Bisphenol A Exposure And Anthropometry In Turkish Children Aged 8-9 Years In Konya

Yalçın S.[1], Yalçın S.S.[2*]

[1]Department of Food Hygiene and Technology Faculty of Veterinary Medicine Selçuk University, Konya, Turkey.

[2]Department of Pediatrics, Facuty of Medicine, Hacettepe University, Ankara, Turkey.

*corresponding author: S. Songül YALÇIN

e-mail: siyalcin@hacettepe.edu.tr

Abstract. This study aimed to determine the levels of Bisphenol A (BPA) and the relationship between BPA and anthropometric measurements of children aged 8-9 years in a sample representing urban and rural areas of Konya in Turkey. Urine samples were collected in glass vials in the morning and were stored at −20 °C until analysis. BPA analyses were performed using LC–MS/MS. Weight-for-age, height-for-age, body mass index -for-age were expressed in Z score (WAZ, HAZ, BAZ, respectively). BPA were divided into three categories [low<20%; 20%≤middle≤80%; high>80%]. Of 587 enrolled children, 65.8% were from urban areas, 50.3% male. Urinary BPA concentrations were detectable in 79.6%. A median (25p-75p) concentration of creatinine-corrected BPA concentrations was 5.9 (2.1-12.0) µg/g-creatinine. Children from urban residence had significantly lower BPA concentrations than rural ones. BPA concentrations were not associated with gender and BAZ. Children with low creatinine-corrected BPA levels (<20%) had significantly higher HAZ than those with high BPA levels (p=0.017). After adjusting age, residence and gender, BPA levels significantly affected HAZ of children. As a result, BPA exposure changed with residence of children. BPA exposure might negatively affect height during prepubertal period. Further studies are necessary to evaluate the effect of BPA exposure on child growth.

Keywords: Bisphenol A, exposure, urine, children, anthropometry, height

1. Introduction

Bisphenol A (BPA) has been widely used for decades in consumer goods, however, it is a suspected endocrine-disrupting chemical and can have a role in multiple diseases including urino-genital abnormalities in male newborns, early onset of puberty in girls, metabolic disorders including insulin resistant (type 2) diabetes and obesity (Bhandari *et al*., 2013; Braun and Hauser 2011; DiVall 2013; Eng 2013; LaKind *et al*., 2014; Rochester 2013). On the other hand, there is no published study concerning the effect of the BPA exposure on child's height.

This study aimed to determine the levels of BPA and the relationship between BPA and antropometric measurements [weight, height, body mass index (BMI)] of children aged 8-9 years in a sample representing urban and rural areas of Konya in central region of Turkey.

2. Methods

Konya is the biggest and the 7th crowded city in Turkey. The study was a representative cross-sectional study in Konya.

Turkish Statistical Institute (TURKSTAT) calculated sample size by child population density for rural and urban areas of Konya. The blocks of 25 household lists were selected as primary sampling units. Then, household lists were checked for children aged 8-9 years by a field operation. After written informed consent was obtained from one parent, anthropometric measurements (height, weight) were taken twice by an expert nurse and the averages were recorded. Urine samples were collected in glass vials from the enrolled children in the morning and were stored at −20 °C until analysis.

The study was approved by Local Ethic Committee of Medical Research of Hacettepe University Faculty of Medicine (291207TBK07/14).

Body weight was measured in light clothing using an electronic scale to the nearest 0,1 kg. Height was measured without shoes to the nearest 0,1 cm. We divided weight by the squared height to calculate BMI (in kg/m2). Using WHO AnthroPlus, z scores for weight-for-age, height-for-age, body mass index -for-age were calculated (WAZ, HAZ, BAZ, respectively) (WHO 2009). HAZ less than "-1" z score was defined as short and BAZ higher than"+1" z score were defined as overweight.

Urinary creatinine was measured using a Jaffe rate reaction. Urinary BPA analyses were performed using LC–MS/MS (Applied Biosystems API-3200; Foster City, CA). The limit of detection (LOD) was 0.3 µg/L and the limit of quantification (LOQ) was 0.9 µg/L.

Statistical analysis was performed using IBM SPSS Statistics 23. Descriptive statistical analyses (median, mean, SD, 95%CI, geometric mean) were performed.

BPA was expressed in µg/L urine and for creatinine adjusted concentrations in µg/g-creatinine. Concentrations below the LOQ were substituted with the LOQ divided by the square root of two. The urinary creatinine-corrected BPA levels were not normally distributed (Shapiro–Wilk

test, $p < 0.05$) and were not corrected after log-transformation. The urinary creatinine-corrected BPA were divided into three categories [low<20%; 20%≤middle≤80%; high>80%] and further categorized into the quintiles (<0.9 μg/L, 0.9-3.9 μg/L, 4.0-6.9 μg/L, 7.0-11.9 μg/L, >11.9 μg/L).

The chi-square test was used to check for gender, regional, HAZ and BAZ differences in relation to three BPA categories. The analysis of variance were carried out to check for differences in the mean WAZ, HAZ, BAZ, MAUC and TSF in three BPA categories and Duncan test was used for subgroup analysis. Spearman correlation coefficients assessed correlations between anthropometric measurement and urinary BPA levels.

Multiple logistic regression analyses were conducted to determine whether the urinary BPA quintiles, age, gender and residence of children predicted short children (HAZ<"-1" z score). Additionally, logistic regression analyses were conducted to determine whether urinary BPA quintiles, age, gender and residence of children predicted overweight.

3. Results

Of 587 enrolled children, 65.8% were from urban area, 50.3% male (Table 1), 16.1% overweight or obese and 16.6% short. The means (±SD) for WAZ, HAZ and BAZ were -0.14±1.17, -0.05±1.04 and -0.22±1.31 respectively.

Urinary BPA concentrations were detectable in 79.6%. A median (25p-75p) concentration of creatinine-corrected BPA concentrations was 5.9 (2.1-12.0) μg/g-creatinine (Table 2).

Children from urban residence had significantly lower BPA concentrations than rural ones [median (25p-75p); 4.9 (1.8-9.9) and 7.9 (3.7-14.8) μg/g-creatinine, respectively]. Males and females had similar urinary BPA concentrations (Table 3). Children with low creatinine-corrected BPA levels (<20%) had significantly higher HAZ than others (p=0.017). Overall, the risk of being short children increased with BPA categories; 8.5 %, 16.6% and 24.8% (P=0.004, Table 3). Overweight children had similar rates of BPA categories to normal weight children.

BPA concentrations were negatively correlated with WAZ (r=-0.101, p=0.015) and HAZ (r=-0.156, p<0.001).

After adjusting age, gender and residence, the risk of being short was found be higher in the 4th and 5th BPA quintiles than the first quintile (Table 4).

Table 1. General characteristics of children

	mean±SD	95%CI
Age, years	8.98±0.29	8.95-9.00
Male, n (%)	295 (50.3)	
Urban, n (%)	386 (65.8)	
WAZ	-0.14±1.17	-0.24, 0.05
HAZ	-0.05±1.04	-0.14, 0.03
BAZ	-0.22±1.31	-0.33, -0.11

WAZ, z scores for weight-for-age; HAZ, z scores for height-for-age; BAZ, z scores for body mass index-for-age.

Table 2. Urinary Bisphenol A levels

Bisphenol A	%<LOQ	mean	geometric mean	25	50	75	90	95	Maximum
μg/L	20.40	8.8	4.4	2.1	5.6	9.7	20.5	30.5	153.0
μg/g-creatinine		11.1	5.0	2.1	5.9	12.0	24.9	44.2	129.5

Table 3. Differences in age, gender region and anthropometry of children by urinary creatinine-corrected BPA categories

	Urinary creatinine-corrected Bisphenol A categories			
	Low: <LOQ	Middle: 21-80 %	High: >80%	p
n	120	350	117	
Age, years	8.96±0.29	8.97±0.30	9.04±0.31	0.076
Male, n(%)	51 (42.5)	185 (52.9)	59 (50.4)	0.147
Urban residence, n(%)	85 (70.8)	240 (68.6)	61 (52.1)	0.002
WAZ	0.02	-0.15	-0.28	0.146
	[-0.19, 0.23]	[-0.28, -0.03]	[-0.51, -0.05]	
HAZ	0.17	-0.08	-0.19	0.017

	[0.01, 0.34][a]	[-0.19, 0.03][b]	[-0.40, 0.02][b]	
HAZ<-1 z score	10 (8.5)	58 (16.6)	29 (24.8)	0.004
BAZ	-0.20	-0.21	-0.28	0.841
	[-0.44, 0.05]	[-0.34, -0.07]	[-0.52, -0.04]	
BAZ>1 z score	23 (19.5)	54 (15.5)	16 (14.5)	0.517

Mean [95%CI], Different letters in the same row were different, p<0.05. WAZ, z scores for weight-for-age; HAZ, z scores for height-for-age; BAZ, z scores for body mass index -for-age.

Table 4. The effect of Bisphenol A (BPA) quintiles (Q) on child's anthropometry

	HAZ<"-1" z score			BAZ>"+1" z score		
	Exp(B)	95% C.I.	Sig.	Exp(B)	95% C.I.	Sig.
BPA-Q1			0.010			0.842
BPA-Q2 vs.Q1	1.30	[0.53-3.16]	0.564	0.74	[0.37-1.46]	0.386
BPA-Q3 vs.Q1	2.18	[0.97-4.90]	0.060	0.70	[0.35-1.41]	0.317
BPA-Q4 vs.Q1	2.93*	[1.33-6.43]	0.007	0.76	[0.38-1.52]	0.441
BPA-Q5 vs.Q1	3.34*	[1.53-7.29]	0.002	0.72	[0.36-1.45]	0.355
Age	1.43	[0.67-3.03]	0.353	1.83	[0.86-3.91]	0.119
Rural vs. Urban	0.86	[0.53-1.38]	0.528	1.62	[0.96-2.72]	0.072
Female vs. male	0.93	[0.60- 1.45]	0.747	0.72	[0.46-1.13]	0.151

BPA, Bisphenol A; Q, quintiles; HAZ, z scores for height-for-age; BAZ, z scores for body mass index -for-age.

4. Discussion

The median and geometric mean of the urinary unadjusted BPA (creatinine-adjusted BPA) concentration was 5.6 and 4.4 µg/L (5.9 and 5.0 µg/g-creatinine) with a 95th percentile of 30.5 µg/L (44.2 µg/g-creatinine) in Turkish preadolescence children. Urinary concentrations of BPA in Turkish children were comparable to the values reported in 9–11 year old Spanish children [Median (P25, P75) 4.76 (2.77, 9.03) µg/L] (Perez-Lobato *et al*., 2016), donated urine samples of 8-11 year old children from 2003-2006 National Health and Nutrition Examination Survey (NHANES), (mean:6.43 µg/L, Li *et al*., 2017) and urine samples of children aged 6–18 years from NHANES 2003–2008 (mean: 4.8 µg/L, Bhandari *et al*., 2013). Urinary BPA levels in our study were much higher in comparison to those reported in Belgium (GM: 2.24 ng/ mL) (Geens *et al*. 2014), USA (GM: 3.7 ng/ mL) (Calafat *et al*. 2008), Canada (GM: 1.50 ng/mL) (Bushnik *et al*., 2010), Denmark (Median: 0.80 ng/mL) (Frederiksen *et al*., 2014), Germany (GM: 2.42 µg/L) (Becker etal., 2009), China (GM: 3.0 µg/L) (Li *et al*., 2013). Varying BPA concentrations among populations of children may be due to cultural differences in diet and behavior.

Some cross-sectional studies suggest that BPA exposure is associated with obesity in children (Bhandari *et al*., 2013; Eng *et al*., 2013; Li *et al*., 2013; Trasande *et al*., 2012; Wang *et al*., 2012; Wells *et al*., 2014), however, prospective cohort studies examining early-life BPA exposure in association with childhood obesity report contradictory findings: One found higher BMI among children with higher prenatal BPA exposure (Valvi *et al*., 2013), and the two others reported lower BMI with higher early childhood exposure (Braun *et al*.,2014; Harley *et al*., 2013). Similarly, study results in adults are also conflicting; eight studies with positive association and ten studies with no association (Oppeneer *et al*., 2015). Despite no relationships between BPA levels and measures of fat mass, BPA was reported to be associated with the adipokines, adiponectin and leptin and with the gut-hormone ghrelin in a previous study (Rönn *et al*., 2014). On the other hand, obese children may have greater exposure to BPA due to higher dietary intakes and diet is an exposure route. In addition, there was no relationship between BAZ and urinary BPA levels in our study.

In our study the level of BPA exposure increased the risk of being stunded in preadolescent children. To our knowledge, there are no other studies so far on the effect of early life BPA exposure on height other than adiposity. Given an endocrine distruptors, BPA exposure might affect height, growth of children. Previous studies reported that BPA exposure altered thyroid function and disturbed thyroid hormone (TH) homeostasis (Andrianou *et al* 2016; Geens 2015; Park *et al* 2017).

In conclusion, our study might support to potential effects of BPA on prepubertal growth. However, because of the short half-life and the likely episodic nature of BPA, our findings based on concentrations of the target biomarkers in a single urine sample may be affected by exposure misclassification. As a limitation of the study, the cross-sectional design does not permit the ascertainment of temporal associations between BPA and height. In addition, the cross-sectional design could give data concerning current exposures. The use of spot urine samples is a potential limitation of our study. Further longitudinal studies are needed in other populations with large sample size to confirm or disprove our findings.

Conflict of interest: The authors have no competing interests to declare, financial or otherwise.

Acknowledgments: This survey was funded by TÜBİTAK SBAG-107S407. The authors would like to thank Osman Aykut for laboratory asistance.

References

Andrianou X.D., Gängler S., Piciu A., Charisiadis P., Zira C., Aristidou K., Piciu D., Hauser R., Makris K.C. (2016), Human Exposures to Bisphenol A, Bisphenol F and Chlorinated Bisphenol A Derivatives and Thyroid Function, *PLoS One*, **11**(10), e0155237.

Becker K., Göen T., Seiwert M., Conrad A., Pick-Fuss H., Müller J., Wittassek M., Schulz C., Kolossa-Gehring M. (2009), GerES IV: phthalate metabolites and bisphenol A in urine of German children. *International Journal Of Hygiene And Environmental Health*, **212**, 685-692.

Bhandari R., Xiao J., Shankar A. (2013), Urinary bisphenol A and obesity in U.S. children. *American Journal Of Epidemiology*, **177**, 1263-1270.

Braun J.M., Hauser R. (2011), Bisphenol A and children's health. *Current Opinion in Pediatrics*, **23**, 233-239.

Braun J.M., Lanphear B.P., Calafat A.M., Deria S., Khoury J., Howe C.J., Venners S.A. (2014), Early-life bisphenol a exposure and child body mass index: a prospective cohort study. *Environmental Health Perspectives*, **122**, 1239-1245.

Bushnik T., Haines D., Levallois P., Levesque J., Van Oostdam J., Viau C. (2010), Lead and bisphenol A concentrations in the Canadian population. *Health Reports*, **21**, 7-18.

Calafat, A.M., Ye, X., Wong, L.Y., Reidy, J.A., Needham, L.L., (2008), Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003–2004. *Environmental Health Perspectives*,116, 39–44.

DiVall S.A. (2013), The influence of endocrine disruptors on growth and development of children. *Current Opinion In Endocrinology, Diabetes, And Obesity*, **20**, 50-55.

Eng D.S., Lee J.M., Gebremariam A., Meeker J.D., Peterson K., Padmanabhan V. (2013), Bisphenol A and chronic disease risk factors in US children, *Pediatrics*, **132**, e637e45.

.Frederiksen H., Jensen T.K., Jørgensen N., Kyhl H.B., Husby S., Skakkebæk N.E., Main K.M., Juul A., Andersson A.M. (2014), Human urinary excretion of non-persistent environmental chemicals: an overview of Danish data collected between 2006 and 2012, *Reproduction*, **147**, 555-565.

Geens T., Dirtu A.C., Dirinck E., Malarvannan G., Van Gaal L., Jorens P.G., Covaci A. (2015), Daily intake of bisphenol A and triclosan and their association with anthropometric data, thyroid hormones and weight loss in overweight and obese individuals, *Environment international*, 76, 98-105.

Geens T., Bruckers L., Covaci A., Schoeters G., Fierens T., Sioen I., Vanermen G., Baeyens W., Morrens B., Loots I., Nelen V., de Bellevaux B.N., Larebeke N.V., Hond E.D. (2014), Determinants of bisphenol A and phthalate metabolites in urine of Flemish adolescents, *Environmental Research*, **134**, 110-117.

Harley K.G., Aguilar Schall R., Chevrier J., Tyler K., Aguirre H., Bradman A., Holland N.T., Lustig R.H., Calafat A.M., Eskenazi B. (2013), Prenatal and postnatal bisphenol A exposure and body mass index in childhood in the CHAMACOS cohort. *Environmental Health Perspectives*, **121**, 514-520.

Lakind, J.S., Goodman, M., Mattison, D.R., (2014),. Bisphenol A and indicators of obesity, glucose metabolism/type 2 diabetes and cardiovascular disease: a systematic review of epidemiologic research. *Critical Reviews In Toxicology*, **44**, 121-150.

Li J., Lai H., Chen S., Zhu H., Lai S. (2017), Gender differences in the associations between urinary bisphenol A and body composition among American children: The National Health and Nutrition Examination Survey, 2003-2006, *Journal of Epidemiology*, Jan 27. pii: S0917-5040(16)30163-0.

Li, D.K., Miao, M., Zhou, Z., Wu, C., Shi, H., Liu, X., Wang, S., Yuan, W., (2013), Urine bisphenol-A level in relation to obesity and overweight in school-age children, *PLoS One*, **8,** e65399.

Oppeneer S.J., Robien K. (2015), Bisphenol A exposure and associations with obesity among adults: a critical review. *Public Health Nutrition*, **18**, 1847-1863.

Park C., Choi W., Hwang M., Lee Y., Kim S., Yu S., Lee I., Paek D., Choi K. (2017), Associations between urinary phthalate metabolites and bisphenol A levels, and serum thyroid hormones among the Korean adult population - Korean National Environmental Health Survey (KoNEHS) 2012-2014. *The Science Of The Total Environment*, **584-585**, 950-957.

Perez-Lobato R., Mustieles V., Calvente I., Jimenez-Diaz I., Ramos R., Caballero-Casero N., López-Jiménez F.J., Rubio S., Olea N., Fernandez M.F. (2016), Exposure to bisphenol A and behavior in school-age children. *Neurotoxicology*, **53**, 12-19.

Rochester J.R. (2013), Bisphenol A and human health: a review of the literature. *Reproductive Toxicology*, **42**, 132-155.

Rönn M., Lind L., Örberg J., Kullberg J., Söderberg S., Larsson A., Johansson L., Ahlström H., Lind P.M. (2014), Bisphenol A is related to circulating levels of adiponectin, leptin and ghrelin, but not to fat mass or fat distribution in humans. *Chemosphere*, 112, 42-48.

Trasande L., Attina T.M,. Blustein J. (2012), Association between urinary bisphenol A concentration and obesity prevalence in children and adolescents. *Journal of the American Medical Association*, 308, 1113–1121.

Valvi D., Casas M., Mendez M.A., Ballesteros-Gomez A., Luque N., Rubio S., *et al*. (2013), Prenatal bisphenol A urine concentrations and early rapid growth and overweight risk in the offspring. *Epidemiology*, **24**, 791–799.

Wang H.X., Zhou Y., Tang C.X., Wu J.G., Chen Y., Jiang Q.W. (2012), Association between bisphenol A exposure and body mass index in Chinese school children: a cross-sectional study. *Environmental Health*, **11**: 79.

Wells E.M., Jackson L.W., Koontz M.B. (2014), Association between bisphenol A and waist-to-height ratio among children: National Health and Nutrition Examination Survey, 2003-2010. *Annals Of Epidemiology*, **24**, 165-167.

WHO. (2009), WHO AnthroPlus for personal computers manual: software for assessing growth of the world's children and adolescents, Geneva: WHO.