

### The Association of Mercury and ALT with Obesity in Korean Adults Using Data from the Korea National Health and Nutrition Examination Survey for 11 Years (KNHANES 2005, 2008–2017)

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**Abstract:** The association between heavy metals in the blood and obesity has been examined in many studies. However, inconsistencies have been observed in the results of these studies. The present study was conducted using data from 119,181 participants of the Korea National Health and Nutrition Examination Survey (KNHANES) for 11 years in 2005 and between 2008 and 2017. The subjects with missing heavy metal blood tests, health interview data, and health examination data were excluded from the study. The study population comprised 1,844 individuals (972 men, and 872 women) who were eligible for inclusion. It was found that obesity and abdominal obesity were associated with an increase in both blood mercury (P < 0.001) and alanine aminotransferase (ALT) (P < 0.001). After adjusting the confounding factors, those with concurrent high levels of ALT and the highest tertile of mercury showed an increased risk of obesity (odds ratio 4.46, 95% confidence interval 2.23–8.90, P < 0.001) as well as abdominal obesity (odds ratio 5.36, 95% confidence interval 2.57–11.17, P < 0.001). The interrelationship of mercury and ALT with the parameters of body mass index (P for interaction = 0.009) and waist circumference (P for interaction = 0.012), respectively, have been observed to be significant, suggesting that the reciprocal relationship could contribute to obesity and abdominal obesity.

**Keywords:** Abdominal obesity; Alanine aminotransferase; Mercury; National health and nutrition examination survey; Obesity

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### **1. Introduction**

Mercury can be found everywhere in our daily lives and is a heavy metal that can exhibit toxicity in the human body <sup>[1]</sup>. Mercury released into the atmosphere through fossil fuels can enter the human body through inhalation. Mercury-contaminated soil or water can enter the food chain through bacteria, plants, livestock, and seafood, ultimately exposing humans and accumulating in their bodies. Mercury is also present in various everyday products such as dental amalgam, thermometers, sphygmomanometers, barometers, fluorescent lamps, batteries, vaccine preservatives, food, cosmetics, and medical drugs.

Mercury exists in different forms, including elemental mercury, inorganic mercury compounds, and organic mercury compounds. Particularly, organic mercury compounds are soluble and can be absorbed in the gastrointestinal tract, entering red blood cells and potentially passing through the blood-brain barrier <sup>[2]</sup>, accumulating in the pituitary gland <sup>[3]</sup>, and crossing the placenta into the fetus, potentially being associated with conditions like precocious puberty and autism <sup>[4,5]</sup>. Even low levels of mercury accumulation in the human body can exhibit toxicity in various organ systems such as the nervous system, cardiovascular system, renal system, and endocrine system <sup>[6]</sup>. Recent studies have suggested that mercury accumulation can lead to obesity or abdominal obesity across all age groups from children to adults <sup>[7-9]</sup>. However, other studies have also analyzed the potential relationship between obesity and other heavy metals like lead and cadmium, indicating that the specific association between certain heavy metals and obesity is not yet clear <sup>[10,11]</sup>.

A study from the National Health and Nutrition Examination Survey (NHANES) conducted between 2003 and 2004 in the United States suggested that an increase in blood mercury levels is associated with an increase in alanine aminotransferase (ALT)<sup>[12]</sup>. ALT is found in small amounts in the kidneys, heart, and muscles but is predominantly detected in the liver. Therefore, an increase in serum ALT levels, even within the normal range, has been shown in several studies to be an independent predictor of nonalcoholic fatty liver disease risk <sup>[13,14]</sup>. Additionally, various reports have indicated a relationship between obesity and ALT elevation in adults without diabetes <sup>[15,16]</sup>. Considering these factors, it is implied that the accumulation of mercury and the elevation of ALT may increase the risk of obesity and nonalcoholic fatty liver disease.

To clarify the relationship between specific heavy metals and obesity, this study utilized Korea NHANES data from 2005 and the 11-year period from 2008 to 2017. An association analysis of mercury, lead, and cadmium with obesity and abdominal obesity was conducted. This study aimed to analyze the mutual relationship between mercury and ALT from the perspective of obesity or abdominal obesity.

### 2. Methods

### 2.1. Study population

The total number of participants in the KNHANES in 2005 and from 2008 to 2017 was 119,818. The Korea Centers for Disease Control and Prevention (KCDC) conducted heavy metal testing on a subset of participants. From those who underwent heavy metal testing, a final parent group consisting of 1,844 participants who had both health survey and health examination data was selected (**Figure 1**) <sup>[17]</sup>. This study was conducted after obtaining an exemption from the review of the Chung-Ang University Institutional Review Board (IRB approval number: 1044297-HR-202109-010-01).



Figure 1. Flow diagram of the present study

### 2.2. Definition of obesity and abdominal obesity

Obesity and abdominal obesity were defined in accordance with the guidelines of the Korean Society for the Study of Obesity (KSSO). Obesity was defined as a body mass index (BMI) of 25 kg/m<sup>2</sup> or higher, while abdominal obesity was defined as a waist circumference of 90 cm or more for adult men and 85 cm or more for

adult women [18].

#### **2.3. Blood tests and others**

Mercury analysis was performed using the DMA-80 device (Milestone, Sorisole, Italy) with the gold amalgamation method. Lead and cadmium were analyzed using the PerkinElmer AAnalyst 600 device (PerkinElmer Inc., Turku, Finland) based on atomic absorption spectrophotometry. ALT was measured using a UV method without the addition of pyridoxal-5'-phosphate, while creatinine was measured using a compensatory kinetic Jaffe method to minimize the influence of bilirubin. The ALT and creatinine tests were conducted using the Hitachi Automatic Analyzer 7600-210 (Hitachi, Tokyo, Japan), and hemoglobin measurement was performed using the XN-9000 device (Sysmex, Kobe, Japan) based on the SLS hemoglobin method.

Education level was classified into the following categories: elementary school or lower, middle school, high school, and college or higher. Alcohol consumption frequency was categorized as non-drinking, less than once a month (< 1 time/month), and once or more a month ( $\geq$  1 time/month). Smoking status was classified as non-smoker, former smoker, or current smoker. Subjective health status was divided into five categories: very bad, bad, average, good, or very good. The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI method <sup>[19]</sup>. In the case of hypertension, diabetes, and hyperlipidemia, these were defined based on the diagnosis by a physician in the self-reported health survey provided by KCDC <sup>[17]</sup>.

The metabolic equivalent of task (MET) represents the amount of energy or oxygen needed during specific physical activities. Physical activity level was calculated based on the data from the NHANES for one week. The MET minutes/week for vigorous physical activity was calculated as  $8.0 \times$  the time spent on vigorous physical activity in hours  $\times$  the number of days with vigorous physical activity. The MET minutes/week for moderate physical activity was calculated as  $4.0 \times$  the time spent on moderate physical activity in hours  $\times$  the number of days with vigorous physical activity in hours  $\times$  the number of days with moderate physical activity. The MET minutes/week for moderate physical activity as calculated as  $4.0 \times$  the time spent on moderate physical activity was calculated as  $3.3 \times$  the time spent on walking physical activity in hours  $\times$  the number of days with walking physical activity. The total physical activity level was calculated as the sum of MET minutes/week for vigorous, moderate, and walking physical activities.

### 2.4. Data analysis

SPSS 24.0 (IBM, Chicago, IL, USA) and GraphPad Prism 9 (GraphPad Software, San Diego, CA, USA) were used for data analysis. NHANES employed a two-stage stratified cluster sampling design for sample selection. To ensure unbiased standard errors of the estimates, we calculated integrated weights for the periods between 2005 and 2017 using the association analysis weights provided by KCDC. Complex sample chi-squared, complex samples multiple logistic regression, and complex samples general linear model analyses were performed, considering weighted complex sample characteristics. In all analyses, missing data were treated as valid values. A significance level of P < 0.05 was set.

### 3. Result

### **3.1.** General characteristics of the study population

A total of 1,844 study participants (972 males and 872 females) are presented in **Table 1**. The mean age for males and females were 44.4 years and 44.8 years, respectively. The mean BMI and waist circumference for the study participants were 23.8 kg/m<sup>2</sup> and 80.6 cm, respectively. The prevalences of obesity and abdominal obesity were 32.9% (606 individuals) and 22.3% (411 individuals), respectively. Statistically significant differences

were observed between males and females in terms of obesity prevalence, abdominal obesity prevalence, education level, alcohol consumption status, and smoking status (P < 0.001). However, household income, subjective health status, diabetes, hypertension, and hyperlipidemia did not show significant differences (P > 0.05). The weighted mean concentrations of mercury, lead, and cadmium were 4.0 µg/L, 2.1 µg/L, and 1.01 µg/L, respectively. Males had significantly higher mean concentrations of mercury and lead than females (P < 0.001), while females had significantly higher cadmium concentrations than males (P < 0.001). The mean ALT level was 22.0 IU/L, with males having a mean ALT level of 26.8 IU/L and females having a mean ALT level of 17.3 IU/L. Males had significantly higher ALT levels than females (P < 0.001).

Variable	Total ( <i>n</i> = 1,844)	Men ( <i>n</i> = 972)	Women ( <i>n</i> = 872)	<i>P</i> -value
Age, years	$44.60\pm0.40$	$44.40\pm0.40$	$44.80\pm0.50$	0.529 <sup>a</sup>
BMI (kg/m <sup>2</sup> )	$23.80\pm0.10$	$24.40\pm0.12$	$23.20\pm0.14$	$< 0.001^{a}$
Obesity*, <i>n</i> (%)				$< 0.001^{b}$
No	1,238 (67.1)	594 (61.1)	644 (73.9)	
Yes	606 (32.9)	378 (38.9)	228 (26.1)	
Waist circumference (cm)	$80.60\pm0.31$	$84.00\pm0.34$	$77.20\pm0.43$	$< 0.001^{a}$
Abdominal obesity**, n (%)				$< 0.001^{b}$
No	1,433 (77.7)	723 (73.4)	710 (81.4)	
Yes	411 (22.3)	249 (25.6)	162 (18.6)	
Mercury (µg/L)	$4.00\pm0.08$	$4.70\pm0.13$	$3.30\pm0.09$	$< 0.001^{a}$
Lead (µg/L)	$2.10\pm0.03$	$2.40\pm0.04$	$1.80\pm0.03$	$< 0.001^{a}$
Cadmium (µg/L)	$1.01\pm0.02$	$0.93\pm0.03$	$1.08\pm0.02$	$< 0.001^{a}$
ALT (IU/L)	$22.00\pm0.72$	$26.80 \pm 1.32$	$17.30\pm0.48$	$< 0.001^{a}$
Education, $n$ (%)				$< 0.001^{b}$
Elementary school or lower	234 (12.7)	89 (9.2)	145 (16.6)	
Middle school	180 (9.8)	97 (10.0)	83 (9.5)	
High school	547 (29.7)	281 (28.9)	266 (30.5)	
College or higher	883 (47.9)	505 (52.0)	378 (43.3)	
Household income, $n$ (%)				0.673 <sup>b</sup>
Low	485 (26.3)	253 (26.0)	231 (26.5)	
Middle-low	449 (24.3)	234 (24.1)	215 (24.7)	
Middle-high	457 (24.8)	240 (24.7)	217 (24.9)	
High	453 (24.6)	244 (25.1)	209 (24.0)	
Drinking status, <i>n</i> (%)				$< 0.001^{b}$
Nondrinker	284 (15.4)	105 (10.8)	179 (20.5)	
< 1 time/month	358 (19.4)	105 (10.8)	253 (29.0)	
$\geq$ 1 time/month	1,202 (65.2)	762 (78.4)	440 (50.5)	
Smoking status, <i>n</i> (%)				$< 0.001^{b}$
Nonsmoker	992 (53.8)	230 (23.7)	762 (87.4)	

 Table 1. General characteristics of participants

Table 1.	(continued)
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Variable	Total ( <i>n</i> = 1,844)	Men ( <i>n</i> = 972)	Women ( <i>n</i> = 872)	<i>P</i> -value
Former smoker	373 (20.2)	332 (34.2)	41 (4.7)	
Current smoker	479 (26.0)	410 (42.2)	69 (7.9)	
Subjective health status, $n$ (%)				0.169 <sup>b</sup>
Very bad	53 (2.9)	23 (2.4)	30 (3.4)	
Bad	255 (13.8)	130 (13.4)	125 (14.3)	
Average	900 (48.8)	459 (47.2)	441 (50.6)	
Good	539 (29.2)	300 (30.9)	239 (27.4)	
Very good	97 (5.3)	60 (6.2)	37 (4.2)	
Physical activity (MET minutes/week)	$2,218.9 \pm 77.4$	$2,737.9 \pm 111.4$	$1,\!699.8\pm98.3$	$< 0.001^{a}$
eGFR (mL/min per 1.73 m <sup>2</sup> )	$97.10\pm0.39$	$93.70\pm0.54$	$100.50\pm0.55$	$< 0.001^{a}$
Hemoglobin (g/dL)	$14.20\pm0.03$	$15.30\pm0.04$	$13.10\pm0.04$	$< 0.001^{a}$
Diabetes, n (%)				0.453 <sup>b</sup>
No	1,634 (88.6)	851 (87.6)	783 (89.8)	
Yes	210 (11.4)	121 (12.4)	89 (10.2)	
Hypertension, n (%)				0.366 <sup>b</sup>
No	1,509 (81.8)	777 (79.9)	732 (83.9)	
Yes	335 (18.2)	195 (20.1)	140 (16.1)	
Hyperlipidemia, n (%)				0.301 <sup>b</sup>
No	1,551 (84.1)	823 (84.7)	728 (83.5)	
Yes	293 (15.9)	149 (15.3)	144 (16.5)	

Values are presented as weighted mean  $\pm$  weighted standard error or weighted percent. <sup>a</sup>Calculated by complex samples general liner model. <sup>b</sup>Calculated by complex samples chi-squared test. \* defined as body mass index  $\geq 25 \text{ kg/m}^2$ . \*\* defined as waist circumference  $\geq 90 \text{ cm}$  for Korean men and  $\geq 85 \text{ cm}$  for Korean women. Abbreviations: ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate; MET, metabolic equivalent of task.

# **3.2.** Distribution of blood mercury, lead, cadmium, and serum ALT concentrations by obesity and abdominal obesity

The distribution of blood concentrations of mercury, lead, cadmium, and serum ALT based on tertiles is presented in **Table 2** for obesity and abdominal obesity. As the tertile of mercury increased, there was a statistically significant difference in the prevalence of obesity (P < 0.001) and abdominal obesity (P < 0.001). Additionally, there were statistically significant differences in the prevalence of obesity (P < 0.001) and abdominal obesity (P < 0.001) as ALT tertiles increased. While the prevalence of obesity showed a statistically significant difference as lead tertiles increased (P = 0.04), the prevalence of abdominal obesity (P > 0.08). Cadmium tertiles did not show statistically significant differences in obesity and abdominal obesity (P > 0.05).

Variable	1st tertile	2nd tertile	3rd tertile	<i>P</i> -value
Mercury (µg/L)	$1.82\pm0.02$	$3.48\pm0.03$	$7.60\pm0.18$	
Lead (µg/L)	$1.22\pm0.01$	$1.97\pm0.01$	$3.21\pm0.04$	
Cadmium (µg/L)	$0.46\pm0.01$	$0.96\pm0.01$	$1.79\pm0.04$	
ALT (IU/L)	$10.70\pm0.10$	$16.80\pm0.09$	$36.40 \pm 1.74$	
		Mercury µg/L (%)		
Obesity*				<0.001 <sup>a</sup>
No ( <i>n</i> = 1,238)	1.81 ± 0.02 (73.1)	$3.42 \pm 0.03$ (66.7)	$7.13 \pm 0.16 \ (59.8)$	
Yes ( <i>n</i> = 606)	$1.83 \pm 0.04 \; (26.9)$	$3.60 \pm 0.04$ (33.3)	$8.3\pm 0.36\ (40.2)$	
Abdominal obesity**				<0.001 <sup>a</sup>
No ( <i>n</i> = 1,433)	$1.82 \pm 0.02$ (82.7)	$3.45 \pm 0.03$ (76.4)	7.41 ± 0.18 (72.7)	
Yes ( <i>n</i> = 411)	$1.78 \pm 0.05 \; (17.3)$	$3.58 \pm 0.06$ (23.6)	8.08 ± 0.41 (27.3)	
		Lead µg/L (%)		
Obesity*				0.04 <sup>a</sup>
No ( <i>n</i> = 1,238)	$1.20 \pm 0.02$ (71.2)	1.97 ± 0.01 (66.4)	3.20 ± 0.06 (63.9)	
Yes ( <i>n</i> = 606)	$1.27 \pm 0.02 \ (28.8)$	$1.98 \pm 0.02$ (33.6)	$3.23 \pm 0.07$ (36.1)	
Abdominal obesity**				$0.08^{a}$
No ( <i>n</i> = 1,433)	$1.20 \pm 0.01 \ (80.0)$	$1.96 \pm 0.01$ (77.9)	$3.22 \pm 0.05$ (75.1)	
Yes ( <i>n</i> = 411)	$1.29\pm 0.02\;(20.0)$	$2.02\pm 0.02\;(22.1)$	$3.18 \pm 0.06 \ (24.9)$	
	(	Cadmium μg/L (%)		
Obesity*				0.30 <sup>a</sup>
No ( <i>n</i> = 1,238)	$0.46 \pm 0.01 \; (68.2)$	$0.96 \pm 0.01 \; (68.9)$	$1.81 \pm 0.05 \ (63.2)$	
Yes ( <i>n</i> = 606)	$0.46 \pm 0.02 \; (31.8)$	0.97 ± 0.01 (31.1)	$1.77\pm 0.04\;(36.8)$	
Abdominal obesity**				0.14 <sup>a</sup>
No ( <i>n</i> = 1,433)	$0.46 \pm 0.01 \; (80.0)$	$0.95 \pm 0.01$ (79.3)	$1.79 \pm 0.05$ (72.4)	
Yes ( <i>n</i> = 411)	$0.46 \pm 0.02 \ (20.0)$	$0.97 \pm 0.01 \ (20.7)$	$1.81 \pm 0.05 \ (27.6)$	
		ALT IU/L (%)		
Obesity*				< 0.001ª
No ( <i>n</i> = 1,238)	10.70 ± 0.11 (86.4)	$16.60\pm 0.10\ (72.5)$	35.50 ± 3.28 (47.2)	
Yes ( <i>n</i> = 606)	11.30 ± 0.21 (13.6)	$17.20 \pm 0.18$ (27.5)	37.30 ± 1.19 (52.8)	
Abdominal obesity**				<0.001 <sup>a</sup>
No ( <i>n</i> = 1,433)	$10.70 \pm 0.10 \; (92.7)$	$16.70\pm0.10\;(81.9)$	35.40 ± 2.50 (62.1)	
Yes ( <i>n</i> = 411)	11.10 ± 0.35 (7.3)	$17.30 \pm 0.24$ (18.1)	38.10 ± 1.54 (37.9)	

**Table 2.** Distribution of blood mercury, lead, cadmium, and serum ALT concentrations by obesity and abdominal<br/>obesity (n = 1,844)

Values are presented as weighted mean  $\pm$  weighted standard error. <sup>a</sup>Calculated by complex samples chi-squared test. \* defined as body mass index  $\geq 25 \text{ kg/m}^2$ . \*\* defined as waist circumference  $\geq 90 \text{ cm}$  for Korean men and  $\geq 85 \text{ cm}$  for Korean women.

# **3.3.** Odds ratios for the risks of obesity and abdominal obesity according to the combination of blood mercury and serum ALT levels

In this study, mercury is divided into three groups based on tertiles and ALT into two groups (low:  $\leq 40$  IU/L; high: > 40 IU/L), resulting in six groups. The calculated odds ratios (ORs) for obesity and abdominal obesity are shown in **Table 3**. In the complex sample logistic regression analysis adjusted for age and gender (Model 1), the group with high ALT and belonging to the highest tertile of mercury had significantly higher ORs for obesity (4.73, 95% confidence interval [CI] 2.39–9.37, P < 0.001) and abdominal obesity (5.66, 95% CI 2.82–11.34, P < 0.001) compared to the low ALT and lowest mercury tertile group (reference group). After additional adjustments for physical activity, education level, household income, alcohol consumption, smoking, and subjective health status (Model 2), the ORs increased slightly to 5.13 (obesity; 95% CI 2.62–10.05) and 6.44 (abdominal obesity; 95% CI 3.20–12.94), both still significant (P < 0.001) compared to Model 1. Further adjustment for eGFR, hemoglobin, diabetes, hypertension, and hyperlipidemia (Model 3) resulted in lower ORs of 4.46 (obesity; 95% CI 2.23–8.90) and 5.36 (abdominal obesity; 95% CI 2.57–11.17) compared to Model 2, but the ORs remained significantly higher compared to the reference group (P < 0.001).

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Model	ALI***	Mercury -	OR	<i>P</i> -value	OR	<i>P</i> -value
Adjusted model 1 <sup>a</sup>		1st tertile	1.00 (reference)		1.00 (reference)	< 0.001
	Low	2nd tertile	1.15 (0.85–1.56)		1.31 (0.92–1.86)	
		3rd tertile	1.50 (1.12–2.01)	- < 0.001	1.51 (1.06–2.15)	
	High	1st tertile	3.30 (1.66-6.55)		4.37 (1.97–9.70)	
		2nd tertile	4.73 (2.39–9.37)		5.62 (2.86–11.03)	
		3rd tertile	6.04 (3.08–11.87)		5.66 (2.82–11.34)	
		1st tertile	1.00 (reference)		1.00 (reference)	< 0.001
	Low	2nd tertile	1.20 (0.89–1.62)	- < 0.001	1.42 (1.00-2.00)	
Adjusted model 2 <sup>b</sup>		3rd tertile	1.65 (1.21–2.26)		1.74 (1.21–2.50)	
	High	1st tertile	3.19 (1.56–6.49)		4.29 (1.97–9.33)	
		2nd tertile	5.13 (2.62–10.05)		5.80 (2.87–11.71)	
		3rd tertile	6.23 (3.20–12.10)		6.44 (3.20–12.94)	
Adjusted model 3 <sup>°</sup>	Low	1st tertile	1.00 (reference)	- < 0.001	1.00 (reference)	< 0.001
		2nd tertile	1.20 (0.87–1.64)		1.42 (0.99–2.03)	
		3rd tertile	1.52 (1.09–2.12)		1.58 (1.09–2.31)	
	High	1st tertile	2.70 (1.30-5.63)		3.50 (1.62–7.59)	
		2nd tertile	4.46 (2.23-8.90)		5.11 (2.52–10.40)	
		3rd tertile	5.70 (2.89–11.22)		5.36 (2.57–11.17)	

Table 3. Adjusted odds ratios for the risk of obesity and abdominal obesity according to the combination of blood
mercury and serum ALT levels

Adjusted models were calculated by applying complex samples multiple logistic regression with adjustment for (a) age and gender; (b) age, gender, physical activity, education, household income, drinking status, smoking status, and subjective health status; (c) age, gender, physical activity, education, household income, drinking status, smoking status, subjective health status, eGFR, hemoglobin, diabetes, hypertension, and hyperlipidemia. \* defined as body mass index  $\geq$  25 kg/m<sup>2</sup>. \*\* defined as waist circumference  $\geq$  90 cm for Korean men and  $\geq$  85 cm for Korean women. \*\*\* Low ALT defined as  $\leq$  40 IU/L, high ALT defined as > 40 IU/L. Abbreviations: ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate; OR, odds ratio.

### **3.4.** Analysis of the relationship between mercury and ALT with body mass index and waist circumference

A complex sample general linear analysis for BMI and waist circumference was conducted using six groups formed by dividing mercury into three tertiles and ALT into two groups (low:  $\leq 40$  IU/L; high: > 40 IU/L). For BMI, the group with high ALT and belonging to the highest tertile of mercury had a significantly higher mean (27.6 kg/m<sup>2</sup>, 95% CI 26.2–29.1) compared to the low ALT and lowest mercury tertile group's mean (24.0 kg/m<sup>2</sup>, 95% CI 23.5–24.5) after Bonferroni post hoc test (P < 0.001, **Figure 2A**). For waist circumference, the group with high ALT and belonging to the highest tertile of mercury had a significantly higher mean (91.4 cm, 95% CI 88.0–94.8) compared to the low ALT and lowest mercury tertile group's mean (82.0 cm, 95% CI 80.6–83.4) after Bonferroni post hoc test (P < 0.001, **Figure 2B**). After adjusting for age, gender, physical activity, education level, household income, alcohol consumption, smoking, subjective health status, eGFR, hemoglobin, diabetes, hypertension, and hyperlipidemia, there were statistically significant interactions between ALT and mercury for both BMI (P for interaction = 0.009, **Figure 2A**) and waist circumference (P for interaction = 0.012, **Figure 2B**).



**Figure 2.** Interrelationship of mercury and ALT in complex samples general linear model adjusted for age, sex, physical activity, education level, household income, drinking status, smoking status, eGFR, hemoglobin, diabetes, hypertension, and hyperlipidemia. **(A)** Obesity; **(B)** Abdominal obesity.

#### 4. Discussion

In a study by Eom *et al.*, a sample of 2,114 healthy Korean adults who were not occupationally exposed to mercury was collected using a multistage, gender- and age-stratified probability sampling method from 2010 to 2011 <sup>[20]</sup>. The average blood mercury concentration in this study was 3.9  $\mu$ g/L, and it showed that as blood mercury levels increased, the OR for abdominal obesity increased by 2.09-fold compared to the reference group <sup>[20]</sup>. The mean blood mercury concentration in the present study was 4.0  $\mu$ g/L, which is similar to the findings in Eom *et al.*'s report. Moreover, the present study also showed significant differences in the prevalence of abdominal obesity based on tertiles of mercury (*P* < 0.001), and the OR for abdominal obesity increased by 5.36-fold as

the mercury tertiles increased (P < 0.001). This suggests that the present study is in line with the previous study conducted by Eom *et al*.

In a study by Kim *et al.*, the daily dietary mercury intake of Korean adults was reported to be primarily from fish and seafood (75.6%, 10.26  $\mu$ g), followed by grains (17.7%, 2.40  $\mu$ g), and legumes (2.6%, 0.35  $\mu$ g)<sup>[21]</sup>. They also reported that blood mercury levels increased with higher consumption of fish and seafood <sup>[21]</sup>. Additionally, another study found that as individuals got older, mercury accumulates, with men having higher levels in their 40s and 50s and women having significantly higher levels in their 50s <sup>[22]</sup>. This suggests that higher mercury accumulation may occur as seafood consumption increases and individuals age.

A study that reported a positive association between blood mercury levels in Korean adolescents and the prevalence of overweight and abdominal obesity, using data from the KNHANES (2010–2013), indicated that mercury accumulation might affect obesity starting from adolescence <sup>[9]</sup>.

The mechanism behind the association between mercury accumulation and obesity is not yet fully understood. However, it has been suggested that it may involve factors such as increased oxidative stress, increased vascular inflammation, decreased metalloenzymes, glutathione depletion, mitochondrial dysfunction, increased lipid peroxidation, increased platelet aggregation, impaired vascular smooth muscle function, endothelial dysfunction, decreased immune function, impaired lipid metabolism, and impaired glucose metabolism<sup>[23,24]</sup>. These mercury-related phenomena may increase the risk of obesity, dyslipidemia, diabetes, hypertension, metabolic syndrome, and cardiovascular disease [25,26]. One Finnish study also found that high hair mercury content increased carotid intima-media thickness and atherosclerosis <sup>[27]</sup>. In the Wisconsin Sleep Cohort study involving 101 participants, participants in the top quartile of blood mercury levels had a 1.9 times higher likelihood of developing hypertension, and those in the top quartile of hair mercury had a 4 times higher risk of developing hypertension<sup>[28]</sup>. This suggests that hair mercury may be a better predictor of hypertension risk than blood mercury. A cross-sectional cohort study of 2,114 Korean adults found a positive association between mercury levels and the prevalence of metabolic syndrome<sup>[20]</sup>. Additionally, a prospective cohort study of 1,512 mother-infant pairs in Boston found that increased maternal mercury levels resulting in fetal exposure increased the risk of preterm birth by 2.4 times <sup>[5]</sup>. However, there are also studies reporting no relationship between blood mercury levels and cardiovascular disease. In a study that composed a group of 54 mercury miners and 58 workers as a control group near Slovenia, no relationship was found between blood mercury and cardiovascular disease [29]. Given the lack of consistency in these studies, it has been emphasized that analysis of the relationship between mercury and diseases is difficult because mercury exposure often accompanies other environmental pollutants in meta-analyses. Therefore, prospective cohort studies should be used to remove confounding variables and consider interactions with other factors <sup>[30]</sup>.

The present study found significant associations between blood mercury levels and both obesity and abdominal obesity. In obesity, the average blood mercury concentration for the highest tertile was 8.30  $\mu$ g/L, and for abdominal obesity, it was 8.08  $\mu$ g/L. While there was no significant difference observed for the latter (not presented in **Table 2**), this suggests that mercury may play an important role in the development of both obesity and abdominal obesity. Notably, the OR for abdominal obesity (5.36-fold in Model 3) was higher than that for obesity (4.46-fold in Model 3), suggesting that mercury may have a more significant role in the formation of abdominal obesity (**Table 3**). The significant interaction between mercury and ALT for both BMI (*P* for interaction = 0.009) and waist circumference (*P* for interaction = 0.012) in the present study suggests that this interaction may accelerate the development of obesity and abdominal obesity. This is consistent with previous research <sup>[26]</sup>. Prospective cohort studies are needed to confirm the relationship between mercury and ALT factors in relation to obesity and abdominal obesity.

Obesity is typically caused by excessive nutrient intake and energy imbalance leading to fat accumulation. While a sedentary lifestyle contributes to energy imbalance, there is growing evidence that environmental exposures may also contribute to obesity. The primary treatments for obesity include dietary therapy, exercise therapy, and behavioral therapy, with drug therapy being an adjunct therapy. If there is no more than a 5% weight loss within three months of starting drug therapy, changing or discontinuing the drug is recommended. However, if these treatments do not result in weight loss in severely obese patients, surgical treatment may be considered <sup>[18]</sup>. In this context, the results of the present study suggest that managing mercury and ALT may be important in the course of obesity treatment.

The present study has several limitations. First, as a cross-sectional study based on the KNHANES, it is difficult to explain causality. Second, in the process of integrating 11 years of data from the KNHANES, it was not possible to create variables for seafood consumption, as blood mercury levels from food intake must be measured within three days, hence this was not included in the study. Third, genetic mutations, epigenetic changes, and other molecular considerations were not considered in relation to obesity and abdominal obesity. Fourth, data on various products containing mercury and various lifestyle factors were not available in the KNHANES, so future research should analyze and confirm these factors.

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### **Disclosure statement**

The author declares no conflict of interest.

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