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Effect of dietary patterns on the blood/urine concentration of the selected toxic metals (Cd, Hg, Pb) in Korean children

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Abstract This study was aimed to examine the association the blood/urinary concentration of toxic metal (Hg, Pb, and Cd) with children's dietary patterns. This cross-sectional study included 1026 school children aged 8–17 years. Dietary patterns were defined using factor loading scores for 108 foods from a Semi-Quantitative Food Frequency Questionnaire. A high blood Hg level was found in boys with a high score in the 'fish' pattern ($p = 0.02$), and in girls with a high score in 'fruit' pattern ($p = 0.04$). The concentration of Pb was related to the 'imprudent' pattern in high school boys ($p = 0.02$). The effect of the 'vegetable' pattern on high excretion of urinary Cd was observed in low grade elementary ($p = 0.04$) and middle school students ($p < 0.0001$), and the effect of the 'fruit' pattern on the urinary Cd was observed in high grade elementary school students ($p = 0.02$). This study suggests that the concentration of selected toxic metals in blood/urine could be affected by children's dietary pattern.

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Introduction

Toxic metals are exposed to humans through various environments such as soil, dust, beverages, air, and foods [9]. It has been reported that toxic metals cause fatal diseases such as renal failure, cardiovascular disease, central nervous system disorder, liver failure, bone disease and cancer [11]. In addition, chronic exposure to toxic metals is especially harmful to children [20] and pregnant women [4]. Excess Cadmium (Cd) exposure has adverse health effects on human beings and contributes to a well-defined spectrum of diseases [6]. Epidemiologically, it has been reported a relationship between the toxic metal level and chronic disease or health problem: Cd and the lung cancer [34], and urinary Cd and the breast cancer [29]; mercury (Hg) and neurotoxicity among children [15]; and Pb exposure and nervous, hematopoietic, hepatic, and renal systems resulting in serious disorders [14].

Mercury, lead, and cadmium were observed in various resources including water, food, dust, soil or other industrial wasters, etc. [23]. Among those resources, food consumption could be a main sources [31] and easily and frequently exposed to children [28, 41]. The German Lexnken Project supplied that specific food including cereal, fish, and vegetable was main sources of Cd exposure regardless of residence or country [31]. In addition, the Belgium study reported the most highly contaminated foods by Cd were cereal products and potatoes [40]. For the Korean foods, rice [27] and salted radishes [10] were reported as main contributors to daily consumption of Cd. It also has been reported that methyl Hg (MeHg) concentration is affected by fish consumption in Korea [43], and generally accumulated in the human body with a fish consumption [12].

Korea Health Statistics 2010 has reported that adults in Korea showed approximately 2–4 times higher blood concentration of Hg and Pb than those in America, suggested a high prevalence of toxic metal exposure in Korea. Considering their behavior, diet, metabolism, and physiological characteristics, children are very sensitive to toxic metal exposure [28]. As exposed to toxic metal, children's body was more rapidly absorbed the toxic metals than adult was Wigle et al. [41]. Even a small level of exposure to toxic metals could seriously affect children's systems exerting harmful effect to their health [35], including neurotoxicity and neurodevelopmental risks [15]. Regardless of those noted risks to children, there has been a lack of research examining the effect of dietary toxic metal exposure on the health, especially for children and adolescents. Therefore, this study is aimed to observe the distribution of the blood/urine toxic metal concentration (Hg, Pb, Cd) and to examine the effect of dietary patterns on the blood/urine toxic metal concentration among school children in Korea.

Materials and methods

Study design and subjects

This study used data from the Korean Research Project on the Integrated Exposure Assessment to Hazardous Materials for Food Safety (KRIEFS) which was designed as a population-based cross-sectional study (Korea Food and Drug and Administration). A total of 1111 children and adolescents aged 7–18 years were recruited by school-based cluster sampling during 2010–2011 school year; elementary (1st to 3rd grade aged 7–9 years, LGES; 4th to 6th grade aged 10–12 years, HGES), middle school aged 13–15 years, and high school aged 16–18 years. The participated students also classified by residence: metropolitan (210 boys and 221 girls), urban (181 boys and 143 girls),

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and rural (179 boys and 177 girls). In addition, the study sites were classified as interior (347 boys and 325 girls) and coastal (223 boys and 216 girls) depending on whether the area is located in seaside or not.

After exclusion of subjects without dietary and blood toxic metal information (11 boys and 16 girls) and with abnormal total energy intake [$\leq$ 800 kcal or $\geq$ 4000 kcal in boys (n = 39) and $\leq$ 500 kcal or $\geq$ 3500 kcal in girls (n = 19)], one thousand twenty six subjects (520 boys and 506 girls) participated in the study (Fig. 1). The study protocol was approved by the ethics committee of Dankook University Hospital (KUHIRB2010-04-0093).

The parents of participating children provided written consent for participation in this study. Personal interviews and sample collections were performed with a structured questionnaire by trained interviewers, who had similar group instruction and provided individual quality control. The survey questionnaire included information about demographic characteristics, parent's education level, smoking habits, and alcohol consumption, residence, past medical history, and diet.

Measurement of toxic metal in blood and urine

Blood sampling was performed by experienced nurses who were educated for the standard sampling protocol. Whole blood collected into the heparin-treated tubes was aliquoted into several cryotubes and then stored at $-$ 80 °C.

Concentration of total Hg in whole blood was presented in our previous study [23] using a thermal decomposition (gold) amalgamation atomic absorption spectrophotometer (TDA/AAS) designed for direct Hg analysis (Direct MercuryAnalyzer-80; Milestone Inc., Italy) based on the US Environmental Protection Agency (EPA) Method 7473. Validation of measurement of total Hg was done in terms of linearity and limit of detection (LOD). Calibration curve was drawn with 0 (blank), 0.05, 0.1, 0.2, 0.5, 1, 2 and 5 ng using quartz boats with standards to pre-adjust each of its concentrations to obtain a linearity of $R^2 = 0.9998$. The LOD was calculated using the equation LOD = 3.14 9 r, where r was the standard deviation of the seven measurements of 0.5 lg/L of Hg standard. The LOD for total Hg
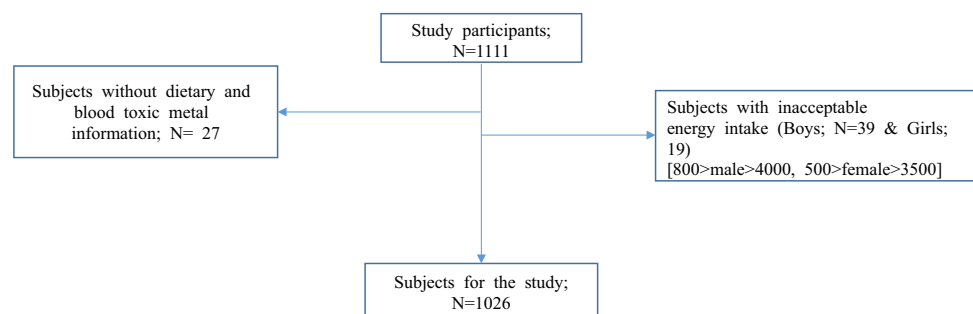
was established as 0.2 lg/L. The experiment was validated by the standard reference material (SRM 955c, Level 2) from the National Institute of Standards Technology (NIST). The mean and standard deviation of SRM analysis were 5.17 $\pm$ 0.35 lg/L (n = 15) for SRM level 2 (reference value 4.95 $\pm$ 0.76 lg/L). 2.16% of LOD sample value were below limit of blank (LOB). LOB was calculated as: LOB = mean (blank) + 1.645 (SD; blank).

Concentration of Pb and Cd in whole blood was determined using graphite furnace atomic absorption spectrophotometer (GFAAS, iCE 3000 series, Thermo scientific, USA) with Zeeman background correction. The calibration curve was drawn between 0.5 and 20 µg/L to obtain a linearity of $R^2 = 0.9999$ for Pb and $R^2 = 0.9998$ for Cd. The LOD was calculated using the equation LOD = 3.14 $\times$ σ, where σ was the standard deviation of the seven measurements of 0.5 µg/L of Pb and Cd standard. The LOD for Pb and Cd were established as 0.2 and 0.1 µg/L, respectively. Also, the LOD for urinary Cd was established as 0.3 µg/L. The mean and standard deviation of SRM analysis were 13.85 $\pm$ 0.84 µg/L (n = 5) for Pb analysis and 1.98 $\pm$ 0.13 µg/L (n = 3) for Cd analysis for SRM level 2 (reference value 13.95 $\pm$ 0.08 µg/L of Pb, 2.14 $\pm$ 0.24 µg/L of Cd). 1.16 and 3.02% of LOD sample value were below LOB for Pb and Cd respectively.

Assessment of dietary intake

Semi-Quantitative Food-Frequency Questionnaire (SQFFQ) was used to collect dietary data which had nine categories (almost never, once a month, 2–3 times a month, 1–2 times a week, 3–4 times a week, 5–6 times a week, once a day, twice a day, and more than 3 times a day) and 3 serving size (less than one vs one vs more than one serving size). Nutrient intake was calculated from the reported usual intake of 108 food items based on the Food Composition Table in the Recommended Dietary Allowances for Koreans (The Korean Nutrition Society). Considering the seasonal variation for fruit consumption, the duration (monthly) of fruit consumption was converted by the interviewer into an annual average value and recorded. The SQFFQ used in the study was previously developed and

Fig. 1 Participant flow chart

Study participants; N=1111

Subjects without dietary and blood toxic metal information; N= 27

Subjects with inacceptable energy intake (Boys; N=39 & Girls; 19) [800>male>4000, 500>female>3500]

Subjects for the study; N=1026

validated with nutrients by Lim and Oh [21]. The correlation coefficients of this SQFFQ ranged from 0.3 to 0.6 for validity and from 0.6 to 0.8 for reproducibility.

Dietary pattern derivation

Factor analysis was used to derive dietary patterns and to determine factor loadings for 108 individual foods from SQFFQ. The factors were rotated with Varimax rotation to maintain uncorrelated factors and enhance interpretability. We examined both the scree plots and factors on their own to see which set of factors most interpretably described the distinct food consumption patterns after adjustment for total energy intake. The factor score for each pattern was calculated by summing intakes of all food groups weighted by their factor loadings. A factor score was then calculated for each subject for each of the four factors, in which the standardized intakes of each of the 108 foods were weighted by their factor loadings and summed. The sums were standardized again [(score − mean score)/standard deviation of score]. From these analyses, four dietary patterns with the highest loadings were identified and included as the list of dietary patterns given in Table 1. Factor loadings were calculated for each food across the four dietary patterns. Factors were thereby interpreted as dietary patterns and named after the food groups having the highest loading (loading > 0.30). The 'vegetable' pattern and the 'fruit' pattern was heavily loaded with vegetables and fruits respectively. The 'imprudent' pattern was characterized by high intakes of fast food and low intakes of milk and tofu. The 'fish' pattern was heavily loaded with both fish and shell fish (Table 1).

Statistical analyses

Differences in etiological characteristics between subgroups were found based on the Least Square Mean (LSM) using general linear model and Turkey–Kramer post hoc test [18] performed when comparing among more than three subgroups at a time. To evaluate the association between each dietary pattern (factor score) and the concentration of toxic metal in blood (Hg, Pb, and Cd) and urine (Cd), multiple regression was performed after adjustment for age (years), gender (boys or girls), BMI (in kg/m^2; ≤ 23 or > 23), city size (metropolitan, urban or rural), residence area (interior or seaside), parents education level (low, combine or high) and family income (in USD; ≤ 99, 100–199, 200–399 or ≥ 400). An alpha level of less than 0.05 was accepted in all tests as statistically significant. Statistical significance was evaluated using a two-sided design with alpha set to 0.05 and analysis conducted by SAS version 9.4; SAS Institute Inc, Cary, NC.

Results and discussion

General characteristics and dietary patterns

The distributions of general characteristics of the four derived dietary patterns are presented in Table 2. Approximately, 27.3 and 26.7% of study participants were middle (average 13 years old) and high school (average 16 years old) students, respectively. Middle school students showed dietary factor scores of high 'vegetable' and low 'fruit' and 'fish' patterns. The low scores 'vegetable' and high 'imprudent' and 'fish' patterns was observed in high school students. Obese students reported higher score of 'vegetable' and lower score of 'imprudent' pattern compared to non-obese students which could be expected in cross-sectional study. Although no children observed in different of each dietary pattern score as city size and residence area, students in costal were higher score in 'fruit' pattern than students in interio. In addition, the 'fruit' pattern was observed a cross-sectional association with parents' education level; when both father and mother had higher education, their children was shown in the high score of 'fruit' pattern.

No children and adolescents who participated in this study exceeded the level of PTWI for Hg and Pb (for Hg, 4 µg/kg body-weight/week; and for Pb, 25 µg/kg body-weight/week); however, six children exceeded PTWI of Cd (7 µg/kg body-weight/week) (data not shown in table). The comparisons of toxic metal concentrations in blood/urine based on the different dietary patterns are shown in Tables 3 and 4 presents the information stratified by age group.

Mercury and dietary patterns

A high concentration of blood Hg was shown in children with high scores in the 'fish' pattern (Hg), predominantly in boys. On the other hand, the blood Hg was higher in girls with high score of 'fruit' pattern than with the low score (Table 3). A larger effect of the 'fruit' pattern on the high concentration of blood Hg was observed in low grade elementary school students than in the other grades. Noeffect of the 'fish' pattern on blood Hg was observed in Korean children, except of borderline significance in HGES ($p = 0.061$) or high school students ($p = 0.059$) (Table 4). Inorganic Hg compounds (IHg) can be converted to MeHg which has higher toxicity. The bio-accumulative properties of MeHg make aquatic species vulnerable and top level predators such as humans are especially susceptible to high MeHg exposure [24]. It was reported that the Hg intake of Korean adults is 18.8 µg/day, and more than 90% of Hg exposure results from food

Table 1 Dietary patterns in Korean children and adolescents

No.	Factor 1		Factor 2		Factor 3		Factor 4	
	Food items	FL	Food items	FL	Food items	FL	Food items	FL
1	Radish	.59	Watermelon	.69	Chocolate	.40	White fish with roasted or boiled	.60
2	Bean sprout	.58	Grape	.68	Hamburger	.37	Blue color fish with fried or pan-fried	.59
3	Chinese cabbage	.56	Strawberry	.67	Pizza	.35	White fish with fried or pan-fried	.51
4	Vegetable in Japchae	.55	Apple	.67	Soda	.30	Blue color fish with roasted or boiled	.43
5	Balloon flower/Deodeok	.53	Peach/plum	.65	Milk	− .33	Shell fish	.32
6	Spinach	.52	Citrus/orange	.64	Tofu	− .37	Dumpling soup	.30
7	bracken/sweet potato vines/taro stem	.47	Melon	.62	Mixed cereal	− .47		
8	Mushroom	.46	Pear	.60				
9	Vegetable in Bibimbap	.43	Banana	.53				
10	Radish kimchi	.42						
11	Other green veg.	.40						
12	Squash	.39						
13	Garlic	.39						
14	Soy paste	.34						
15	Perilla leaf	.33						
16	Onion	.33						
17	Lettuce/cabbage	.33						
18	Tomato	.32						
19	Other kimchi	.32						
20	Cucumber	.32						

FL: Factor load in each dietary pattern

intake [25]. The infrastructural environment of Korea, such as peninsula, lakes, rivers, and tributaries, allow Koreans to be easily exposed to seafood including various kinds of fish. Blood Hg concentration of Korean adults is 5–8 times higher than adults in other countries [26]. In a domestic survey of Hg exposure factors in elementary school students, the preference for and the amount of fish intake were positively related to blood Hg concentration [16]. Tian et al. [37] reported in a Canadian study that sea food, especially fish, was positively associated with biomarkers of mercury in children. Blood Hg concentration showed significantly positive association with "fish" pattern in our study, consistent to other studies [16, 30, 37] (UnitedNationsEnvironmentProgramme.). One Japan study reported that the higher intake of raw fishes and shellfishes, especially predatory fish such as tuna, is main contributor to significantly increase total Hg concentration in adults compared to other countries [30]. Based on the US FDA monitoring program (1990–2010), some predator fish species such as shark, swordfish, and fresh and frozen tuna exceeded the tolerance of 0.5 ppm in US adults (U.S. Food and Drug Administration).

On the other hand, Hong et al. suggested the ameliorated effect of high frequency consumption of vegetable and fruit on the low concentration of blood Hg [32], supported by

Beyrouty and Chan [2]; co-consumption of vitamin E and selenium supplement can reduced the toxicity of methyl mercury. Nevertheless, this study was not shown the beneficial effect of the 'vegetable' and 'fruit' pattern; even students with high score of 'fruit' pattern was observed the increased blood Hg concentration. Nevertheless, we couldn't suggested the harmful effect of 'fruit' pattern on blood Hg concentration, because this presented study was focused on the dietary pattern not each food items or groups, the high score in 'fruit' pattern was positively correlated with 'fish' pattern ($r = 0.4$).

Lead and dietary patterns

The 'imprudent' pattern was observed in positive association with the concentration of lead (Pb) in boys (Table 3). In particular, the concentration of blood Pb was highly shown in high school students with low score of 'vegetable' pattern or high score of 'imprudent' pattern (Tables 4, 5). Childhood exposure of lead negatively affect cognitive development and result in increased behavioral problem [22]. According to our previous report [19], vegetables such as radish kimchi, cooked bean sprouts, and soybean paste soup with turnip greens had the highest Pb concentrations. Consistent with report from European

Table 2 Comparison of demographic characteristics by dietary pattern

	All (N = 1026)	Vegetable pattern						Fruit pattern					
		Q1	Q2	Q3	Q4	Q5	Score LSM* ± SE	Q1	Q2	Q3	Q4	Q5	Score LSM ± SE
Grade of school (%)													
LGES	220 (20.4)	11.4	19.1	32.7	24.1	12.7	0.05 ± 0.10[a]	5.0	17.7	28.6	26.8	21.8	0.08 ± 0.09[a]
HGES	252 (20.6)	19.4	23.4	17.1	21.0	19.1	0.07 ± 0.09[ab]	12.3	23.0	22.2	21.1	21.4	− 0.11 ± 0.09[a]
Middle school	280 (27.3)	12.9	16.4	18.2	22.9	29.6	0.43 ± 0.08[c]	31.4	21.1	20.4	14.6	12.5	− 0.36 ± 0.08[b]
High school	274 (26.7)	34.7	21.5	13.9	13.1	16.8	− 0.19 ± 0.08[ad]	27.4	17.9	11.3	18.6	24.8	0.01 ± 0.08[a]
Gender (%)													
Boys	520 (50.7)	25.8	21.2	18.6	14.2	20.2	0.01 ± 0.07	28.1	22.1	15.6	16.9	17.3	− 0.18 ± 0.07
Girls	506 (49.3)	14.0	19.0	21.1	26.1	19.8	0.17 ± 0.07*	11.7	17.8	24.9	22.9	22.7	− 0.02 ± 0.07*
BMI (kg/m^2)													
≤ 23	895 (87.2)	20.5	19.4	20.1	21.1	18.9	− 0.01 ± 0.06	18.3	20.2	21.0	20.7	19.8	− 0.07 ± 0.05
> 23	131 (12.8)	16.8	24.4	18.3	13.0	27.5	0.19 ± 0.10*	31.3	18.3	14.5	14.5	21.4	− 0.13 ± 0.10
City size													
Metropolitan	400 (39.0)	20.8	17.7	21.0	19.5	21.0	0.15 ± 0.08	19.0	18.4	19.8	20.5	22.3	− 0.08 ± 0.08
Urban	307 (29.9)	23.1	19.5	19.0	19.2	19.2	0.05 ± 0.08	22.5	19.5	17.6	20.2	20.2	− 0.04 ± 0.08
Rural	319 (31.1)	16.0	23.5	19.4	21.7	19.4	0.07 ± 0.08	18.8	22.3	23.2	18.8	16.9	− 0.17 ± 0.08
Residence area (%)													
interior	628 (61.2)	20.2	21.8	17.8	19.8	20.4	0.05 ± 0.07	22.0	20.2	19.9	19.4	18.5	− 0.17 ± 0.07
Seaside	398 (38.8)	19.6	17.3	23.1	20.6	19.4	0.13 ± 0.08	16.8	19.6	20.6	20.6	22.4	− 0.02 ± 0.08*
Parents education													
Low	288 (31.1)	23.6	17.4	19.1	18.7	21.2	0.09 ± 0.08	23.6	21.2	24.0	16.3	14.9	− 0.17 ± 0.08[a]
Combine	218 (23.5)	18.4	21.1	20.6	20.2	19.7	0.08 ± 0.09	22.5	21.1	19.7	19.7	17.0	− 0.15 ± 0.09[ab]
High	421 (45.4)	19.2	20.2	20.2	21.4	19.0	0.11 ± 0.08	15.4	17.8	19.5	21.2	26.1	0.04 ± 0.08[c]
Family income[†]													
≤ 99	33 (3.50)	21.2	18.2	18.2	18.2	24.2	0.06 ± 0.21	42.4	12.1	15.2	18.2	12.1	− 0.45 ± 0.20
100–199	134 (14.2)	17.9	24.6	22.4	18.7	16.4	0.01 ± 0.10	20.9	25.4	21.6	15.7	16.4	− 0.04 ± 0.09
200–399	414 (43.9)	21.0	17.9	18.6	20.8	21.7	0.08 ± 0.06	19.6	19.8	22.2	20.8	17.6	− 0.05 ± 0.06
400 ≤	362 (38.4)	18.2	22.6	21.0	20.4	17.7	0.03 ± 0.07	16.9	18.4	18.0	21.3	25.4	0.04 ± 0.06

	Imprudent pattern						Fish pattern					
	Q1	Q2	Q3	Q4	Q5	Score LSM ± SE	Q1	Q2	Q3	Q4	Q5	Score LSM ± SE
Grade of school (%)												
LGES	20.5	25.4	22.7	23.2	8.2	− 0.32 ± 0.10[a]	14.1	18.2	27.7	33.6	6.40	0.02 ± 0.08[a]
HGES	29.0	23.0	21.0	15.5	11.5	− 0.42 ± 0.10[ab]	19.8	25.0	25.4	20.7	9.10	− 0.08 ± 0.08[ab]
Middle school	20.4	20.0	20.4	20.6	18.6	− 0.07 ± 0.09[ac]	38.6	28.5	17.5	10.0	5.40	− 0.38 ± 0.07[c]
High school	11.0	12.8	17.2	20.7	38.3	0.32 ± 0.08[d]	5.8	8.1	11.7	18.6	55.8	0.81 ± 0.07[d]
Gender (%)												
Boys	25.2	18.1	19.4	15.6	21.7	− 0.19 ± 0.08	26.0	20.1	17.7	17.7	18.5	− 0.01 ± 0.06
Girls	14.6	21.9	21.0	24.5	18.0	− 0.06 ± 0.08*	13.8	19.9	22.5	22.3	21.5	0.20 ± 0.06*
BMI (kg/m^2)												
≤ 23	19.8	19.8	20.6	19.6	20.2	0.00 ± 0.06	20.6	20.1	20.0	20.4	18.9	0.06 ± 0.05
> 23	21.4	21.4	17.6	22.0	17.6	− 0.25 ± 0.11*	16.0	19.1	20.6	16.8	27.5	0.13 ± 0.08
City size												
Metropolitan	19.0	22.2	19.8	20.5	18.5	− 0.13 ± 0.09	19.5	23.0	18.5	19.7	19.3	0.07 ± 0.07
Urban	23.1	18.9	21.8	18	18.2	− 0.17 ± 0.09	21.8	19.2	18.6	16.3	24.1	0.05 ± 0.07
Rural	18.2	18.2	19.1	21.3	23.2	− 0.08 ± 0.09	18.8	16.9	23.5	23.9	16.9	0.16 ± 0.06
Residence area (%)												

Table 2 continued

	Imprudent pattern						Fish pattern					
	Q1	Q2	Q3	Q4	Q5	Score LSM ± SE	Q1	Q2	Q3	Q4	Q5	Score LSM ± SE
Interior	21.8	20.0	20.7	19.3	18.2	− 0.17 ± 0.08	21.2	21.0	19.6	18.9	19.3	0.05 ± 0.06
Seaside	17.1	19.8	19.4	21.1	22.6	− 0.08 ± 0.08	18.1	18.3	20.9	21.6	21.1	0.13 ± 0.06
Parents education												
Low	18.1	15.9	17.7	21.9	26.4	− 0.04 ± 0.09	21.5	18.1	20.5	17	22.9	0.11 ± 0.07
Combine	18.8	19.7	25.2	18.4	17.9	− 0.15 ± 0.10	22.5	19.3	18.8	21.5	17.9	0.06 ± 0.07
High	23.0	23.3	19.2	19.8	14.7	− 0.17 ± 0.08	15.9	21.4	20.9	22.6	19.2	0.10 ± 0.06
Family income[†]												
≤ 99	27.3	12.1	9.1	18.2	33.3	− 0.19 ± 0.23	30.3	12.1	21.2	21.2	15.2	0.31 ± 0.16
100–199	11.9	17.9	27.6	21.0	21.6	− 0.00 ± 0.11	17.2	24.6	21.6	22.4	14.2	− 0.03 ± 0.08
200–399	20.5	22.2	19.6	20.1	17.6	− 0.10 ± 0.07	19.1	20.8	22.5	21.7	15.9	0.01 ± 0.05
400 ≤	22.4	20.4	20.2	17.9	19.1	− 0.17 ± 0.07	20.7	19.6	17.7	18.2	23.8	0.07 ± 0.05

LSM*: least squares means of each effect by demographic characteristics, a, ab, c, ad, ac, d: post hoc test of Tukey–Kramer adjustment, [†]million won/month

LGES low grade elementary school, *HGES* high grade elementary school

country, higher grade students were related to lower Pb concentration, which might cause dilution of the Pb concentration in blood because of the body size [3]. It was reported that Pb were introduced into the food through the food processing [42]. In this study, Pb were higher as the score of 'imprudent' pattern increased, especially in high school students, supported by Wyasu's study [42]. In particular, the 'imprudent' pattern was related to the low Ca intake in our study (data not in table), which could increase the absorption of Pb [7]. Calcium rich food, such as banana peels [33], and commercial citric acid [5] removed 87.44 and 100% of Pb from automotive waste water, suggesting that the consumption of fruits could ameliorate the Pb toxicity. In particular, students with parents in low education level or low house-income are exposed to higher "imprudent" pattern and lower "fruit" pattern in the present study, which could suggest to increase the chance of exposure to lead toxicity.

Cadmium and dietary patterns

Although there was no significant difference in blood Cd concentration among all participants, urinary Cd excretion showed strongly positive association with the high score of 'vegetable' pattern, especially among girls (Table 2). High school student with the low score of 'vegetable' pattern or high score of 'imprudent' pattern was shown in a high excretion of blood Cd among high school students (Tables 4, 5). Although the middle school students with high score of 'fish' pattern had a low concentrations of blood Cd, no different concentration of blood Cd was observed in students for each dietary pattern score. On the

other hand, the urinary Cd excretion was lower among low grade elementary school and middle school students who had a high scores of 'vegetable' pattern. Considering that urinary Cd is a biomarker of body burden but blood Cd is indicator of the on-going Cd exposure in the body, the high excretion of urinary Cd could be considered a possible benefit of toxic metal exposure reduced exposure of the toxic metal among children with high score of 'vegetable' and 'fruit' pattern. Further, regarding the excretion of Cd, exposure to Cd (II) increases nitric oxide (NO) and anthocyanins (Ay) can reduce NO contents by directly scavenging, suggesting that Ay from blueberry extract, which is a fruit that may be useful as a therapeutic agent in combating Cd (II)-induced tissue injury [8]. Degreased coffee beans, which contain sulfur and small amounts of calcium, can remove harmful metal ions including Cd (II) [13]. For the urinary Cd excretion, we found the association with the 'vegetable' pattern in predominantly female students. Even that, it is difficult to suggest the effect was observed in only girls, because the absolute amount of vegetable intake of boys was lower than that among girls. Therefore, the effect of the 'vegetable' pattern on the urinary toxic metal excretion should be evaluated with a number of male subjects.

Limitations and strength of the study

Although this study used relatively large number of children and the experts measured toxic metal concentration in both urine and blood, this study has several limitations. First, causal effects of dietary patterns on blood and urinary

Table 3 Comparison of blood and urine level by dietary pattern

	Total							Boys							Girls						
	Q1	Q2	Q3	Q4	Q5	β*	p	Q1	Q2	Q3	Q4	Q5	β*	p	Q1	Q2	Q3	Q4	Q5	β*	p
Vegetable pattern																					
Hg (μg/L)	2.51§	2.53	2.34	2.37	2.55	0.02	0.73	2.65	2.31	2.34	2.42	2.50	0.01	0.93	2.26	2.80	2.34	2.32	2.59	0.02	0.83
Pb (μg/dL)	1.47	1.46	1.50	1.53	1.51	0.03	0.12	1.64	1.63	1.68	1.61	1.70	0.04	0.18	1.30	1.30	1.31	1.40	1.30	0.01	0.56
Cd (μg/L)	0.35	0.34	0.35	0.38	0.37	0.01	0.31	0.34	0.32	0.36	0.42	0.38	0.02	0.15	0.37	0.36	0.34	0.35	0.37	0.00	0.98
Urinary Cd (μg/g)	0.38	0.41	0.38	0.40	0.44	**0.14**	**<.0001**	0.33	0.35	0.35	0.29	0.33	0.00	0.69	0.39	0.47	0.42	0.48	0.55	**0.30**	**<.0001**
Fruit pattern																					
Hg (μg/L)	2.45	2.44	2.34	2.50	2.57	0.04	0.48	2.48	2.60	2.25	2.43	2.46	− 0.03	0.68	2.30	2.24	2.39	2.58	2.67	**0.17**	**0.04**
Pb (μg/dL)	1.50	1.52	1.47	1.50	1.48	− 0.01	0.47	1.69	1.70	1.65	1.59	1.62	− 0.02	0.46	1.21	1.35	1.28	1.41	1.34	0.02	0.44
Cd (μg/L)	0.38	0.33	0.37	0.33	0.37	− 0.01	0.57	0.38	0.34	0.38	0.33	0.36	− 0.01	0.55	0.38	0.32	0.37	0.33	0.38	0.00	0.96
Urinary Cd (μg/g)	0.35	0.45	0.38	0.37	0.46	0.03	0.06	0.30	0.35	0.32	0.33	0.38	0.03	0.03	0.37	0.54	0.44	0.42	0.53	0.04	0.26
Imprudent pattern																					
Hg (μg/L)	2.68	2.35	2.39	2.50	2.38	− 0.08	0.08	2.82	2.36	2.27	2.28	2.43	− 0.12	0.06	2.48	2.34	2.50	2.65	2.27	− 0.05	0.43
Pb (μg/dL)	1.37	1.51	1.51	1.51	1.59	**0.05**	**0.01**	1.54	1.64	1.71	1.71	1.72	**0.04**	**0.09**	1.20	1.37	1.30	1.31	1.44	0.04	0.06
Cd (μg/L)	0.37	0.37	0.35	0.35	0.35	− 0.01	0.54	0.34	0.34	0.36	0.39	0.37	0.00	0.73	0.39	0.38	0.34	0.34	0.34	− 0.01	0.28
Urinary Cd (μg/g)	0.38	0.41	0.39	0.34	0.48	0.02	0.10	0.32	0.36	0.36	0.30	0.33	0.00	0.90	0.42	0.47	0.43	0.41	0.63	0.04	0.11
Fish pattern																					
Hg (μg/L)	2.31	2.12	2.67	2.46	2.74	**0.15**	**0.01**	2.48	2.11	2.37	2.35	2.35	**0.19**	**0.02**	2.05	2.17	2.90	2.52	2.47	0.11	0.22
Pb (μg/dL)	1.44	1.49	1.50	1.53	1.51	− 0.02	0.40	1.57	1.64	1.66	1.75	1.69	0.02	0.61	1.33	1.37	1.33	1.29	1.32	− 0.04	0.12
Cd (μg/L)	0.36	0.37	0.32	0.39	0.34	− 0.01	0.41	0.34	0.40	0.32	0.40	0.33	− 0.01	0.64	0.39	0.34	0.32	0.40	0.36	− 0.01	0.58
Urinary Cd (μg/g)	0.37	0.49	0.40	0.36	0.39	− 0.01	0.78	0.31	0.35	0.35	0.31	0.40	0.01	0.70	0.42	0.62	0.44	0.42	0.43	− 0.01	0.73

β*: parameter of blood/urine level estimation value for factor score, p: p-trend of factor adjusted for age group, gender, BMI, city size, residence area, parents education level, family income, §least squares means of blood and urine level by dietary pattern (all such values)

Bold values are statistically significant

Table 4 Comparison of blood and urine level by dietary pattern in elementary school students

	LGES							HGES						
	Q1	Q2	Q3	Q4	Q5	β*	p	Q1	Q2	Q3	Q4	Q5	β*	p
Vegetable pattern														
Hg (µg/L)	2.46§	2.62	2.29	2.14	2.39	−0.14	0.41	2.38	2.57	2.38	2.19	2.46	−0.06	0.52
Pb (µg/dL)	1.59	1.65	1.63	1.54	1.53	−0.02	0.83	1.58	1.56	1.63	1.65	1.56	−0.04	0.31
Cd (µg/L)	0.35	0.34	0.30	0.26	0.36	0.00	0.99	0.27	0.32	0.29	0.39	0.34	0.01	0.53
Urinary Cd (µg/g)	0.40	0.45	0.42	0.40	0.51	**0.09**	**0.04**	0.44	0.46	0.42	0.56	0.36	0.00	0.90
Fruit pattern														
Hg (µg/L)	2.53	2.19	2.18	2.32	2.69	0.21	0.03	2.15	2.44	2.43	2.28	2.59	0.11	0.29
Pb (µg/dL)	1.22	1.60	1.57	1.67	1.63	0.02	0.74	1.75	1.60	1.57	1.53	1.59	− 0.05	0.24
Cd (µg/L)	0.28	0.25	0.30	0.28	0.41	0.03	0.17	0.35	0.32	0.38	0.26	0.31	− 0.03	0.23
Urinary Cd (µg/g)	0.36	0.52	0.44	0.41	0.39	− 0.02	0.45	0.40	0.49	0.41	0.36	0.56	**0.07**	**0.02**
Imprudent pattern														
Hg (µg/L)	2.24	2.13	2.22	2.71	2.64	0.15	0.13	2.72	2.31	2.23	2.21	2.34	− 0.15	0.12
Pb (µg/dL)	1.37	1.70	1.61	1.69	1.55	0.02	0.72	1.52	1.62	1.62	1.57	1.71	0.05	0.20
Cd (µg/L)	0.30	0.36	0.28	0.32	0.25	− 0.01	0.73	0.35	0.32	0.30	0.28	0.35	− 0.02	0.26
Urinary Cd (µg/g)	0.42	0.52	0.41	0.40	0.34	− 0.02	0.52	0.43	0.47	0.49	0.41	0.47	0.00	0.86
Fish pattern														
Hg (µg/L)	2.59	1.84	2.48	2.43	2.36	0.10	0.64	2.28	2.12	2.51	2.48	2.92	0.30	0.06
Pb (µg/dL)	1.48	1.60	1.68	1.61	1.43	0.02	0.84	1.53	1.56	1.65	1.62	1.62	0.00	1.00
Cd (µg/L)	0.34	0.35	0.24	0.32	0.40	− 0.01	0.74	0.32	0.36	0.29	0.37	0.20	− 0.04	0.31
Urinary Cd (µg/g)	0.36	0.44	0.44	0.42	0.58	0.07	0.16	0.45	0.52	0.44	0.41	0.42	− 0.06	0.24

β*: parameter of blood/urine level estimation value for factor score, p: p-trend of factor adjusted for age group, gender, BMI, city size, residence area, parents education level, family income, §least squares means of blood and urine level by dietary pattern (all such values)

LGES: low grade elementary school, HGES: high grade elementary school

Bold values are statistically significant

toxic metal concentrations could not be explored as this is a cross-sectional study. Second, we could not take smoking habits into consideration for children and adolescents. Although the survey questionnaire included smoking habits for children and adolescents, we did not find any differences between case and control groups. This could contribute to information bias, because children and adolescents under 20 years old were prohibited from smoking in Korea and they would not report smoking habit honestly. As such, we could not compare the smoking effect on the level of toxic metal in blood/urine. Third, contribution of dietary Pb to the blood concentration in the body would be lower than that from environmental conditions as Pb is known to be more of an occupational and environmental exposure factor including lead-based paint, water from leaded pipes and air pollution than a dietary one. Forth, the dietary Cd concentration would be affected by soil contamination, because vegetables and fruits absorb and accumulate nutrition from soil. Korea, however, is small country and the subjects were evenly distributed, a primary and common non-occupational source of Cd would

not be different by area and city. Fifth, although the iron and menarche status of subjects affects the blood concentration level of certain metals and iron deficiency induced metal transporters may play a role for Cd, but not for Hg and Pb [1], we could not present it because of the unavailability of the information.

In conclusion, this study suggests a possible effect of school children's dietary patterns on blood/urinary toxic metal (Cd, Pb, and Hg) concentrations by gender and age group in Korea. Urinary Cd excretion was higher in younger and/or female students with relatively higher factor scores for 'vegetable' dietary patterns. Conversely, high school students with high factor score of 'imprudent' pattern showed high concentration of blood Pb. Blood Hg concentration showed predictively positive association with 'fish' pattern. Although children and adolescents in Korean were within the appropriate ranges based on the PTWI standard, it is valuable to consider the harmful effects of toxic metal depending on the dietary patterns of children and adolescents.

Table 5 Comparison of blood and urine level by dietary pattern in middle and high school students

	Middle school							High school						
	Q1	Q2	Q3	Q4	Q5	β*	p	Q1	Q2	Q3	Q4	Q5	β*	p
Vegetable pattern														
Hg (μg/L)	2.23	2.33	2.03	2.72	2.58	0.10	0.10	2.77	2.59	2.71	2.32	2.60	− 0.02	0.89
Pb (μg/dL)	1.64	1.42	1.45	1.58	1.56	0.01	0.66	1.21	1.26	1.36	1.43	1.29	0.11	0.00
Cd (μg/L)	0.42	0.36	0.40	0.36	0.38	0.00	0.74	0.39	0.35	0.40	0.51	0.41	0.02	0.39
Urinary Cd (μg/g)	0.32	0.44	0.38	0.39	0.52	**0.27**	**<.0001**	0.30	0.33	0.28	0.24	0.34	− 0.01	0.57
Fruit pattern														
Hg (μg/L)	2.53	2.28	0.18	2.54	2.69	0.03	0.79	2.57	2.76	2.39	2.99	2.47	− 0.06	0.55
Pb (μg/dL)	1.55	1.54	1.47	1.50	1.56	0.00	0.94	1.22	1.39	1.33	1.32	1.23	− 0.01	0.72
Cd (μg/L)	0.42	0.34	0.37	0.36	0.39	− 0.02	0.31	0.40	0.40	0.46	0.41	0.38	− 0.01	0.61
Urinary Cd (μg/g)	0.36	0.48	0.35	0.40	0.65	0.13	0.05	0.28	0.31	0.31	0.32	0.31	0.01	0.37
Imprudent pattern														
Hg (μg/L)	2.71	2.30	2.40	2.41	2.28	− 0.12	0.07	3.09	2.55	2.68	2.62	2.54	− 0.14	0.18
Pb (μg/dL)	1.49	1.51	1.51	1.52	1.61	0.01	0.65	1.24	1.17	1.26	1.24	1.37	**0.07**	**0.02**
Cd (μg/L)	0.41	0.37	0.42	0.33	0.38	0.00	0.82	0.33	0.42	0.39	0.44	0.40	0.00	0.95
Urinary Cd (μg/g)	0.36	0.37	0.38	0.32	0.71	0.07	0.06	0.27	0.31	0.32	0.27	0.32	0.01	0.48
Fish pattern														
Hg (μg/L)	2.36	2.32	2.88	2.39	2.10	0.04	0.78	1.68	1.92	2.90	2.44	2.84	0.18	0.06
Pb (μg/dL)	1.52	1.54	1.40	1.62	1.81	0.07	0.21	1.06	1.47	1.23	1.30	1.29	− 0.05	0.08
Cd (μg/L)	0.41	0.35	0.37	0.41	0.30	− 0.04	0.05	0.25	0.46	0.41	0.43	0.40	0.00	0.89
Urinary Cd (μg/g)	0.41	0.53	0.38	0.34	0.28	− 0.02	0.79	0.25	0.35	0.34	0.29	0.30	− 0.01	0.47

β*: parameter of blood/urine level estimation value for factor score, p: p-trend of factor adjusted for age group, gender, BMI, city size, residence area, parents education level, family income

Bold values are statistically significant

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