 44 for creatinine and 117 > 47 for creatinine-d_3. The CE was held at 25 eV, TEM was 400 °C, and the IS was 4500 V.

Quality Assurance/Quality Control. For each batch of 30 samples analyzed, two method blanks, a spiked blank, a pair of matrix spiked samples, and duplicate samples were processed. BPA was not detected in method blanks or sample containers (i.e., polypropylene tubes). The average recoveries of BPA from spiked matrix and spiked blanks were 103 ± 15% and 96 ± 11%, respectively. The relative standard deviation (RSD) of replicate analysis was <12.6%. The regression coefficient of calibration standards, injected at concentrations ranging from 0.05 ng/mL to 20 ng/mL, was >0.999. A calibration curve was prepared every day at the beginning and at the end of every batch of 30 samples analyzed. As a check for instrumental drift in response factors, a midpoint calibration standard was injected after every 10 samples. To check for carry-over of BPA from sample to sample, a pure solvent (methanol) was injected after every 10 samples. The limit of quantitation (LOQ) of BPA was 0.1 ng/mL, which was determined based on the lowest point of the calibration standard and a nominal sample volume of 0.5 mL, used in this study. Quantification was by isotope-dilution. Prior to the analysis of the samples, the recovery and reproducibility of the method was verified by spiking known concentrations of BPA into Milli-Q

Table 1. Concentrations of Urinary BPA [ng/mL (μg/g Creatinine)] in Seven Asian Countries[a]

variable	concentration (ng/mL)			concentration creatinine-adjusted (μg/g)			number of samples (M/F)	average age (years)
	GM (CI 95%)	AM	range	GM (CI 95%)	AM	range		
China	1.10 (0.87−1.63)	3.86	<LOQ-29.4	1.03 (0.85−1.75)	3.86	<LOQ-58.1	116 (61/55)	31 ± 16
Vietnam	1.42 (0.91−2.20)	3.32	0.16−30.1	1.27 (0.79−2.05)	2.79	0.10−22.0	30 (14/16)	49 ± 18
Malaysia	1.00 (0.66−1.59)	1.89	<LOQ-13.4	1.93 (1.21−4.09)	4.47	<LOQ-30.0	29 (10/19)	30 ± 9
India	1.59 (1.14−2.21)	1.97	0.25−5.60	2.51 (1.58−3.99)	4.66	0.31−39.2	21 (7/14)	45 ± 16
Kuwait	1.24 (0.71−2.82)	4.10	<LOQ-27.0	1.09 (0.62−2.48)	3.04	<LOQ-13.5	32 (16/16)	23 ± 14
Japan	0.84 (0.55−1.28)	1.98	0.10−23.2	0.67 (0.43−1.03)	1.67	0.05−16.0	36 (28/8)	32 ± 10
Korea	2.00 (1.31−3.17)	3.47	<LOQ-10.6	2.53 (1.66−4.02)	4.69	<LOQ-29.3	32 (17/15)	37 ± 11
all	1.20 (1.06−1.50)	3.23	<LOQ-30.1	1.25 (1.14−1.68)	3.60	<LOQ-58.1	296 (153/143)	32 ± 17
male	1.27 (1.05−1.70)	3.44	<LOQ-29.4	1.26 (1.02−1.71)	3.45	<LOQ-32.4	153	32 ± 16
female	1.13 (0.93−1.51)	3.01	<LOQ-30.1	1.25 (1.07−1.94)	3.76	<LOQ-58.1	143	33 ± 18
China								
age ≤19	1.65 (0.67−4.08)	5.31	<LOQ-20.6	2.56 (1.11−9.41)	7.67	<LOQ-32.4	17 (10/7)	9 ± 5
age 20−29	1.09 (0.67−1.78)	3.77	<LOQ-29.4	1.00 (0.58−1.74)	3.92	<LOQ-58.1	51 (22/29)	25 ± 3
age 30−39	1.45 (0.60−3.56)	5.07	<LOQ-29.0	0.97 (0.44−3.53)	2.89	<LOQ-15.7	21 (8/13)	34 ± 3
age 40−49	1.09 (0.42−2.87)	2.76	<LOQ-12.7	0.68 (0.24−1.90)	2.67	<LOQ-10.4	14 (5/9)	45 ± 3
age ≥50	0.87 (0.44−1.72)	1.54	0.15−5.90	1.30 (0.62−2.76)	1.77	0.29−12.7	13 (9/4)	64 ± 10
urban	1.17 (0.60−2.27)	3.98	<LOQ-24.8	1.22 (0.64−3.11)	3.65	<LOQ-15.7	32 (16/16)	38 ± 23
rural	1.35 (0.78−2.35)	3.54	<LOQ-29.0	0.93 (0.57−2.13)	2.34	<LOQ-16.9	32 (16/16)	30 ± 13
male	1.40 (0.90−2.19)	4.49	<LOQ-29.4	1.36 (0.86−2.14)	3.89	<LOQ-32.4	61	31 ± 17
female	1.00 (0.57−1.36)	3.16	<LOQ-29.0	0.90 (0.52−1.54)	3.83	<LOQ-58.1	55	31 ± 14

[a] LOQ: 0.1 ng/mL; GM: geometric mean; AM: arithmetic mean; CI: confidence interval; M: male; F: female.

water and selected urine samples. To help reduce variability in BPA concentrations related to fluctuations in urine output, the results are also presented on the basis of creatinine levels. Creatinine adjustment can improve the comparability of chemical measurements across individuals.

Statistical Analysis. Arithmetic mean (AM), geometric mean (GM), and concentration ranges (both unadjusted and creatinine-adjusted) were used to describe the results. Concentrations below the LOQ were substituted with a value equal to the LOQ divided by 2 or by the square root of 2 for the calculation of AM and GM, respectively. Results were examined based on creatinine-adjusted and creatinine-unadjusted BPA concentrations. Samples were categorized into 5 age groups (≤19, 20−29, 30−39, 40−49, and ≥50) to enable interpretation on age-related changes in BPA levels. Data analysis was conducted using SPSS (Version 16.0). Comparisons of urinary BPA concentrations among countries and age groups were conducted using ANOVA (log transformed, Duncan's multiple range test); comparisons between urinary BPA and sex or residence were examined using nonparametric statistical tests (Kruskal−Wallis H and Mann−Whitney U). Statistical significance was set at $p < 0.05$.

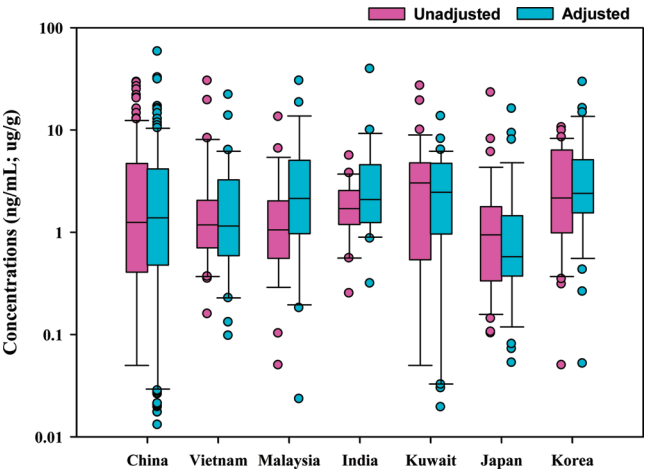

Figure 1. Concentrations (ng/mL and creatinine-adjusted in μg/g) of urinary bisphenol A in seven Asian countries. The lower and upper boundaries of each box represent 25th and 75th percentiles, and the line within the box is the median concentration. The whiskers represent 10th and 90th percentiles, and the dots are outlier samples.

RESULTS AND DISCUSSION

Concentrations. Of the 296 urine specimens analyzed, 153 (51.7%) were from males and 143 (48.3%) were from females. The age of subjects ranged from 2 to 84 years, with an average age of 32 ± 17 years (Table 1, Table S3). BPA was detected in 94.3% of the samples at concentrations ranging from <0.1 to 30.1 ng/mL. The AM and GM concentrations were 3.23 and 1.2 ng/mL, respectively (95% confidence interval of the GM was 1.06−1.50 ng/mL). The creatinine-adjusted GM urinary concentration of BPA was 1.25 μg/g, with a 95% confidence interval of 1.14−1.68 μg/g. Our results indicate widespread human exposure to BPA in Asian countries. The urinary concentrations of BPA varied significantly among the seven Asian countries ($p < 0.05$).

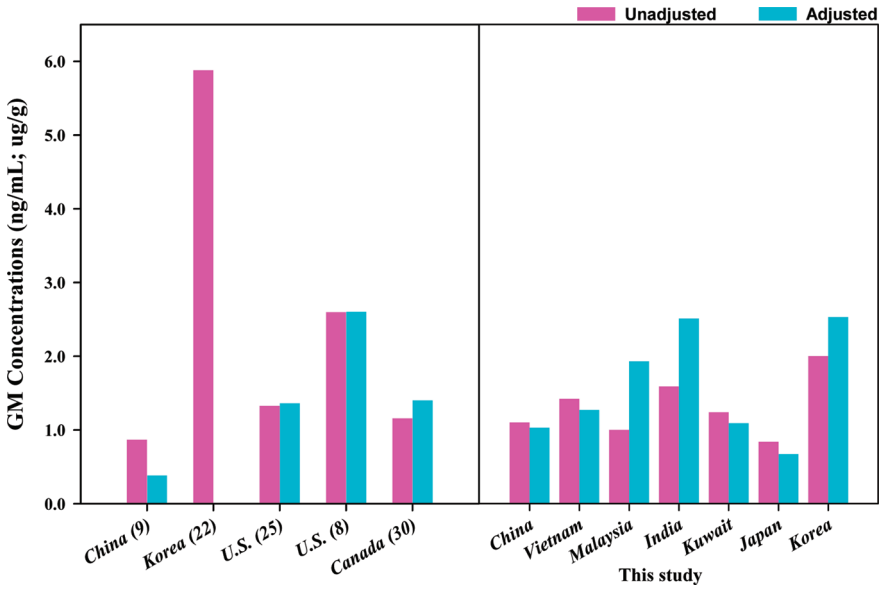

Figure 2. Reported GM concentrations (ng/mL and creatinine-adjusted in μg/g) of BPA in human urine samples from several countries.

When the data were analyzed for individual countries or the entire data set of seven countries, no significant difference existed in urinary BPA concentrations between male and female donors. The GM concentration of BPA in males was 1.27 ng/mL (1.26 μg/g creatinine) and that of females was 1.13 ng/mL (1.25 μg/g creatinine). The highest concentration of urinary BPA was found in samples from Kuwait (median: 3.05 ng/mL, 2.45 μg/g creatinine, Figure 1), followed, in decreasing order, by Korea (2.17 ng/mL, 2.40 μg/g), India (1.71 ng/mL, 2.09 μg/g), Vietnam (1.18 ng/mL, 1.15 μg/g), China (1.10 ng/mL, 1.38 μg/g), Malaysia (1.06 ng/mL, 2.31 μg/g), and Japan (0.95 ng/mL, 0.58 μg/g). However, when data were presented as AM, no significant difference in urinary BPA levels was found among the countries. Because data are not distributed normally, median values are more representative of the population than AM values. Median concentrations of BPA in urine samples from Kuwait were 2−3 times higher than the concentrations measured in samples from Japan ($p < 0.05$).

This is the first study to report urinary concentrations of BPA in several Asian countries, especially for Kuwait, Malaysia, India, and Vietnam. Reported concentrations of BPA in urine samples from several countries have been compiled (Table S1, Figure 2). An earlier study from China[9] showed a higher mean concentration (10.5 ng/mL, 24.9 μg/g creatinine) of urinary BPA than that found in our study. The earlier study from China used HPLC with fluorescence detection (LOQ of 0.31 ng/mL), which is not as sensitive and selective as the MS/MS method used in our study. Another study from China showed highly variable concentrations (<2.7- 395 ng/mL) of urinary BPA.[21] The variability in BPA concentrations between the studies from China can be attributed to high LOQ and small sample size ($n = 20$) analyzed in earlier studies.[9,21] Urinary concentrations of BPA reported for Japan in earlier studies were similar to those found in the present study.[22−24] The median concentrations of urinary BPA reported for Austrian and German adults were 1.1 and 1.2 ng/mL, respectively,[25−30] which were similar to those found in urine samples from the Asian countries. The urinary BPA concentrations in the general U.S. population (for the samples collected from 1988 to 1994) were reported by the Centers for Disease

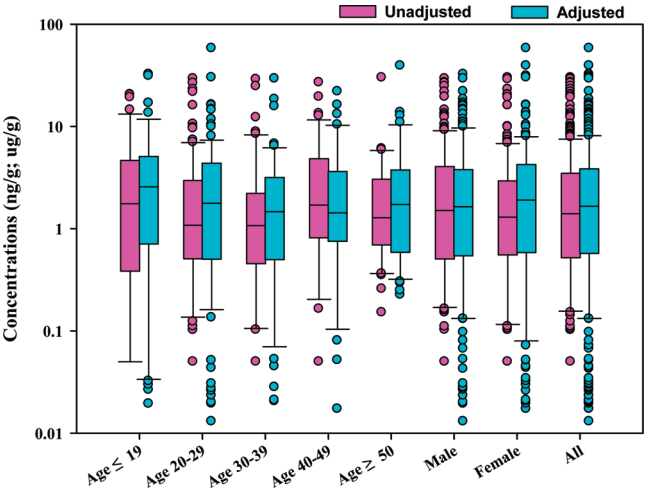

Figure 3. Concentrations (ng/mL and creatinine-adjusted in μg/g) of urinary bisphenol A in various age/sex groups from seven Asian countries. The lower and upper boundaries of each box represent 25th and 75th percentiles, and the line within the box is the median concentration. The whiskers represent 10th and 90th percentiles, and the dots are outlier samples.

Control and Prevention (CDC);[25] BPA was detected in 95% of spot urine samples collected from 394 Americans, with a GM concentration of 1.33 ng/mL (1.36 μg/g creatinine). Similar GM concentrations were found for samples from individual Asian countries in our study (range: 0.84−2.00 ng/mL). Another U.S. study examined spot urine samples from 2517 Americans (>6 years of age) for the 2003−2004 NHANES[8] and reported a detection rate of 92.6%, with a concentration range of 0.4 to 149 ng/mL (GM: 2.6 ng/mL, 2.6 μg/g creatinine). These values were approximately 2- to 3-fold higher than those found for China, Vietnam, Malaysia, Kuwait, India, and Japan but similar to those found for Korea.

The differences in concentrations of BPA between male and female subjects were not statistically different; this was true when

Table 2. Estimated Daily Exposure to BPA in Seven Asian Countries (μg/day)

	China	Vietnam	Malaysia	India	Kuwait	Japan	Korea
median	2.13	2.01	1.80	2.90	5.19	1.61	3.69
mean	6.56	5.65	3.22	3.35	6.99	3.36	5.89
range	0.08−50.0	0.27−51.2	0.08−22.9	0.43−9.52	0.08−45.9	0.17−39.4	0.08−18.0

	children and adolescents (age <20, n = 47)	adults (age ≥20, n = 259)	males	females	all
median	1.16	2.21	2.58	2.22	2.39
mean	2.58	5.28	5.85	5.12	5.50
range	0.03−13.6	0.08−51.2	0.08−50.0	0.08−51.2	0.08−51.2

the entire data set for seven countries was analyzed collectively or when data for individual countries were analyzed separately. Because a large number of samples was available from China, we performed detailed analysis of BPA concentrations for that country. The GM concentrations of urinary BPA in Chinese males and females were 1.40 and 1.00 ng/mL (1.36 and 0.90 μg/g creatinine), respectively (Table 1), and the differences were not statistically significant (p = 0.52). Several studies have reported the lack of significant difference in urinary BPA levels between males and females.[22,25,31]

Age-Related Differences in BPA Concentrations. We categorized the samples into five groups, depending on the age of donors, as ≤19, 20−29, 30−39, 40−49, and ≥50 years. This categorization was performed individually for Chinese donors and for the entire sample set from the seven Asian countries. Among the five age groups selected from China, the highest concentrations of urinary BPA were found in the age group of ≤19 years (Table 1), with GM concentration of 1.65 ng/mL (2.56 μg/g creatinine). The creatinine-adjusted GM concentrations of BPA in age groups 20−29, 30−39, 40−49, and ≥50 years were 1.00, 0.97, 0.68, and 1.30 μg/g, respectively. A similar trend was found for the entire sample set from the seven Asian countries (Table S2, Figure 3).

Previous studies have reported that urinary BPA concentrations in children were higher than those in adults.[8,32] The 2003−2004 NHANES of the U.S. reported that creatinine-adjusted GM concentrations of BPA in children's urine were approximately 2-fold higher (4.3 μg/g) than in adults (2.4 μg/g).[8] Another study from the U.S.[32] in 2005 reported that the median concentration of urinary BPA was lower in adults (0.47 ng/mL) than in children at 9 years (2.4 ng/mL). Higher urinary concentrations of BPA in children than in adults have been reported for other nonpersistent chemicals, such as phthalate metabolites and organophosphate pesticides.[33] Elevated concentrations of urinary BPA in children may be explained by high food consumption, product usage, and air inhalation rates in relation to body weight. The differences also could be related to absorption, distribution, metabolism, or excretion of BPA. Our findings highlight the need for additional research on the sources and pathways of exposure to BPA, especially in children, and the need for epidemiologic studies to target health outcomes related to BPA exposures.

BPA Concentrations in Urban and Rural Residents of Harbin, China. Concentrations of BPA in urine samples collected from urban (n = 32) and rural (n = 32) residents in and around Harbin, China, were examined for the elucidation of differences in exposures. The urinary BPA concentrations in urban and rural residents were in the range of < LOQ-24.8 ng/mL (15.7 μg/g creatinine, Table 1) and < LOQ-29.0 ng/mL (16.9 μg/g creatinine), respectively. The GM concentrations of urinary BPA were 1.17 (1.22 μg/g creatinine) and 1.35 ng/mL (0.93 μg/g creatinine) for urban and rural residents, respectively. This result is similar to what was reported for urban and rural residents of the U.S.[25] No significant difference was found in urinary BPA concentrations between urban and rural residents (p = 0.21).

Human Exposure to BPA. In humans, orally administered BPA conjugates with glucuronic acid in the liver and is rapidly cleared from the bloodstream by elimination in urine within 24 h.[34,35] Thus, BPA levels in urine reflect exposures that occurred within 24 h of sampling.[35,36] The urinary BPA measures have been used in the estimation exposure doses.[37] The urinary BPA concentration (μg/L) was used in the estimation of amount excreted in 24 h based on the volume of urine output (L), that is, daily intake (DI, μg/day) = urinary BPA concentration (μg/L) × urine excretion rate (L/day). The daily urine excretion rates were reported to be 0.66 and 1.7 L for children and adults, respectively.[38,39] A similar approach has been used in the calculation of daily exposure doses of BPA in the U.S., on the basis of urinary BPA concentrations.[36,40,41]

The estimated daily exposure doses of BPA by the populations in seven Asian countries are shown in Table 2. The estimated median daily intakes of BPA were 5.19, 3.69, 2.90, 2.13, 2.01, 1.80, and 1.61 μg/day for the populations in Kuwait, Korea, India, China, Vietnam, Malaysia, and Japan, respectively. Previous studies have estimated daily intake of BPA from urinary concentrations. For instance, Arakawa et al.[36] reported the daily intake of BPA in 36 Japanese males to be <0.21−14 μg/day, with a median value of 1.2 μg/day. Ouichi and Watanabe[40] estimated the daily intake of BPA in 48 females to be 0.6 to 71.4 μg/day. For the calculation of daily intake values adjusted for body weight (bw), the estimated daily intake values were divided by a nominal value of 30 and 60 kg for children and adults, respectively. The estimated median daily intake values of BPA were 0.039 and 0.037 μg/kg bw/day, for children and adults, respectively. Median daily intake rates of BPA by adults and children in the U.S. were reported to be 0.033−0.056 μg/kg bw/day and 0.067−0.077 μg/kg bw/day, respectively.[41] The estimated daily intakes of BPA in Asian countries were similar to the values reported for the U.S.

The European Commission estimated the daily intake of BPA to be 1.6 μg/kg bw/day for infants, 1.2 μg/kg bw/day for children between 4 and 6 years, and 0.4 μg/kg bw/day for adults in the EU countries.[42] The UK Food Standards Agency reported that BPA intakes in adults were 0.36−0.38 μg/kg bw/day, and in infants were 0.83−0.87 μg/kg bw/day.[43] The daily intakes of BPA estimated from the ingestion of foods in Western countries were approximately 10-fold higher than the intake values calculated for

the Asian countries. Further studies are needed to assess the sources (e.g., diet) of human exposures to BPA in Asian countries. The European Food Safety Authority[44] and U.S. Environmental Protection Agency[45] recommended a value of 50 μg/kg bw/day as the tolerable daily intake and reference dose for BPA. The median daily intakes of BPA estimated from urinary concentrations in our study were 3 orders of magnitude lower than the reference dose of 50 μg/kg bw/day.

The number of samples analyzed for individual countries in this study is small, and therefore this study should be considered as a pilot study aimed at elucidating the occurrence, establishing baseline values, and determining exposure doses of BPA in Asian nations. We also acknowledge that considerable controversies surround the issue of exposure doses and threshold concentrations of BPA and our calculation of exposure doses from urinary measurements involve several assumptions.[49] Nevertheless, this study is the first to document the urinary BPA concentrations in several Asian countries and suggests the need for further studies with large sample size along with detailed demographic information.

■ ASSOCIATED CONTENT

Supporting Information. Three tables. This material is available free of charge via the Internet at http://pubs.acs.org.

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