



Association between Urinary Bisphenol A and Waist Circumference in Korean Adults

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Bisphenol A (BPA) is widely used in the production of polycarbonate plastics, epoxy resins, and food and beverage containers. In the present study, we aimed to investigate the relationship between urinary concentrations of BPA and waist circumference in Korean adults. A total of 1,030 Korean adults (mean age, 44.3 ± 14.6 years) were enrolled in the study on the integrated exposure to hazardous materials for safety control, conducted by the Ministry of Food and Drug Safety from 2010 to 2012. Abdominal obesity was defined as having a waist circumference of at least 90 cm and 85 cm for men and women, respectively. The participants were divided into 4 groups according to the urinary BPA concentration quartile. Waist circumference was significantly higher among subjects with a urinary BPA concentration in the highest quartile relative to those in the lowest quartile ($p = 0.0071$). Linear regression analysis revealed a significant positive association between urinary BPA concentrations and body mass index, body fat, after adjusting for potential confounders. Moreover, subjects with urinary BPA concentrations in the fourth quartile were more likely to be obese compared to those with urinary BPA concentrations in the first quartile (odds ratio, 1.938; 95% CI: 1.314~2.857; p for trend = 0.0106). These findings provide evidence for a positive association between urinary BPA concentration and waist circumference in Korean adults.

Key words: Bisphenol A, Waist circumference, Korean adults

INTRODUCTION

Bisphenol A (BPA) is a widely used chemical in the global production of polycarbonate plastics, epoxy resins, and food and beverage containers (1). Due to its broad applications, the general population usually has detectable BPA concentrations in blood, urine, and breast milk (2). BPA exposure can result in a variety of harmful effects, including behavioral and emotional changes, such as anxiety, depression, and hyperactive behaviors (3); male sexual dysfunction (4,5); decreased oocyte retrieval number in women undergoing in vitro fertilization (6); and increased inflammation and oxidative stress (7).

Previous studies have reported a significant association between urinary BPA concentration and obesity (8). In Chinese adults, after adjusting for potential confounders, the odds ratio (OR) for the association between the highest quartile of urinary BPA concentration and generalized obesity was 1.50 (95% confidence interval [CI]: 1.15~1.97) and 1.28 (95% CI: 1.03~1.60) for abdominal obesity relative to the first quartile (9). Similarly, another study found that the highest quartile of urinary BPA concentration was associated with obesity (body mass index [BMI] ≥ 30 kg/m²) relative to the lowest quartile (OR, 1.69; 95% CI: 1.30~2.20) (10).

In particular, waist circumference is known to be a strong indicator of obesity and is significantly associated with cardiovascular disease; meta-regression analysis of prospective studies has shown that waist circumference is significantly associated with the risk of cardiovascular events (11). In healthy men and women, waist circumference is significantly associated with future coronary heart disease, after adjusting for physical activity, smoking, diabetes, systolic blood pressure, low density lipoprotein and high density lipoprotein cholesterol, and inflammatory markers, all of which are well-established conventional risk factors for coronary heart disease (12). A prospective study reported a strong association between waist circumference and all-cause mortality, among

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middle-aged men and women (13). Moreover, waist circumference was found to be a stronger obesity-associated risk factor than BMI among the population participating in National Health and Nutrition Examination Survey (NHANES) (14).

Several studies have reported an association between waist circumference and urinary BPA concentration. Among Chinese adults, waist circumference significantly differed according to the quartile of urinary BPA concentration (9). Among 2,104 adults participating in NHANES 2003~2008, waist circumference was found to be significantly higher in those with urinary BPA concentrations in the highest tertile compared to those in the lowest tertile (15). Although many studies have demonstrated an association between urinary BPA concentration and waist circumference, no studies have reported on this relationship in Korean adults. Therefore, in the present study, we evaluated the relationship between urinary BPA concentration and waist circumference in Korean adults.

MATERIALS AND METHODS

Study subjects. This study was part of the study on the integrated exposure to hazardous materials for safety control conducted in 2010~2012 (16). The study protocol was approved by the Human Investigation Review Board of Dankook University College of Medicine and informed consent for participation was obtained from all subjects. The subjects were Korean adults living in Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, Ulsan, Gyunggi-do, Gangwon-do, Chungcheongbuk-do, Chungcheongnam-do, Jeollabuk-do, Jeollanam-do, Gyeongsangbuk-do, and Gyeongsangnam-do. Among the 1,058 Korean adults, those with missing information on general characteristics ($n = 19$) as well as those with missing data on anthropometric variables or blood profiles ($n = 9$) were excluded. Therefore, a total of 1,030 Korean adults were eligible for this study.

The subjects were individually interviewed by trained technicians using standard protocols. A questionnaire was developed for this study that included questions on age, education, income, smoking status, and alcohol consumption. The education status of the subjects was categorized as "elementary school," "middle school," "high school," and "college." The household monthly income was categorized as $\leq \$2,000$ and $> \$2,000$. Smoking status (never/former/current) and alcohol consumption (non/current) were also obtained via a personal interview. Raw data on waist circumference and urinary BPA concentration were collected from the study on the integrated exposure to hazardous materials for safety control (16). Urinary BPA concentrations were measured using high-performance liquid chromatography tandem mass spectrometry (Agilent 6410 Triple Quad LCMS, Agilent, Santa Clara, USA).

Statistical analysis. Continuous variable were expressed as means and standard deviations, and categorical variable

were expressed as number and percentage. The urinary BPA concentration was categorized into 4 groups on the basis of quartiles. Linear regression analyses were used to examine the relationship between urinary BPA concentration and anthropometric variables, blood pressure, and blood profiles, after adjusting for possible confounders. A general linear model was applied to examine the differences in the anthropometric variables, blood pressure, and blood profiles according to the BPA concentration quartile, including Tukey's post-hoc comparisons, while adjusting for age, sex, and urinary creatinine concentration. Unconditional multivariable logistic regression analysis was used to estimate the OR and 95% CI for the association of abdominal obesity with urinary BPA concentration quartile, while controlling for potential confounders (age, sex, urinary creatinine, education, income, alcohol consumption, and smoking status). All the tests were two-sided and significance was considered when $p < 0.05$, and all statistical analyses were performed using SAS 9.3 software (SAS Institute, Cary, NC, USA).

RESULTS

Study population characteristics. The study subjects had a mean age of 44.3 ± 14.6 years, and 75% of the subjects had at least received a high school education. Approximately 57% of the subjects had a monthly household income of $> \$2,000$. The proportions of subjects who were current smokers and current drinkers were 21.9% and 77.9%,

Table 1. General characteristics of Korean adults

	Values ¹⁾
Age (year)	44.3 \pm 14.6
Sex	
Men	465 (45.2)
Women	565 (54.8)
Education	
\leq Elementary school	155 (15.0)
\leq Middle school	103 (10.0)
\leq High school	350 (34.0)
\geq College	422 (41.0)
Household Monthly income	
\leq \$2,000	379 (36.8)
$>$ \$2,000	588 (57.1)
No response	63 (6.1)
Smoking status	
Never smokers	655 (63.6)
Ex-smokers	149 (14.5)
Current smokers	226 (21.9)
Alcohol consumption	
Never drinkers	228 (22.1)
Current drinkers	802 (77.9)
Urinary BPA concentration ($\mu\text{g/ml}$) ²⁾	1.4 (0.2, 198.7)
Urinary creatinine (mg/dl)	0.8 \pm 0.2

¹⁾Mean \pm standard deviation or frequency (%).

²⁾Median (minimum, maximum).

Table 2. Anthropometric variables, blood pressure and blood biochemical profiles of Korean adults according to the range of urinary BPA concentration¹⁾

	Bisphenol A (µg/ml)					p value	p value ³⁾
	All (n = 1030)	< 0.853 (n = 257)	0.853~1.407 (n = 258)	1.407~2.594 (n = 257)	> 2.594 (n = 258)		
Height (cm)	163.01 ± 8.93	161.84 ± 9.09	162.52 ± 9.17	163.71 ± 8.46	163.96 ± 8.88	0.0208	0.3956
Weight (kg)	63.87 ± 11.80	62.83 ± 10.86	62.95 ± 11.61	64.39 ± 12.02	65.31 ± 12.54	0.0478	0.0719
Body mass index (kg/m ²)	24.01 ± 3.44	24.04 ± 3.56	23.74 ± 3.18	24.03 ± 3.37	24.22 ± 3.63	0.4618	0.1620
Waist circumference (cm) ²⁾	84.51 ± 9.07	83.99 ± 8.45 ^a	83.99 ± 8.56 ^a	84.46 ± 8.32 ^{ab}	85.61 ± 10.68 ^b	0.1371	0.0071
Hip circumference (cm) ²⁾	94.97 ± 6.45	94.51 ± 6.08 ^{ab}	94.30 ± 6.17 ^a	95.14 ± 6.44 ^{ab}	95.93 ± 6.99 ^b	0.0179	0.0329
Body fat (%)	26.54 ± 6.33	27.25 ± 6.74	26.44 ± 5.72	26.23 ± 6.25	26.23 ± 6.54	0.2111	0.7386
Systolic blood pressure (mmHg)	123.36 ± 18.91	124.78 ± 20.58	124.65 ± 20.23	123.40 ± 17.44	120.62 ± 16.94	0.0442	0.3345
Diastolic blood pressure (mmHg)	74.78 ± 12.14	75.88 ± 12.24	75.62 ± 12.07	74.45 ± 12.39	73.18 ± 11.72	0.0457	0.0878
hsCRP (mg/dl)	0.15 ± 0.41	0.12 ± 0.27	0.18 ± 0.64	0.14 ± 0.26	0.15 ± 0.32	0.3805	0.3951
White blood cell (Thous/µl)	6.12 ± 1.63	6.17 ± 1.62	6.11 ± 1.76	6.12 ± 1.56	6.06 ± 1.60	0.8929	0.7966
Total cholesterol (mg/dl)	185.08 ± 35.21	187.23 ± 34.74	186.66 ± 35.84	183.34 ± 33.57	183.11 ± 36.61	0.4058	0.8234
LDL cholesterol (mg/dl)	111.87 ± 31.26	111.18 ± 31.17	112.39 ± 31.44	110.90 ± 29.14	113.03 ± 33.28	0.8504	0.4287
HDL cholesterol (mg/dl)	52.37 ± 11.75	52.69 ± 12.19	52.20 ± 12.23	52.71 ± 11.29	51.87 ± 11.31	0.8176	0.5481
Triglyceride (mg/dl)	130.37 ± 109.61	138.74 ± 133.23	134.84 ± 104.01	123.39 ± 96.09	124.52 ± 101.16	0.2958	0.2908
Fasting blood sugar (mg/dl)	97.54 ± 21.77	99.07 ± 27.15	99.35 ± 25.16	96.85 ± 18.00	94.90 ± 13.94	0.0684	0.3870

¹⁾Values are mean ± SD.

²⁾Values with different alphabets are significantly different among the four groups by GLM at $p < 0.05$ as appropriate; including the post hoc comparisons of Tukey.

³⁾From GLM test; adjusted for age, sex, urinary creatinine.

respectively (Table 1).

Comparison of anthropometric variables, blood pressure, and blood biochemical profiles according to the range of urinary BPA concentration. Table 2 presents the anthropometric variables, blood pressure, and blood biochemical profiles of Korean adults according to the range of the urinary BPA concentration. The mean BMI of all subjects was 24.01 ± 3.44 kg/m²; 64.6% and 35.4% of the subjects had normal weight (< 25 kg/m²) and were obese (≥ 25 kg/m²), respectively. The mean waist circumference was 86.53 ± 8.11 cm in men and 82.85 ± 9.47 cm in women, both of which were in the normal range (data not shown). The mean values of systolic blood pressure, diastolic blood pressure, hsCRP, white blood cell count, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, and fasting blood sugar were all within the normal range. The mean waist circumference was 84.51 ± 9.07 cm. The waist circumference was higher in the highest quartile (85.61 ± 10.68 cm) than in the first (83.99 ± 8.45 cm) and second quartile (83.99 ± 8.56 cm), after adjusting for age, sex, and urinary creatinine ($p = 0.0071$). Moreover, the hip circumference was higher in the highest quartile than in the second quartile ($p = 0.0329$), after adjusting for age, sex, and urinary creatinine.

In gender, the waist circumference was higher in the highest quartile (84.36 ± 11.85 cm) than in the first (82.63 ± 9.01 cm) and second quartile (81.63 ± 8.46 cm), after adjusting for age, urinary creatinine in women ($p = 0.0011$). However, there is no significant association between urinary BPA

concentrations and anthropometric variables, blood pressure and blood biochemical profiles in men (data not shown).

Linear regression analysis of BPA concentration and anthropometric variables, blood pressure, and blood biochemical profiles. Linear regression analysis revealed a positive association between urinary BPA concentration

Table 3. Coefficients from linear regression analysis BPA concentration and anthropometric variables, blood pressure, blood biochemical profiles in Korean adults¹⁾

	Bisphenol A (µg/ml)		
	β	(SE)	p value
Height (cm)	-0.0992	0.0468	0.0341
Weight (kg)	0.0444	0.0255	0.0822
Body mass index (kg/m ²)	0.1866	0.0749	0.0128
Waist circumference (cm)	0.0564	0.0291	0.0533
Hip circumference (cm)	0.0598	0.0394	0.1296
Body fat (%)	0.1091	0.0528	0.0389
Systolic blood pressure (mmHg)	0.0064	0.0145	0.6592
Diastolic blood pressure (mmHg)	0.0213	0.0224	0.3432
hsCRP (mg/dl)	0.0099	0.6221	0.9873
White blood cell (Thous/µl)	0.2006	0.1581	0.2046
Total Cholesterol (mg/dl)	0.0037	0.0074	0.6188
LDL Cholesterol (mg/dl)	0.0121	0.0082	0.1437
HDL Cholesterol (mg/dl)	-0.0237	0.0223	0.2878
Triglyceride (mg/dl)	-0.0017	0.0024	0.4850
Fasting blood sugar (mg/dl)	-0.0110	0.0121	0.3624

¹⁾Adjusted for age, sex, urinary creatinine.

Table 4. Odds ratio and 95% confidence interval of waist circumference (≥ 90 cm and 85 cm for men and women) according to the range of BPA concentration

OR (95% CI)	Quartile of urinary bisphenol A ($\mu\text{g/ml}$)				<i>p</i> for trend
	< 0.853 (<i>n</i> = 257)	0.853~1.407 (<i>n</i> = 258)	1.407~2.594 (<i>n</i> = 257)	> 2.594 (<i>n</i> = 258)	
Model 1 ¹⁾	1.0000	0.977 (0.676~1.411)	1.147 (0.798~1.651)	1.457 (1.018~2.086)	0.0167
Model 2 ²⁾	1.0000	1.086 (0.738~1.599)	1.343 (0.915~1.971)	1.901 (1.294~2.792)	0.0100
Model 3 ³⁾	1.0000	1.117 (0.757~1.649)	1.337 (0.908~1.967)	1.938 (1.314~2.857)	0.0106

¹⁾Unadjusted.

²⁾Adjusted for age, sex, urinary creatinine.

³⁾Adjusted for age, sex, urinary creatinine, education, income, alcohol consumption, smoking status.

and BMI ($\beta = 0.1866$; $p = 0.0128$), waist circumference ($\beta = 0.0564$; $p = 0.0533$), and body fat ($\beta = 0.1091$; $p = 0.0389$), after adjusting for the other covariates in the model (Table 3).

Association of waist circumference with urinary BPA concentration. A significant positive relationship was observed between obesity, as determined by waist circumference (≥ 90 cm for men; 85 cm for women), and urinary BPA concentration when comparing the highest quartile to the lowest (OR, 1.938; 95% CI: 1.314~2.857; p for trend = 0.0106) and after adjusting for age, sex, urinary creatinine, education, income, alcohol consumption, and smoking status (Table 4).

DISCUSSION

In the present study on Korean adults, waist circumference was higher among subjects with urinary BPA concentrations in the highest quartile compared to those with urinary BPA concentrations in the first and second quartile. Moreover, the hip circumference was higher for those with urinary BPA concentrations in the highest quartile relative to those with urinary BPA concentrations in the second quartile, after adjusting for age, sex, and urinary creatinine. In addition, after adjusting for potential confounders, linear regression analysis revealed a positive association between urinary BPA concentrations and BMI, waist circumference, and body fat. These findings are corroborated by the results of other studies among the general population (17-19).

Previous studies have reported a significant positive association, after adjusting for potential confounders, between obesity (BMI ≥ 30 kg/m²) and the highest quartile of urinary BPA concentration compared to the lowest (OR, 1.76, 95%CI: 1.06~2.94) among adults in the NHANES 2003~2006 (17). Among Chinese adults without micro- and macroalbuminuria, urinary BPA concentration was positively associated with BMI and waist circumference (18). Among healthy premenopausal women, the urinary BPA concentration was significantly correlated with body weight, BMI, waist circumference, hip circumference, and waist-hip ratio (19).

For children, the likelihood of having a BMI in the $\geq 95^{\text{th}}$ percentile was greater in those with a urinary BPA concentration in the highest quartile relative to those with concentrations in the lowest quartile. Additionally, those with a urinary BPA concentration in the highest quartile were significantly more likely to have waist circumferences in the $\geq 75^{\text{th}}$ percentile and $\geq 90^{\text{th}}$ percentile than those with BPA concentrations in the lowest quartile (20). Among Chinese school children, the mean urinary BPA concentration for obese children was observed to be significantly higher than that for those of normal weight (21). Among children aged 9 years participating in the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), the urinary BPA concentration was positively associated with BMI z-score, waist circumference, and body fat (22).

According to literature reviews, the mechanisms associated with health effects such as obesity and BPA exposure are still unclear. However, several studies have reported a significant association between urinary BPA concentrations and waist circumference (17-20). In addition waist circumference is a strong indicator of health effects and is significantly related with cardiovascular disease (11,12).

In the present study, the mean urinary BPA concentration of the subjects was 2.63 ± 8.11 ng/ml (mean age, 44 ± 15 years). The urinary BPA concentration of our subjects was higher than that reported in other studies conducted in Malaysia (mean urinary BPA, 1.89 ng/ml; mean age, 30 ± 9 years), India (mean urinary BPA, 1.97 ng/ml; mean age, 45 ± 16 years), and Japan (mean urinary BPA, 1.98 ng/ml; mean age, 32 ± 10 years), but lower than that of other studies conducted in China (mean urinary BPA, 3.86 ng/ml; mean age, 31 ± 16 years), Vietnam (mean urinary BPA, 3.32 ng/ml; mean age, 49 ± 18 years), and Kuwait (mean urinary BPA, 4.10 ng/ml; mean age, 23 ± 14 years) (23).

Our study had a number of strengths. To our knowledge, this is the first study to report on the relationship between urinary BPA concentrations and waist circumference in Korean adults. This study was sponsored by the Ministry of Food and Drug Safety and performed on a large scale with detailed epidemiologic data. Moreover, our subjects were enrolled from different regions in the country, thus making

it more generalizable to the Korean population as a whole. Furthermore, as our study measured the BPA concentration in 12 hr urine samples, our results may be more reflective of BPA exposure as compared to measurements from spot urine tests.

Despite its strengths, this study also has several limitations. First, our results are not supported by mechanistic data, and thus, it is plausible that our observed association between urinary BPA concentration and obesity is an incorrect statistical finding due to confounding or random chance. However, potential confounding factors were included in the analysis, thus limiting their effects. Second, we cannot infer causality because of the cross-sectional nature of the study. Third, our results indicated that the well-established traditional risk factors for cardiovascular disease, including waist circumference, BMI, blood pressure, hsCRP, total cholesterol, low density lipoprotein and high density lipoprotein cholesterol, triglycerides, and fasting blood sugar were all within the normal range. Unlike other indices, urinary BPA concentration was positively associated with waist circumference. Thus, we believe that prospective studies among the Korean population should be conducted to explore the association of urinary BPA concentration with cardiovascular events (11,12).

In conclusion, we have observed a positive association between urinary BPA concentration and waist circumference in Korean adults.

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