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ORIGINAL ARTICLE

# Blood mercury concentration in relation to metabolic and weight phenotypes using the KNHANES 2011–2013 data

**Kayoung Lee**[1]

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**Abstract**
*Purpose* We assessed the association of blood mercury concentration with metabolic and weight phenotypes.
*Methods* Blood mercury concentration, metabolic syndrome components, and body mass index (BMI) were measured in 6006 Korean adults (2963 men, 3043 women, mean age 44.7 ± 14.7 years), using the 2011–2013 Korean National Health and Nutrition Examination Survey data. Metabolic and weight phenotypes were classified based on BMI and metabolic syndrome (MetS) presence as metabolically healthy and normal weight (MHNW), metabolically unhealthy and normal weight (MUNW), metabolically healthy and obese (MHO), and metabolically unhealthy and obese (MUO).
*Results* The geometric mean of blood mercury concentration was 3.37 μg/L (95% CI 3.32–3.43). A higher quartile of blood mercury concentration was associated with older age, male sex, higher education, alcohol use, current smoking, low physical activity, greater energy intake, and hypertension history. After adjusting for confounding factors (age, sex, education, income, health behaviors, and energy intake), blood mercury concentration tended to increase across the MHNW, MUNW, MHO, and MUO groups in all subjects and each sex ($P$ for trend < 0.01). Compared to the lowest mercury quartile group, adjusted odds ratios (95% CI) for MHO and MUO in those with the highest mercury quartile were, respectively, 1.67 (1.34, 2.09) and 2.02 (1.59, 2.56) in all subjects: 1.58 (1.25, 1.99) and 1.72 (1.37, 2.16) for men; 1.33 (0.94, 1.88) and 1.90 (1.34, 2.70) for women.
*Conclusions* Blood mercury concentration was associated with both metabolic syndrome and obesity, and the association was dose dependent across metabolic and weight phenotypes.

**Keywords** Blood mercury · Metabolic syndrome · Obesity · Phenotype

## Introduction

Metabolic syndrome (MetS), an obesity-associated complex metabolic disturbance including high blood pressure, high waist circumference, low HDL cholesterol, and high triglyceride and high fasting plasma glucose levels (National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) 2002; Alberti et al. 2005) has a significant public health burden because of its high prevalence (George et al. 2006), with consequences including increased cardiovascular mortality (Mottillo et al. 2010) and cancer mortality (Gathirua-Mwangi et al. 2017). Although abdominal obesity per se is one component of MetS, metabolically healthy or metabolically unhealthy obesity has been classified according to the presence or absence of MetS in obese persons. This differentiation is important because obese persons without MetS have a lower risk for cardiovascular disease and for the incidence of type 2 diabetes than obese persons with MetS (Bell et al. 2014; Eckel et al. 2016). In addition, the metabolically healthy obese group had a potential to develop metabolically unhealthy obesity (Mongraw-Chaffin et al. 2016); so the identification of factors related to this pathway is critical. As MetS

✉ Kayoung Lee
kayoung.fmlky@gmail.com

[1] Department of Family Medicine, Busan Paik Hospital, Inje University College of Medicine, 75 Bokjiro, Busan Jin-Gu, Busan 47392, South Korea

consists of multiple metabolic components, the development of MetS may be involved in complex pathophysiological mechanisms such as oxidative stress, endoplasmic reticulum stress, and inflammatory reaction (Tinkov et al. 2015). These pathogenic mechanisms may occur through environmental exposure to heavy metals (Eom et al. 2014; Lee and Kim 2013; Moon 2014). World Health Organization considered mercury as one of the top 10 chemicals of major public health concern. Health effects of mercury differ according to the type of mercury such as elemental, inorganic (mainly exposed through occupation), and organic (e.g., methyl mercury, mainly exposed through diet such as fish and shellfish), dose, age or developmental stage of the person exposed, duration of exposure, and route of exposure (World Health Organization 2017).

Mercury has been considered to play a role in the development of MetS due to its pathophysiologic mechanisms (Tinkov et al. 2015). However, previous findings on associations of mercury with MetS and obesity are inconsistent (Rothenberg et al. 2015; Park et al. 2017; Ettinger et al. 2014; Eom et al. 2014; Lee and Kim 2013; Moon 2014). The association between mercury level and MetS was significant (Eom et al. 2014) or non-significant (Moon 2014; Lee and Kim 2013; Ettinger et al. 2014). In those studies conducted in the Korean population (Lee and Kim. 2013; Moon 2014; Eom et al. 2014) and African descent, (Ettinger et al. 2014) weight status was not taken into account. On the other hand, the directions of associations of obesity indicators and weight status with mercury level were different in the Korean population (Park et al. 2017) and the U.S. population (Rothenberg et al. 2015). Given the inconsistent findings of previous studies and there are concerns regarding higher exposure to bio-accumulated mercury (Lamborg et al. 2014), investigating the relationship between mercury and metabolic and weight phenotypes may enhance information regarding the hazardous effect of mercury.

To the best of our knowledge, any relationship between mercury and the combined phenotypes of MetS and obesity has not been reported. Then, the present study aimed to examine the association between blood mercury concentrations and metabolic and weight phenotypes, using data from the 2011–2013 Korea National Health and Nutrition Examination Survey (KNHANES).

## Methods

### Study population

KNHANES 2011–2013 was a cross-sectional, nationally representative survey for individuals from the non-institutionalized civilian population of South Korea (The Sixth Korea National Healthy and Nutition Examination Survey (KNHANES VI-1) 2013). Among the 18,972 adults aged ≥ 19 years, the current study included participants who had a complete dataset for blood mercury concentration, components of MetS, and BMI. 6030 participants had data of blood mercury concentration, 16, 618 participants had data of MetS, and 17,907 participants had data of BMI. Therefore, participants who did not have data of blood mercury concentration, data of MetS, or data of BMI were excluded ($N = 12{,}966$). Finally, 6006 Korean adults (2963 men, 3043 women, mean age 44.7 ± 14.7 years) were included in the present study. Compared to the excluded participants, individuals who were included were less likely to have MetS (22.8 vs. 27.4%, $P < 0.001$). However, there was no significant difference in prevalence of obesity (i.e. BMI ≥ 25 kg/m$^2$) between the two groups (32.1 vs. 32.1%). All procedures involving human participants were approved by the Institutional Review Board of the Korean Center for Disease Control and Prevention.

### Measurements of mercury, metabolic and weight phenotypes, and confounding factors

Measurements of blood mercury concentration and components of MetS were conducted in each participant after at least an 8-h fast. Blood samples were analyzed in the central laboratory certified by the Korean Ministry of Health and Welfare. Blood mercury concentration was measured using a gold-amalgam collection method with a DMA-80 (Milestone, Bergamo, Italy), while fasting plasma glucose (FPG), triglyceride (TG), and high density lipoprotein cholesterol (HDL) levels were measured using an automatic analyzer (Automatic Chemistry Analyzer 7600, Hitachi, Tokyo, Japan). Blood pressure (BP) was assessed manually, using a standard mercury sphygmomanometer. Waist circumference (WC) was measured at the narrowest point between the lower rib margin and the iliac crest. The definition of MetS was adapted from the Harmonized definition, which requires that three of five MetS components should be present (Alberti et al. 2009). The MetS criteria used in this study were as follows: WC > 90 cm in men or > 85 cm in women (Park et al. 2008); BP ≥ 130/85 mmHg, or a history of hypertension; an FPG concentration ≥ 5.6 mmol/L or a history of diabetes; a HDL concentration < 1.03 mmol/L for men or < 1.29 mmol/L for women; and a TG concentration ≥ 1.63 mmol/L.

BMI was calculated as measured weight (kg)/measured height (m)$^2$, and the weight status was dichotomized as a BMI < 25 kg/m$^2$ for normal weight vs. ≥ 25 kg/m$^2$ for obesity (Park et al. 2008). Using combined categories of metabolic and weight status, four metabolic and weight phenotypes were created: without MetS and normal weight (MHNW), with MetS and normal weight (MUNW), without

MetS and obesity (MHO), and with MetS and obesity (MUO).

The potential confounding factors were age, sex, educational attainment, income level, current smoking status (current smoker vs. current non-smoker), alcohol drinking status (low risk vs. high risk), regular physical activity (no vs. yes), and calorie intake per day. Low-risk alcohol drinking was defined using the definition of National Institute on Alcohol Abuse and Alcoholism: For women, low-risk drinking is defined as no more than 3 drinks on any single day and no more than 7 drinks per week. For men, it is defined as no more than 4 drinks on any single day and no more than 14 drinks per week (NIAAA's Definition of Drinking at Low Risk for Developing Alcohol Use Disorder 2017). Regular physical activity was defined when engaging in regular, high-intensity exercise for > 20 min per session at least 3 times per week; regular, moderate-intensity exercise for > 30 min per session at least 5 times per week, or regular walking for > 30 min per session at least 5 times per week. These factors were assessed using a self-reported standardized questionnaire.

### Statistical analysis

Blood mercury concentration was categorized as quartiles or dichotomized by the US Environmental Protection Agency's recommended mercury reference value (≤ 5.8 vs. > 5.8 μg/L) (Agency for Toxic Substances and Disease Registry (ATSDR) 2017; Fernandes Azevedo et al. 2012). Mercury values were log10 transformed prior to comparison between quartiles, and a quartile-specific geometric mean was calculated. Demographic factors, health behaviors, weight status, and MetS components were compared among the four groups of blood mercury quartiles by a Chi-squared test for trend or an analysis of variance and polynomial test. The associations between the metabolic and weight phenotypes, and subgroups of blood mercury concentration, were analyzed using a Chi-squared test for trend. Analysis of covariance (ANCOVA) was conducted for the association between the metabolic and weight phenotypes, and log10 transformed blood mercury concentration as a continuous variable, after adjusting for confounding factors. Multiple comparison of ANCOVA among subgroups of four phenotypes was conducted using the Sidak method, while a linear regression test was applied to a trend. Multinomial logistic regression analysis was conducted for the associations between the phenotypes and subgroups of mercury, after adjusting for confounding factors. As there was a significant association between sex and metabolic and weight phenotypes, sex-specific relationships between metabolic and weight phenotypes and blood mercury concentration were performed. All analyses were performed using SPSS Statistics Version 23 (IBM, Armonk, NY, USA).

## Results

In the study participants, the prevalence of MetS was 22.9% and the prevalence of obesity was 32.1%, with 7.7, 16.9, and 15.2% classified as MUNW, MHO, and MUO, respectively. The geometric mean of blood mercury concentration was 3.37 μg/L (95% CI 3.32–3.43) and 18.7% of participants had blood mercury concentration > 5.8 μg/L. Table 1 shows demographic factors, health behaviors, weight status, and MetS components of the study population in accordance with quartiles of blood mercury concentration. A higher mercury quartile was positively associated with old age, male sex, higher income, current smoking, current alcohol use, history of hypertension, presence of MetS, and greater energy intake, while inversely associated with regular physical activity. As shown in Table 2, the higher mercury quartile group or those who had blood mercury concentrations > 5.8 μg/L in all subjects tended to have obesity or MetS, or both. The associations between quartiles of blood mercury concentration and metabolic and weight phenotypes were consistently significant regardless of sex. However, the associations with dichotomized blood mercury concentrations were significant in men but not in women (Table 2).

The geometric mean of blood mercury concentration tended to increase across MHNW, MUNW, MHO, and MUO groups in overall analysis as well as each sex after adjusting for confounding factors ($P$ for trend < 0.001). The marginal estimated geometric means of blood mercury concentration in all categories of metabolic and weight phenotypes were greater in men than in women (Table 3). In the multivariable multinomial logistic model, higher mercury quartiles were associated with both MetS and obesity. After adjusting for confounding factors, the highest mercury quartile group had 1.67 and 2.02 times higher odds for having MHO and MUO, respectively, than the lowest mercury quartile group. In addition, individuals with a blood mercury concentration > 5.8 μg/L had 1.38 times and 1.54 times higher odds for having MHO and MUO, respectively, than those with a blood mercury concentration ≤ 5.8 μg/L. The relationships of quartiles and dichotomized categories of mercury concentration and metabolic and weight phenotype were significant in men, while in women, the associations were significant for quartiles of mercury concentration but not for dichotomized mercury concentration (Table 4).

## Discussion

In the present study using data representative of the Korean population, blood mercury concentration was positively associated with both obesity and MetS. Individuals who had blood mercury concentrations higher than the recommended reference value were 38 and 54% more likely to have MHO

**Table 1** The relationships between quartiles of blood mercury concentration (Hg) and demographic, behavioral, and metabolic characteristics ($n = 6006$)

| | Blood mercury quartiles | | | | $P^*$ |
|---|---|---|---|---|---|
| | Lowest ($N = 1500$) | 2nd ($N = 1503$) | 3rd ($N = 1502$) | Highest ($N = 1501$) | |
| Mercury, range (μg/L) | 0.34–2.18 | 2.18–3.25 | 3.25–5.02 | 5.02–60.68 | < 0.001 |
| Mercury, geometric mean (μg/L) | 1.59 ± 1.30 | 2.67 ± 1.12 | 3.40 ± 1.13 | 7.62 ± 1.43 | < 0.001 |
| Age (years) | 41.7 ± 16.5 | 43.2 ± 15.0 | 45.2 ± 13.7 | 48.8 ± 12.6 | < 0.001 |
| Men | 483 (32.2) | 641 (42.6) | 813 (54.1) | 1026 (68.4) | < 0.001 |
| Graduated ≥ high school | 1082 (74.6) | 1096 (75.2) | 1093 (74.8) | 1032 (72.3) | 0.164 |
| Income ≥ middle high[a] | 620 (41.8) | 722 (48.5) | 768 (51.6) | 825 (55.4) | < 0.001 |
| Current smoker | 237 (16.3) | 302 (20.7) | 396 (27.1) | 450 (31.6) | < 0.001 |
| Low-risk alcohol drinking[b] | 860 (59.2) | 825 (56.6) | 780 (53.4) | 651 (45.7) | < 0.001 |
| Regular physical activity | 715 (47.7) | 700 (46.6) | 684 (45.5) | 652 (43.4) | 0.017 |
| Energy intake (cal) | 1893 ± 774 | 2025 ± 849 | 2147 ± 936 | 2180 ± 870 | < 0.001 |
| Dx of hypertension | 213 (14.7) | 192 (13.2) | 233 (15.9) | 294 (20.6) | < 0.001 |
| Dx of diabetes | 122 (8.5) | 100 (7.0) | 116 (8.0) | 135 (9.7) | 0.173 |
| Obesity[c] | 371 (24.9) | 425 (28.3) | 522 (34.8) | 605 (40.3) | < 0.001 |
| Metabolic syndrome[d] | 266 (17.7) | 280 (18.6) | 365 (24.3) | 461 (30.7) | < 0.001 |
| High waist circumference | 245 (16.3) | 300 (20.0) | 379 (25.2) | 430 (28.6) | < 0.001 |
| High blood pressure | 425 (28.3) | 414 (27.5) | 534 (35.6) | 675 (45.0) | < 0.001 |
| High fasting plasma glucose | 309 (20.6) | 361 (24.0) | 438 (29.2) | 560 (37.3) | < 0.001 |
| High triglycerides | 350 (23.3) | 362 (24.1) | 480 (32.0) | 569 (37.9) | < 0.001 |
| Low HDL | 490 (32.7) | 463 (30.8) | 462 (30.8) | 416 (27.7) | 0.005 |

Values are represented as arithmetic mean ± SD, geometric mean ± SD, or number (%)

*Q* quartile, *Dx* diagnosis, *HDL* high density lipoprotein cholesterol

* Using Chi-squared test for trend or one-way analysis of variance (polynomial test)

[a]Income categories are classified into quartiles using a standardized table of individual's monthly income

[b]Low-risk alcohol drinking is defined as no more than 3 drinks on any single day and no more than 7 drinks per week for women; no more than 4 drinks on any single day and no more than 14 drinks per week for men

[c]Obesity is defined as a body mass index ≥ 25 kg/m$^2$

[d]Metabolic syndrome is defined when there are at least three of five following components: high waist circumference (> 90 cm in men or > 85 cm in women); high blood pressure (≥ 130/85 mmHg, or a history of hypertension); high fasting plasma glucose (≥ 5.6 mmol/L or a history of diabetes);high triglycerides (≥ 1.63 mmol/L); low HDL (< 1.03 mmol/L for men or < 1.29 mmol/L for women)

and MUO, respectively, than those with the recommended mercury value, after adjusting for age, sex, education, income, heath behaviors, and energy intake. After adjusting for confounding factors, the geometric mean of blood mercury concentration tended to increase across MHNW, MUNW, MHO, and MUO groups. This dose-dependent association between blood mercury concentration and metabolic and weight phenotypes was consistent across sex. These findings may be the first to demonstrate relationships between mercury and phenotypes of metabolic and weight status, whereas previous studies focused on the relationship of blood mercury concentration with either MetS or obesity.

Previous studies on the association between blood mercury concentration and MetS did not show consistent results. For example, Moon did not find significant associations between quartiles of blood mercury concentration and MetS, after adjusting for confounding factors including BMI using KNHANES 2009–2010 data (Moon 2014). Another study using KNHANES 2005–2010 data also did not find an association between tertiles of blood mercury concentration and MetS after adjusting for BMI and other confounding factors (Lee and Kim 2013). In another study involving a small number of multi-ethnic participants, dichotomized blood mercury concentration was not associated with MetS components, regardless of adjustment for confounding factors (Ettinger et al. 2014). By contrast, Eom et al. reported a significant association between tertiles of blood mercury concentration and MetS, after adjusting for confounding factors in Koreans, although they did not adjust for BMI as a confounding factor (Eom et al. 2014). Therefore, previous findings suggest that the association between blood mercury concentration and MetS (or its components) may be influenced by the adjustment of obesity indicators.

**Table 2** The distribution of subgroups of blood mercury concentration according to metabolic/weight phenotypes ($n = 6006$)

| | MHNW | MUNW | MHO | MUO | $P^*$ |
|---|---|---|---|---|---|
| Overall | ($N = 3619$) | ($N = 461$) | ($N = 1015$) | ($N = 911$) | |
| Quartile of mercury | | | | | < 0.001 |
| Lowest quartile ($n = 1500$) | 1017 (67.8) | 109 (7.3) | 217 (14.6) | 157 (10.5) | |
| 2nd quartile ($n = 1503$) | 981 (65.3) | 97 (6.5) | 242 (16.1) | 183 (12.2) | |
| 3rd quartile ($n = 1502$) | 867 (57.7) | 113 (7.5) | 270 (18.0) | 252 (16.8) | |
| Highest quartile ($n = 1501$) | 754 (50.2) | 142 (9.5) | 286 (19.1) | 319 (21.3) | |
| Dichotomized mercury | | | | | < 0.001 |
| ≤ 5.8 μg/L ($n = 4880$) | 3060 (62.7) | 355 (7.3) | 798 (16.4) | 667 (13.7) | |
| > 5.8 μg/L ($n = 1126$) | 559 (49.6) | 106 (9.4) | 2317 (19.3) | 244 (21.7) | |
| Men | ($N = 1609$) | ($N = 254$) | ($N = 571$) | ($N = 529$) | |
| Quartile of mercury | | | | | < 0.001 |
| Lowest quartile ($n = 483$) | 297 (61.5) | 48 (9.9) | 81 (16.8) | 57 (11.8) | |
| 2nd quartile ($n = 641$) | 395 (61.6) | 40 (6.2) | 117 (18.3) | 89 (13.9) | |
| 3rd quartile ($n = 813$) | 444 (54.6) | 64 (7.9) | 154 (18.9) | 151 (18.6) | |
| Highest quartile ($n = 1026$) | 473 (46.1) | 102 (9.9) | 219 (21.3) | 232 (22.6) | |
| Dichotomized mercury | | | | | < 0.001 |
| ≤ 5.8 μg/L ($n = 2167$) | 1256 (58.0) | 177 (8.2) | 398 (18.4) | 336 (15.5) | |
| > 5.8 μg/L ($n = 796$) | 353 (44.3) | 77(9.7) | 173 (21.7) | 193 (24.2) | |
| Women | ($N = 2010$) | ($N = 207$) | ($N = 444$) | ($N = 382$) | |
| Quartile of mercury | | | | | < 0.001 |
| Lowest quartile ($n = 1017$) | 720 (70.8) | 61 (6.0) | 136 (13.4) | 100 (9.8) | |
| 2nd quartile ($n = 862$) | 586 (68.0) | 57 (6.6) | 125 (14.5) | 94 (10.9) | |
| 3rd quartile ($n = 689$) | 423 (61.4) | 49 (7.1) | 116 (16.8) | 101 (14.7) | |
| Highest quartile ($n = 475$) | 281 (59.2) | 40 (8.4) | 67 (14.1) | 87 (18.3) | |
| Dichotomized mercury | | | | | 0.124 |
| ≤ 5.8 μg/L ($n = 2713$) | 1804 (66.5) | 178 (6.6) | 400 (14.7) | 331 (12.2) | |
| > 5.8 μg/L ($n = 330$) | 206 (62.4) | 29 (8.8) | 44 (13.3) | 51 (15.5) | |

Values are represented as number (%)

*MHNW* metabolically healthy and normal weight, *MUNW* metabolically unhealthy but normal weight, *MHO* metabolically healthy but obese, *MUO* metabolically unhealthy and obese

* Using Chi-squared test for trend

With respect to the associations between blood mercury concentration and weight status, in a sample of the Korean population, there were positive associations between blood mercury concentration and obesity indicators such as BMI, WC, and visceral adipose tissue (Park et al. 2017). In contrast, in the U.S. National Health and Nutrition Examination Survey, blood mercury concentration was lower in obese (BMI ≥ 30 kg/m$^2$) participants than in overweight (25 ≤ BMI < 30 kg/m$^2$)/normal weight (18.5 ≤ BMI < 25.0 kg/m$^2$) participants (Rothenberg et al. 2015). However, the point to be considered is that blood mercury concentrations in the U.S. population may be lower compared to the Korean population. For example, the blood mercury concentrations in the U.S. participant and current Korean participants were, respectively, 1.4 vs. 3.8 μg/L for those with BMI ≥ 30 kg/m$^2$; 1.8 vs. 3.8 μg/L for those with 25 ≤ BMI < 30 kg/m$^2$; 1.9 vs. 3.2 μg/L for those with 18.5 ≤ BMI < 25.0 kg/m$^2$ (Rothenberg et al. 2015).

Based on the current findings, the association with combined phenotypes of MetS and obesity appears to be dose dependent. Given the evidence for metabolically healthy obesity as a transient state in the pathway to metabolically unhealthy obesity (Mongraw-Chaffin et al. 2016), blood mercury concentration could be regarded as one risk factor for the progression from a normal weight to a metabolically unhealthy obese status. Blood mercury concentration is considered to represent integrated dose of mercury over the past 5–6 months (Weil et al. 2005). The geometric mean of blood mercury concentration in the current population was 3.37 μg/L (95% CI 3.32–3.43), while it was 1.58 μg/L (95% CI 1.29–1.93) in Asians and 0.69 μg/L (95% CI 0.58–0.81) in non-Hispanic Whites in the U.S. (Mortensen et al. 2014). The prevalence of individuals with a blood mercury concentration > 5.8 μg/L was 18.7% in the current population, while the prevalence of individuals with a methyl mercury concentration > 5.8 μg/L was 15.8% in Asians and 2.8% in

**Table 3** Estimated geometric mean of blood mercury concentration according to metabolic/weight phenotypes ($n = 6006$)

| | MHNW ($N = 3619$) | MUNW ($N = 461$) | MHO ($N = 1015$) | MUO ($N = 911$) | $P^*$ | $P^{**}$ |
|---|---|---|---|---|---|---|
| Overall | | | | | | |
| Age/sex-adjusted model (μg/L) | $3.24 \pm 1.01^a$ | $3.29 \pm 1.03^a$ | $3.61 \pm 1.02^b$ | $3.79 \pm 1.02^b$ | < 0.001 | < 0.001 |
| Full-adjusted model (μg/L) | $3.23 \pm 1.01^a$ | $3.33 \pm 1.03^a$ | $3.65 \pm 1.02^b$ | $3.80 \pm 1.02^b$ | < 0.001 | < 0.001 |
| Men | | | | | | |
| Age-adjusted model (μg/L) | $3.72 \pm 1.02^a$ | $3.91 \pm 1.04^{ab}$ | $4.39 \pm 1.03^{bc}$ | $4.65 \pm 1.03^c$ | < 0.001 | < 0.001 |
| Full-adjusted model (μg/L) | $3.63 \pm 1.02^a$ | $3.78 \pm 1.04^{ab}$ | $4.16 \pm 1.03^{bc}$ | $4.37 \pm 1.03^c$ | < 0.001 | < 0.001 |
| Women | | | | | | |
| Age-adjusted model (μg/L) | $2.80 \pm 1.01^a$ | $2.74 \pm 1.04^{ab}$ | $2.97 \pm 1.03^{ab}$ | $3.06 \pm 1.03^b$ | 0.007 | 0.001 |
| Full-adjusted model (μg/L) | $2.98 \pm 1.02^a$ | $3.01 \pm 1.04^{ab}$ | $3.29 \pm 1.03^{bc}$ | $3.38 \pm 1.03^{bc}$ | < 0.001 | < 0.001 |

Values are represented as estimated marginal geometric mean ± SE of blood mercury concentration using ANCOVA

Full-adjusted model after adjusting for age, education, income, smoking status, alcohol use, physical activity, energy intake, and sex (only for overall subjects)

*MHNW* metabolically healthy and normal weight, *MUNW* metabolically unhealthy but normal weight, *MHO* metabolically healthy but obese, *MUO* metabolically unhealthy and obese

* Using one-way analysis of covariance

** Using linear regression test

[a,b]Same letters indicate no statistical significance based on Sidak multiple comparison

**Table 4** The associations between metabolic/weight phenotypes and subgroups of blood mercury concentration ($n = 6006$)

| | MUNW OR (95% CI) | MHO OR (95% CI) | MUO OR (95% CI) |
|---|---|---|---|
| Overall | | | |
| Quartiles of mercury ($Q$) | | | |
| 2nd $Q$ vs. 1st $Q$ | 0.90 (0.66, 1.23) | 1.15 (0.93, 1.42) | 1.16 (0.91, 1.48) |
| 3rd $Q$ vs. 1st $Q$ | 1.07 (0.79, 1.46) | 1.41 (1.14, 1.74) | 1.62 (1.28, 2.05) |
| 4th $Q$ vs. 1st $Q$ | 1.26 (0.93, 1.71) | 1.67 (1.34, 2.09) | 2.02 (1.59, 2.56) |
| Dichotomized mercury | | | |
| > 5.8 μg/L vs. ≤ 5.8 μg/L | 1.25 (0.97, 1.62) | 1.38 (1.14, 1.66) | 1.54 (1.27, 1.86) |
| Men | | | |
| Quartiles of mercury ($Q$) | | | |
| 2nd $Q$ vs. 1st $Q$ | 0. 56 (0.34, 0.91) | 1.14 (0.82, 1.58) | 1.09 (0.74, 1.60) |
| 3rd $Q$ vs. 1st $Q$ | 0.78 (0.50, 1.22) | 1.30 (0.94, 1.79) | 1.55 (1.08, 2.21) |
| 4th $Q$ vs. 1st $Q$ | 0.97 (0.64, 1.47) | 1.79 (1.30, 2.46) | 1.97 (1.39, 2.79) |
| Dichotomized mercury | | | |
| > 5.8 μg/L vs. ≤ 5.8 μg/L | 1.28 (0.93, 1.52) | 1.58 (1.25, 1.99) | 1.72 (1.37, 2.16) |
| Women | | | |
| Quartiles of mercury ($Q$) | | | |
| 2nd $Q$ vs. 1st $Q$ | 1.39 (0.92, 2.09) | 1.22 (0.93, 1.61) | 1.35 (0.97, 1.88) |
| 3rd $Q$ vs. 1st $Q$ | 1.52 (0.98, 2.35) | 1.65 (1.24, 2.20) | 1.80 (1.29, 2.51) |
| 4th $Q$ vs. 1st $Q$ | 1.36 (0.86, 2.16) | 1.33 (0.94, 1.88) | 1.90 (1.34, 2.70) |
| Dichotomized mercury | | | |
| > 5.8 μg/L vs. ≤ 5.8 μg/L | 0.99 (0.66, 1.23) | 0.90 (0.63, 1.30) | 1.03 (0.72, 1.47) |

Multinomal logistic regression model compared to MHNW group after adjusting for age, education, income, smoking status, alcohol use, physical activity, energy intake, and sex (only for overall subjects)

*MHNW* metabolically healthy and normal weight, *MUNW* metabolically unhealthy but normal weight, *MHO* metabolically healthy but obese, *MUO* metabolically unhealthy and obese, *OR* odds ratio, *CI* confidence interval

non-Hispanic whites (Mortensen et al. 2014). While exposure to mercury may occur chronically through a variety of pathways such as dietary consumption, industrial processes, occupational use, dental amalgams, and mercury containing vaccines, blood mercury concentration is related mostly to the dietary intake of organic forms, particularly methylmercury (Centers for Disease Control and Prevention 2017). In a recent study in the Korean population, fish and shellfish consumption explained 78% of dietary mercury intake and this consumption was strongly associated with blood mercury concentration (Kim et al. 2016). Therefore, in clinical context, evaluating blood mercury concentration and potential source (such as consumption of fish and shell fish) of exposure to mercury and designing intervention to reduce the exposure could be considered for those at risk for obesity or MetS.

The mechanisms for blood mercury concentration in relation to obesity and MetS are not clearly understood. To explain the positive association between blood mercury concentration and obesity, one potential mechanism may be that a high blood mercury concentration reflects a low accumulation of mercury in adipose tissue for those with a higher susceptibility to metabolic dysfunction. In diabetes-prone mice with a high percentage of body fat, a higher mercury concentration in the blood and organs and a lower accumulation of mercury in adipose tissue than that in control mice were observed (Yamamoto et al. 2014). Another potential mechanism to explain higher blood mercury concentration in obese individuals could be impaired mercury excretion through the biliary system (Skalnaya et al. 2014; Park et al. 2017). As mercury induces oxidative stress, endoplasmic reticulum stress, and inflammation, these mechanisms could promote the development of MetS components, such as insulin resistance, hypertension, and dyslipidemia (Tinkov et al. 2015). Mercury is a potent promotor of oxidative stress, and mercury exposure enhances an increase in the free radical oxidation process and a reduction in the activity of antioxidant enzymes (Genchi et al. 2017; Kobal et al. 2004; Tinkov et al. 2015). In addition, chronic low dose exposure to mercury may result in endothelial dysfunction by reducing the bioavailability of vasodilators such as nitric oxide (Fernandes Azevedo et al. 2012). Whether obesity plays a role as an inducer, promotor, or modifier in the relationship between mercury exposure and MetS remains to be elucidated (Ettinger et al. 2014). Genetic susceptibility may play a role in the differential development of MetS and obesity even in those of similar exposure to mercury. Studies have suggested that response to mercury may be influenced by molecular variants in regulatory glutathione detoxification system genes involved in absorption, distribution, metabolism and excretion process, natural chelating agents such as metallothioneins, selenogenes, and transporters for mercury (Andreoli and Sprovieri 2017). Nevertheless, important questions remain about causality in the relationship between mercury accumulation and obesity (or visceral obesity). Future prospective studies are necessary to disentangle high blood mercury level as a cardiometabolic risk factor or an innocent bystander of true culprits.

There are several limitations to this study. First, this current cross-sectional study may not be able to elucidate temporal relationships across mercury exposure, obesity, and MetS. In addition, blood mercury concentration tends to reflect recent mercury exposure compared to hair and urine mercury concentration (Agency for Toxic Substances and Disease Registry 2017). Therefore, our findings may not apply to cumulative exposure to mercury. Moreover, the apparent associations found may be influenced by unadjusted residual factors, such as selenium, an antagonistic element of mercury (Hu et al. 2017).

Despite these limitations, representative population-based findings have strengths in terms of being potentially generalizable to Koreans. Furthermore, this study provides noteworthy results for the importance of blood mercury concentration in relation to obesity and MetS. In conclusion, using KNHANES 2011–2013 data, blood mercury concentration was associated with both metabolic syndrome and obesity, and the association was dose-dependent across metabolic and weight phenotypes. Given widely dispersed circumstances to mercury exposure, biocumulative potential and persistent effects of mercury, and high prevalence of obesity and MetS, the impact of mercury exposure on public health will be significant. Therefore, current findings demonstrate the importance of evaluating risk for exposure to mercury and implementing intervention program to control the risk.

**Compliance with ethical standards**

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**Conflict of interest** No conflicts of interests exist.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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