



The association of total blood mercury levels and overweight among Korean adolescents: analysis of the Korean National Health and Nutrition Examination Survey (KNHANES) 2010–2013

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Purpose: Obesity has been associated with higher total blood mercury levels, based on animal studies; however, studies that focus on children and adolescents are lacking. We aimed to assess the association between total blood mercury levels and the incidence of overweight and abdominal obesity in Korean adolescents.

Methods: The study population comprised 1,567 adolescents (793 boys and 774 girls; aged 10–19 years), who participated in the Korea National Health and Nutrition Examination Survey 2010–2013. We analyzed total blood mercury levels according to obesity status in all participants.

Results: The geometric mean of total blood mercury levels was 1.93 µg/L. Participants with overweight (2.20 µg/L) and obesity (2.17 µg/L) had higher levels than those with normal weight (1.86 µg/L, $P < 0.0001$). The prevalence of overweight significantly increased with elevation of the total blood mercury quartile in both sexes. Increased incidence of abdominal obesity corresponding to increased total blood mercury level was observed in boys. After adjusting for covariates, those in the highest total blood mercury quartile were found to be at higher risk of overweight/obesity than those in the lowest quartile in both sexes (odds ratio [95% confidence interval]: boys, 3.27 [1.66–6.41]; girls, 1.90 [1.03–3.49]). The association between total blood mercury quartile and abdominal obesity was significant after controlling for covariates in boys (2.35 [1.05–5.24]).

Conclusion: Our results suggest an association between total blood mercury levels and overweight in Korean adolescents.

Key words: Adolescent, Blood, Mercury, Obesity, Overweight

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Received: 11 September, 2017
Revised: 22 October, 2017
Accepted: 25 October, 2017

Introduction

Mercury exists naturally in the Earth's crust. It is naturally emitted into the atmosphere from soil and water, or released artificially through human activities such as metal mining, coal-burning (in power stations and homes), and the breakage of products containing mercury (fluorescent lamps, batteries, and pharmaceuticals).¹⁾ The general population is exposed to mercury predominantly through contaminated foods—in particular, the products of fisheries and plants, which accumulate mercury in the form of methylmercury. Mercury exposure, in humans, has toxic effects on various organ systems, including the nervous, cardiovascular, renal and endocrine systems.¹⁾

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Mercury is considered an endocrine disruptor, since it has direct cytotoxic effects on most of the human endocrine tissues, such as pancreas and thyroid gland.²⁾ In addition, mercury exposure cause disturbances in carbohydrate and lipid metabolism³⁾ and induction of oxidative stress and systemic inflammation.³⁾ These effects, caused by mercury exposure, could lead to an increased risk of the development of obesity-related metabolic disorders. In recent times, numerous studies have investigated the relationship between mercury exposure and an increased risk of obesity,^{4–6)} and mercury has emerged as a possible obesogen. However, these findings were not consistent with some other studies, which reported that there was no association⁷⁾ between total blood mercury concentrations and adiposity. Moreover, the number of studies conducted on the pediatric population, in this context, is limited.^{8,9)}

Children and adolescents are considered more vulnerable to the toxic effects of heavy metal exposure, as they may ingest larger amounts of contaminated foods, in relation to their body weight.¹⁰⁾ In addition, the immature nature of their metabolic excretory pathways can limit the detoxification and elimination of heavy metals, after exposure; this may increase the toxic effects on this population.¹⁰⁾

In this study, we aimed to investigate the association of total blood mercury levels and overweight/obesity (defined by the body mass index [BMI]), and with abdominal obesity (defined by the waist to height ratio [WHtR]), in a population of Korean adolescents, using data from the Korean National Health and Nutrition Survey (KNHANES) 2010–2013.

Materials and methods

1. Study participants

The data for this study were obtained from the KNHANES 2010–2013—a community-based survey performed by the Korea Centers for Disease Control and Prevention, to evaluate the health and nutritional statuses of Korean citizens. A stratified, multistage, probability sampling design was used to select participants, who were representative of South Korea's civilian, noninstitutionalized population. The cross-sectional analysis was performed in 1,567 children and adolescents, aged 10–19 years (793 boys and 774 girls), who completed the health examination survey and the laboratory assessment for the estimation of the total blood mercury levels. Written informed consent was obtained from all the participants or their parents. This study was exempt from the approval of the institutional review board, since it used a publicly available deidentified dataset.

2. Data collection and study variables

The participants were divided into 3 age groups (10–12, 13–15, and 16–19 years). The BMI status was determined in accordance with the sex- and age-specific percentiles of the national reference

standards.¹¹⁾ For participants aged <19 years, the BMI status was defined as follows: underweight (BMI<5th percentile), normal (BMI≥5th percentile, and <85th percentile), overweight (BMI≥85th percentile and <95th percentile), and obese (BMI≥95th percentile). For subjects aged 19 years, the BMI status was determined in accordance with the criteria defined by the International Obesity Task Force, for adults in the Asian and Pacific regions.¹²⁾ In this, the BMI status was defined as follows: underweight (BMI<18.5 kg/m²), normal weight (18.5 kg/m²≤BMI<23 kg/m²), overweight (23 kg/m²≤BMI<25 kg/m²), and obese (BMI≥25 kg/m²). Abdominal obesity was defined as a WHtR≥0.5.¹³⁾

We classified the areas of the participants' residence into 2 categories: rural areas (administrative divisions of counties, or small cities with a population of less than 500,000 people) or urban areas (administrative divisions of counties, or cities with a population of more than 500,000 people). The household income level was determined by the quartiles of the monthly household equivalent income, which was calculated by dividing the monthly household income by the square root of the number of household members.

The smoking status of the participants was categorized into 3 groups, according to their smoking habits or exposure to cigarette smoke in the past 30 days: nonsmokers (those who had never smoked), secondhand smoke exposure (those who were exposed to cigarette smoke due to the smoking habits of their family members), and current smokers (those who smoked at least 1 cigarette a day). Drinking habits were categorized into 3 groups, based on the patterns of alcohol consumption in the past year: nondrinkers (those who did not consume alcohol even once a month), light drinkers (those who consumed at least one glass of alcohol every month), and heavy drinkers (those who consumed more than 6 drinks for boys, or 4 drinks for girls, on a single occasion, more than 2 times per week). The level of physical activity was self-reported, using the International Physical Activity Questionnaire, in the KNHANES. Moderate-to-vigorous physical activity was defined as vigorous physical activity lasting at least 20 minutes, per session, more than 3 times a week, or as moderate physical activity lasting at least 30 minutes, per session, more than 5 times a week.

We defined anemia according to the cutoff values provided by the criteria of the¹⁴⁾: Hb<11.5 g/L at 10–11 years, <12.0 g/L at 12–14 years, <13.0 g/L in boys aged ≥15 years, and <12.0 g/L in girls aged ≥15 years.

3. Determination of mercury concentrations in whole blood

Participants' blood samples were drawn into sodium heparin tubes, after an overnight fast. The total blood mercury concentrations were measured using the gold-amalgam collection method, with a Direct Mercury Analyzer 80 (DMA 80, Milestone, Bergamo, Italy). The interassay coefficients of variation were 0.47%–6.08%. The limit of detection (LOD) for the total blood mercury was 0.158 mg/L, and the total blood mercury levels were not below the LOD in

any of the participants.

Table 1. General characteristics of participants

Characteristic	Total (n=1,567)	Boy (n=793)	Girl (n=774)	P value
Age (yr)	15.0±0.1	14.9±0.1	15.0±0.1	0.409
Age group (yr)				0.601
10–12	471 (23.8)	249 (24.7)	222 (22.8)	
13–15	515 (30.2)	267 (30.8)	248 (29.7)	
16–19	581 (46.0)	277 (44.5)	304 (47.5)	
BMI (kg/m ²)	21.0±0.1	21.4±0.2	20.8±0.2	0.006
BMI status				0.808
Underweight	75 (4.8)	36 (5.1)	39 (4.6)	
Normal	1,171 (73.9)	589 (72.7)	582 (75.2)	
Overweight	198 (12.7)	102 (13.3)	96 (12.0)	
Obese	123 (8.6)	66 (8.9)	57 (8.2)	
Waist circumference (cm)	70.3±0.3	72.5±0.4	68.1±0.4	<0.001
Abdominal obesity	157 (11.0)	103 (13.0)	54 (8.7)	0.037
Residential region				0.726
Urban	1,323 (82.8)	668 (82.5)	655 (83.2)	
Rural	244 (17.2)	125 (17.5)	119 (16.8)	
Household income				0.199
Quartile 1	186 (14.0)	85 (12.4)	101 (15.9)	
Quartile 2	414 (28.8)	210 (29.2)	204 (28.3)	
Quartile 3	488 (29.5)	244 (28.7)	244 (30.4)	
Quartile 4	463 (27.6)	249 (29.7)	214 (25.4)	
Smoking status				<0.001
Nonsmoker	851 (53.2)	418 (49.8)	433 (56.8)	
Secondhand smoke exposure	619 (38.9)	304 (38.5)	315 (39.4)	
Current smoker	86 (7.9)	66 (11.7)	20 (3.8)	
Drinking habits				0.001
Nondrinker	1,371 (84.6)	684 (81.9)	687 (87.6)	
Light drinker	139 (11.4)	70 (11.8)	69 (10.9)	
Heavy drinker	45 (4.0)	36 (6.4)	9 (1.5)	
Anemia				<0.001
No	1,545 (98.5)	790 (99.7)	755 (97.2)	
Yes	22 (1.5)	3 (0.3)	19 (2.8)	

Values are presented as mean±standard error or number (%).
BMI, body mass index.

Table 2. Distribution of blood mercury levels (µg/L) in Korean adolescents

	No.	Geometric mean (95% CI)	Selected percentiles (95% CI)			
			50th	75th	90th	95th
Total	1,567	1.93 (1.87–1.98)	1.88 (1.82–1.93)	2.54 (2.47–2.68)	3.51 (3.38–3.73)	4.32 (4.08–4.77)
Sex						
Girl	774	1.85 (1.78–1.92)	1.80 (1.72–1.89)	2.41 (2.30–2.55)	3.23 (3.05–3.45)	3.89 (3.59–4.41)
Boy	793	2.01 (1.93–2.09)	1.94 (1.86–2.04)	2.43 (2.41–2.46)	3.81 (3.62–4.07)	4.77 (4.30–5.15)

CI, confidence interval.

4. Statistical analysis

Statistical analyses were conducted using IBM SPSS ver. 18.0 (IBM Co., Armonk, NY, USA), and sampling weights were used to take the complex sampling design into account. The complex sample descriptive procedure (CSDESCRIPTIVES) was used to evaluate the numerical variables (both discrete and continuous). For categorical or ordinal variables, the complex-samples crosstabs procedure (CSTABULATE) was used. Because of the left-skewed distribution, the blood mercury levels were log-transformed. The geometric means and 95% confidence intervals (CIs) were calculated using a complex samples general linear model (CSGLM), to compare the blood mercury levels by different demographic and lifestyle groups, after adjusting for all the covariates, including age, sex, BMI status, residential region, household income, smoking status, alcohol consumption, and anemia. Multivariate logistic regression analyses were used to determine the adjusted odds ratios (ORs) and 95% CI for the incidences of overweight and abdominal obesity, according to the quartile of total blood mercury concentrations (CSLOGISTIC). For all the analyses, *P* values were two-tailed and *P*<0.05 was considered statistically significant.

Results

1. General characteristics of the study participants

The general characteristics of the study participants are presented in Table 1. The mean age of the study population was 15.0 years. There were no significant differences in age, area of residence, and household income, between the boys and girls. The prevalence of overweight and obesity was 12.7% and 8.6%, respectively, and no significant sex-related difference was found in the BMI status. The prevalence of abdominal obesity, however, was significantly higher in the boys (13.0%) than in the girls (8.7%). The proportions of current smokers (*P*<0.001) and heavy drinkers (*P*=0.001) were also significantly higher among the boys. The prevalence of anemia was significantly higher in the girls than in the boys (*P*<0.001).

2. Total blood mercury concentrations of the study participants

The distribution of the total blood mercury concentrations in the study participants are shown in Table 2. The geometric mean of the total blood mercury levels was 1.93 µg/L (2.01 µg/L in boys,

and 1.85 µg/L in girls), and the 95th percentile values in the boys and girls were 4.77 and 3.89 µg/L, respectively. Table 3 presents the crude and adjusted geometric means of total blood mercury concentrations, according to the participants' characteristics. The crude and adjusted geometric means of the total blood mercury levels were significantly higher in the boys than in the girls ($P < 0.001$).

Table 3. Crude and adjusted geometric means of blood mercury levels (µg/L) according to participant general characteristics

Variable	No.	Geometric mean (95% CI)	
		Crude	Adjusted [†]
Total	1,567	1.93 (1.87–1.98)	
Sex			
Girl	774	1.85 (1.78–1.92)	2.11 (1.88–2.36)
Boy	793	2.01 (1.93–2.09)**	2.25 (2.00–2.52)**
Age (yr)			
10–12 [†]	471	1.89 (1.81–2.18)	2.16 (1.90–2.44)
13–15	515	1.94 (1.84–2.03)	2.21 (1.95–2.49)
16–19	581	1.95 (1.87–2.03)	2.17 (1.95–2.41)
Body mass index status			
Underweight	75	1.92 (1.68–2.19)	2.05 (1.74–2.41)
Normal [†]	1171	1.86 (1.80–1.92)	2.00 (1.80–2.24)
Overweight	198	2.20 (2.02–2.38)***	2.38 (2.08–2.72)***
Obese	123	2.17 (2.00–2.35)***	2.30 (2.02–2.62)**
Residential region			
Urban [†]	1,323	1.91 (1.85–1.97)	2.11 (1.89–2.35)
Rural	244	2.02 (1.88–2.16)	2.25 (1.98–2.55)
Household income			
Quartile 1 [†]	186	1.94 (1.79–2.10)	2.21 (1.94–2.52)
Quartile 2	414	1.81 (1.73–1.90)	2.02 (1.79–2.27)
Quartile 3	488	1.94 (1.84–2.04)	2.18 (1.93–2.46)
Quartile 4	463	2.06 (1.95–2.19)	2.32 (2.06–2.61)
Smoking status			
Nonsmoker [†]	851	1.88 (1.81–1.96)	2.12 (1.88–2.38)
Secondhand smoke exposure	619	1.98 (1.89–2.06)	2.21 (1.98–2.47)
Current smoker	86	2.00 (1.83–2.19)	2.21 (1.93–2.52)
Drinking habits			
Nondrinker [†]	1,371	1.91 (1.85–1.98)	2.10 (1.90–2.32)
Light drinker	139	2.02 (1.88–2.16)	2.21 (1.97–2.48)
Heavy drinker	45	2.15 (1.80–2.56)	2.22 (1.83–2.69)
Anemia			
No [†]	1,545	1.93 (1.88–1.99)	2.15 (1.99–2.31)
Yes	22	1.80 (1.52–2.13)	2.21 (1.84–2.64)

CI, confidence interval.

** $P < 0.001$. *** $P < 0.0001$.

[†]Adjusted for all variables in the table. [†]Reference for comparison of geometric mean in each variables[†].

3. The associations of total blood mercury concentrations with overweight/obesity and abdominal obesity

Significantly higher total blood mercury levels were observed among participants with overweight and obesity than among participants with a normal weight ($P < 0.001$). However, the total blood mercury levels did not differ significantly based on age group, area of residence, household income, smoking/drinking habits, or presence of anemia.

The prevalence of overweight/obesity and abdominal obesity, according to the quartiles of total blood mercury concentrations, are presented in Table 4. The prevalence of overweight/obesity significantly increased with the elevation of the total blood mercury quartile, in both the sexes (P for-trend < 0.05). Increases in the prevalence rates of abdominal obesity, corresponding to the increase of the total blood mercury quartile, were also noted in the boys, but this trend was not observed in the girls.

The adjusted ORs (95% CI) for overweight/obesity and abdominal obesity, according to the quartiles of total blood mercury concentrations, are shown in Table 5. After adjusting for the covariates, including age, household income, daily calorie intake, and level of physical activity, the participants in the highest total blood mercury quartile were found to be at the highest risk for developing overweight/obesity, compared to those in the lowest quartile (OR [95% CI]: boys, 3.27 [1.66–6.41]; girls, 1.90 [1.03–3.49]). The positive association between total blood mercury quartiles and abdominal obesity was significant in the boys (2.35 [1.05–5.24]), but not in the girls.

Table 4. Prevalence of overweight/obesity and abdominal obesity according to blood mercury level quartile

Variable	Blood mercury quartile				<i>P</i> for-trend
	I	II	III	IV	
Boy					
	n=200	n=196	n=199	n=198	
BMI status					0.001
Underweight	8 (5.2)	10 (6.4)	9 (4.8)	9 (3.9)	
Normal	166 (79.8)	147 (70.8)	154 (79.2)	122 (60.9)	
Overweight	16 (9.3)	24 (12.0)	24 (11.8)	38 (20.2)	
Obesity	10 (5.6)	15 (10.8)	12 (4.3)	29 (15.0)	
Abdominal obesity	14 (7.8)	22 (14.0)	27 (10.9)	40 (19.2)	0.043
Girl					
	n=193	n=193	n=191	n=197	
BMI status					0.024
Underweight	10 (5.0)	10 (4.0)	10 (4.2)	9 (5.1)	
Normal	149 (78.5)	155 (80.6)	143 (74.9)	135 (67.2)	
Overweight	27 (13.4)	15 (6.5)	23 (11.0)	31 (16.8)	
Obesity	7 (3.2)	13 (8.9)	15 (9.9)	22 (10.8)	
Abdominal obesity	8 (5.7)	14 (10.0)	13 (9.1)	19 (10.1)	0.618

Values are presented as number (%).

The sex-specific quartile values of blood mercury are as follows: boy (< 1.47 , 1.47–1.93, 1.94–2.67, > 2.67 µg/L), girl (< 1.39 , 1.39–1.79, 1.80–2.41, > 2.41 µg/L).

Table 5. Odds ratio (95% confidence interval) for obesity according to blood mercury level quartile

Variable	Blood mercury quartile			
	I	II	III	IV
Boy				
Overweight/obesity				
Model 1	1.00	1.61 (0.83–3.09)	1.02 (0.49–2.12)	2.89 (1.54–5.40)
Model 2	1.00	1.72 (0.89–3.36)	1.11 (0.53–2.34)	3.00 (1.57–5.72)
Model 3	1.00	1.86 (0.92–3.77)	1.27 (0.58–2.76)	3.27 (1.66–6.41)
Abdominal obesity				
Model 1	1.00	2.06 (0.89–4.78)	1.58 (0.70–3.57)	3.13 (1.44–6.80)
Model 2	1.00	2.06 (0.89–4.78)	1.58 (0.71–3.53)	2.87 (1.33–6.18)
Model 3	1.00	2.09 (0.87–4.97)	1.72 (0.72–4.08)	2.35 (1.05–5.24)
Girl				
Overweight/obesity				
Model 1	1.00	0.92 (0.46–1.83)	1.34 (0.76–2.36)	1.93 (1.10–3.37)
Model 2	1.00	0.90 (0.45–1.79)	1.29 (0.72–2.31)	1.93 (1.09–3.41)
Model 3	1.00	0.83 (0.39–1.79)	1.24 (0.66–2.30)	1.90 (1.03–3.49)
Abdominal obesity				
Model 1	1.00	1.94 (0.65–5.82)	1.71 (0.62–4.76)	1.93 (0.70–5.31)
Model 2	1.00	1.87 (0.63–5.57)	1.65 (0.59–4.60)	1.87 (0.67–5.21)
Model 3	1.00	1.85 (0.58–5.94)	1.41 (0.47–4.26)	1.67 (0.57–4.93)

The sex-specific quartile values of blood mercury are as follows: boy (<-1.47, 1.47–1.93, 1.94–2.67, >2.67 µg/L), girl (<1.39, 1.39–1.79, 1.80–2.41, >2.41 µg/L). Odds ratios were derived from logistic regression analyses.

Model 1, adjusted for age; model 2, model 1 plus adjustment for household income; model 3, model 2 plus adjustment for daily calorie intake (kcal) and fulfillment of moderate-to-vigorous physical activity.

Discussion

In this study, we presented a representative sample of total blood mercury concentrations, in Korean adolescents, and also demonstrated that elevations in the total blood mercury levels were associated with increases in the prevalence of overweight/obesity in both sex and abdominal obesity in boys, using data from the KNHANES 2010–2013.

Only a limited number of studies have focused on the effects of total blood mercury concentrations among adolescent populations, especially those from Asian countries. Recently, two studies reported the total blood mercury levels of children in Japan¹⁵⁾ and China.¹⁶⁾ Although there were differences regarding the number of participants and their ages in those studies, the geometric means of the total blood mercury levels tended to be the highest in Japanese children (4.55 µg/L),¹⁵⁾ followed by in adolescents from Korea (1.93 µg/L in this study) and Chinese children (1.05 µg/L).¹⁶⁾ Importantly, we found that the geometric mean values of the total blood mercury levels, among the children and adolescents in these 3 countries, were markedly higher than those of their counterparts from Canada (0.29 µg/L),¹⁷⁾ the US (0.28 µg/L),¹⁸⁾ and Germany (0.2 µg/L).¹⁹⁾

Total blood mercury comprises 14% to 26% of inorganic mercury and 75% to 90% of methylmercury; exposure to methylmercury predominantly occurs through the consumption of the products

of fisheries.²⁰⁾ Interestingly, the consumption of fish and shellfish, per capita, has been reported to be relatively higher in Japanese (85.4–107 g/day),²¹⁾ Korean (79.6 g/day),²²⁾ and Chinese (29.6 g/day) populations,²³⁾ compared with the consumption, per capita, in the US (12.8 g/day),²⁴⁾ Canada (20 g/day),²⁵⁾ and Germany (15.8–16.2 g/day)²⁶⁾; these results can be expanded to include children and adolescents too. Therefore, the high total blood mercury levels observed in Korean and Japanese adolescents, in comparison to the corresponding levels in adolescents from other countries, could be partly attributed to the higher rates of consumption of fishery products.

Several studies have reported a positive association between blood mercury levels and obesity, in adult populations; however, these findings were not consistent with those of other previously conducted studies. Several investigators have observed an increased risk of overweight/central obesity, based on the BMI^{4,5,27,28)} in Korean adults with higher blood mercury concentrations, using large-scale data. In addition, a recent study demonstrated that blood mercury levels were associated with visceral fat, as estimated using dual-energy X-ray absorptiometry, in healthy Korean adults.⁵⁾ Similarly, Russian investigators demonstrated a positive correlation between hair mercury levels and BMI, and also established an association between increased hair mercury levels and the prevalence of overweight and obesity, in adults.⁶⁾ However, there were some other

studies which suggested that there is no significant relationship between blood mercury concentrations and central obesity.⁷⁾ There were a few studies reported a negative associations between mercury concentrations and BMI.⁹⁾

As mentioned previously, mercury has numerous toxic effects, which could be responsible for the link between mercury exposure and overweight/obesity. However, there have been no prospective studies focusing on whether obesity would be developed or aggravated after mercury exposure. Therefore, it is unclear if elevated concentrations of mercury in the blood and tissues are a cause or an effect of obesity. Obesity has been hypothesized to be an important factor that impacts the tissue distribution and elimination of mercury. *In vivo* studies demonstrated much higher mercury concentrations in the blood and other organs in experimental animals with obesity.^{29,30)} These studies suggested that the higher blood mercury concentrations in overweight organisms could be attributed to their higher body fat mass, and to the lower capacity of mercury accumulation in the fat tissues compared to the other tissues.^{29,30)} In addition, the defective biliary excretion processes and reduced glutathione levels that accompany obesity, may impair the biliary excretion of methylmercury,^{31,32)} thereby leading to accumulation of methylmercury in the blood and multiple organs.

In this study, we demonstrated that total blood mercury concentrations were increased in adolescents with overweight/obesity, irrespective of their sex, as well as in boys with abdominal obesity. To our knowledge, this is a novel finding, in relation to pediatric populations. Only a few studies, till date, have investigated the relationship between mercury exposure and overweight/obesity, in children and adolescents. Two previously conducted studies failed to show significant correlations between total blood mercury concentrations and BMI or obesity, in a population of children and adolescents from the US^{8,9)}; these findings differ from those of the present study. A recent study, which made use of the Vaccine Safety Datalink database, demonstrated that exposure to mercury, through Thimerosal-containing hepatitis B vaccines, was associated with a higher incidence of obesity, in children from the US³³⁾; this is consistent with the present study's results. However, the study by Geier et al.³³⁾ was not adjusted for several important covariates, including ethnicity, socioeconomic status, calorie intake, and physical activity. Our study showed modest but significant associations between incidences of overweight/abdominal obesity and higher blood mercury concentrations, after controlling for socioeconomic status, calorie intake and physical activity in Korean adolescents. It is interesting to note that while total blood mercury concentrations are shown to be positively associated with increased risks of overweight and abdominal obesity in several studies conducted on the Korean population, they are not significantly or even negatively associated with the prevalence of overweight in the US population.^{8,9)} It is unclear if this discrepancy is due to the ethnicity-driven differences in the metabolism and elimination of

mercury, or due to the higher levels of mercury exposure, among Koreans (adult, 3.08 µg/L; children, 1.93 µg/L) relative to US citizens (adult, 1.7 µg/L; children, 0.76 µg/L).⁹⁾ Further studies, conducted in different countries and ethnic groups, are required, for the estimation of the inconsistencies in the study results.

Of note, the associations between blood mercury concentrations and abdominal obesity was significant only in boys, not in girls. Sex differences in tissue distribution and clearance of mercury have been demonstrated in rodent studies.³⁴⁾ However, no previous human data have reported on the sex difference in mercury accumulation within the adipose tissue, therefore, the sex difference in the relationship between the blood mercury level and abdominal obesity cannot be fully explained. We assume that one possible explanation is the sexual dimorphism in fat distribution.³⁵⁾ Men have more visceral adipose tissue and less subcutaneous adipose tissue compared with women, which is explained as effects of sex steroids. In addition, previous studies suggested that mercury predominantly accumulates in visceral adipose tissue than subcutaneous adipose tissue.⁵⁾ For these reasons, the relationship between abdominal obesity and the blood mercury might be more relevant in boys than in girls.

The present study has some limitations. First, because this was a cross-sectional study, causality could not be inferred. Second, the levels of mercury in the hair and toenails, which are the best biomarkers of long-term exposure, were not measured in the KNHANES. Third, we could not assess differences in the consumption of fish/shellfish based on obesity status, as the variable grouping of fish/shellfish types and the frequencies of food consumption were different, between 2010–2011 and 2012–2013. Additionally, the response rate to the food frequency questionnaire, among the participants, was relatively low. Nonetheless, to our knowledge, this is the first study to demonstrate the association of high blood mercury concentrations, and incidences of overweight and abdominal obesity using a representative national sample of adolescents.

In conclusion, this study provides evidence of the positive association between total blood mercury levels and incidences of overweight/abdominal obesity in Korean adolescents compared to their counterparts in Western countries. Adiposity and its distribution should be considered in studies using blood mercury concentrations. Further studies are required to reveal the possible mechanisms that lead to an association between high blood mercury concentrations and obesity.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

We thank the Korea Centers for Disease Control and Prevention for providing the data.

References

1. UNEP(United Nations Environment Programme). Global Mercury Assessment 2013: Sources, Emissions, Releases and Environmental Transport [Internet]. Switzerland: UNEP Chemicals Branch Geneva; c2013 [cited 2017 Jun 1]. Available from: <http://wedocs.unep.org/handle/20.500.11822/7984>.
2. Tan SW, Meiller JC, Mahaffey KR. The endocrine effects of mercury in humans and wildlife. *Crit Rev Toxicol* 2009;39:228-69.
3. Chen YW, Huang CF, Tsai KS, Yang RS, Yen CC, Yang CY, et al. The role of phosphoinositide 3-kinase/Akt signaling in low-dose mercury-induced mouse pancreatic beta-cell dysfunction in vitro and in vivo. *Diabetes* 2006;55:1614-24.
4. Lee S, Yoon JH, Won JU, Lee W, Lee JH, Seok H, et al. The association between blood mercury levels and risk for overweight in a general adult population: results from the Korean National Health and Nutrition Examination Survey. *Biol Trace Elem Res* 2016;171:251-61.
5. Park JS, Ha KH, He K, Kim DJ. Association between blood mercury level and visceral adiposity in adults. *Diabetes Metab J* 2017;41:113-20.
6. Skalnaya MG, Tinkov AA, Demidov VA, Serebryansky EP, Nikonorov AA, Skalny AV. Hair toxic element content in adult men and women in relation to body mass index. *Biol Trace Elem Res* 2014;161:13-9.
7. Lee BK, Kim Y. Blood cadmium, mercury, and lead and metabolic syndrome in South Korea: 2005-2010 Korean National Health and Nutrition Examination Survey. *Am J Ind Med* 2013;56:682-92.
8. Fan Y, Zhang C, Bu J. Relationship between selected serum metallic elements and obesity in children and adolescent in the U.S. *Nutrients* 2017 Feb 3;9(2). pii: E104. <https://doi.org/10.3390/nu9020104>.
9. Rothenberg SE, Korrick SA, Fayad R. The influence of obesity on blood mercury levels for U.S. non-pregnant adults and children: NHANES 2007-2010. *Environ Res* 2015;138:173-80.
10. World Health Organization. Children's exposure to mercury compounds [Internet]. Geneva (Switzerland): World Health Organization; c2010 [cited 2016 Nov 6]. Available from: http://who.int/ceh/publications/children_exposure/en/.
11. Moon JS, Lee SY, Nam CM, Choi JM, Choe BK, Seo JW, et al. 2007 Korean National Growth Charts: review of developmental process and an outlook. *Korean J Pediatr* 2008;51:1-25.
12. World Health Organization. The Asia-Pacific perspective: redefining obesity and its treatment [Internet]. Sydney (Australia): Health Communications Australia; c2000 [cited 2017 Apr 5]. Available from: <http://iris.wpro.who.int/handle/10665.1/5379>.
13. Yoo EG. Waist-to-height ratio as a screening tool for obesity and cardiometabolic risk. *Korean J Pediatr* 2016;59:425-31.
14. World Health Organization. Iron deficiency anaemia: assessment, prevention and control: a guide for programme managers [Internet]. Geneva (Switzerland): World Health Organization; c2014 [cited 2017 Apr 4]. Available from: http://www.who.int/nutrition/publications/en/ida_assessment_prevention_control.pdf.
15. Ilmiawati C, Yoshida T, Itoh T, Nakagi Y, Saijo Y, Sugioka Y, et al. Biomonitoring of mercury, cadmium, and lead exposure in Japanese children: a cross-sectional study. *Environ Health Prev Med* 2015;20:18-27.
16. Chen G, Chen X, Yan C, Wu X, Zeng G. Surveying mercury levels in hair, blood and urine of under 7-year old children from a coastal city in China. *Int J Environ Res Public Health* 2014;11:12029-41.
17. Lye E, Legrand M, Clarke J, Probert A. Blood total mercury concentrations in the Canadian population: Canadian Health Measures Survey cycle 1, 2007-2009. *Can J Public Health* 2013;104:e246-51.
18. Mortensen ME, Caudill SP, Caldwell KL, Ward CD, Jones RL. Total and methyl mercury in whole blood measured for the first time in the U.S. population: NHANES 2011-2012. *Environ Res* 2014;134:257-64.
19. Schulz C, Angerer J, Ewers U, Heudorf U, Wilhelm M; Human Biomonitoring Commission of the German Federal Environment Agency. Revised and new reference values for environmental pollutants in urine or blood of children in Germany derived from the German environmental survey on children 2003-2006 (GerES IV). *Int J Hyg Environ Health* 2009;212:637-47.
20. Kim BG, Jo EM, Kim GY, Kim DS, Kim YM, Kim RB, et al. Analysis of methylmercury concentration in the blood of Koreans by using cold vapor atomic fluorescence spectrophotometry. *Ann Lab Med* 2012;32:31-7.
21. AIST Research Center for CRM. 2007. Japanese exposure factors handbook [Internet]. Tsukuba (Japan): National Institute of Advanced Industrial Science and Technology; c2007 [cited 2017 Jun 9]. Available from: https://unit.aist.go.jp/riss/crm/exposurefactors/english_summary.html.
22. Jang JY, Jo SN, Kim SJ, Myung HN, Kim CI. Food ingestion factors of the Korean exposure factors handbook. *J Prev Med Public Health* 2014;47:18-26.
23. Duan X, Zhao X, Wang B, Chen Y, Cao S. Highlights of the Chinese exposure factors handbook(Adult). Waltham (MA): Academic Press (Elsevier), 2015:28.
24. U. S. Environmental Protection Agency. Exposure Factors Handbook: Chapter 10. Intake of Fish and Shellfish. In: Exposure factors handbook 2011 edition (Final report) [Internet]. Washington, DC: U.S. Environmental Protection Agency; c2011 [cited 2017 Jun 5]. Available from: <https://www.epa.gov/sites/production/files/2015-09/documents/efh-chapter10.pdf>.
25. Agriculture and Agri-Food Canada. Per capita disappearance: protein disappearance of animal protein sources in Canada [Internet]. Canada: Agriculture and Agri-Food Canada; c2017 [cited 2017 Jun 29]. Available from: <http://www.agr.gc.ca/eng/industry-markets-and-trade/market-information-by-sector/poultry-and-eggs/poultry-and-egg-market-information/industry-indicators/per-capita-disappearance/?id=1384971854413>.
26. European Commission's Joint Research Centre. The European exposure factors: Database access: Consumption of cooked meat and fish [Internet]. European Commission; c2002 [cited 2017 Jun 9]. Available from: <http://expofacts.jrc.ec.europa.eu/index.php?category=databases&source=results&>.
27. Moon SS. Additive effect of heavy metals on metabolic syndrome in the Korean population: the Korea National Health and Nutrition Examination Survey (KNHANES) 2009-2010. *Endocrine* 2014;46:263-71.
28. You CH, Kim BG, Kim JM, Yu SD, Kim YM, Kim RB, et al. Relationship between blood mercury concentration and waist-to-hip ratio in elderly Korean individuals living in coastal areas. *J Prev Med Public Health* 2011;44:218-25.
29. Vahter ME, Mottet NK, Friberg LT, Lind SB, Charleston JS, Burbacher TM. Demethylation of methyl mercury in different brain sites of Macaca fascicularis monkeys during long-term subclinical methyl mercury exposure. *Toxicol Appl Pharmacol* 1995;134:273-84.
30. Yamamoto M, Yanagisawa R, Motomura E, Nakamura M, Sakamoto M, Takeya M, et al. Increased methylmercury toxicity related to obe-

- sity in diabetic KK-Ay mice. *J Appl Toxicol* 2014;34:914-23.
31. Aberg B, Ekman L, Falk R, Greitz U, Persson G, Snihs JO. Metabolism of methyl mercury (203Hg) compounds in man. *Arch Environ Health* 1969;19:478-84.
 32. Geier A, Dietrich CG, Grote T, Beuers U, Prüfer T, Fraunberger P, et al. Characterization of organic anion transporter regulation, glutathione metabolism and bile formation in the obese Zucker rat. *J Hepatol* 2005;43:1021-30.
 33. Geier DA, Kern JK, Homme KG, Sykes LK, Geier MR. Thimerosal-containing hepatitis B vaccine exposure is highly associated with childhood obesity: a case-control study using the vaccine safety datalink. *N Am J Med Sci* 2016;8:297-306.
 34. Thomas DJ, Fisher HL, Sumler MR, Marcus AH, Mushak P, Hall LL. Sexual differences in the distribution and retention of organic and inorganic mercury in methyl mercury-treated rats. *Environ Res* 1986;41:219-34.
 35. White UA, Tchoukalova YD. Sex dimorphism and depot differences in adipose tissue function. *Biochim Biophys Acta* 2014;1842:377-92.