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Association of blood mercury concentrations with atopic dermatitis in adults: A population-based study in Korea[☆]

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ABSTRACT

Atopic dermatitis is one of the most common inflammatory skin diseases among children and adults. Although the risk factors for atopic dermatitis have not yet been fully identified, exposure to mercury may be an important environmental risk factor. The objective of this study was to evaluate the association between mercury body burden and prevalence of atopic dermatitis in an adult population. We recruited participants ($n=1990$) aged 20 years or older, using stratified random sampling of Korean census blocks. Demographic characteristics and medical history of atopic dermatitis were collected from participants by questionnaire, and mercury levels were determined by an analysis of blood samples. We found that demographic factors such as sex, age, alcohol drinking status, income, and fish or shellfish consumption were important covariates determining blood mercury concentration. Sex and cigarette smoking status were important demographic variables affecting the prevalence of atopic dermatitis. After adjusting for demographic factors, blood mercury concentrations were positively associated with lifetime prevalence of atopic dermatitis [odds ratio (OR), highest vs. lowest tertile=1.50; 95% confidence interval (CI), 1.02–2.21; p for trend=0.057]. This association became stronger for 1-year prevalence of atopic dermatitis (OR, highest vs. lowest tertile=1.82; 95% CI, 1.17–2.83; p for trend=0.026). Mercury body burden and atopic dermatitis prevalence vary across demographic characteristics, and increased blood level of mercury was related to an incidence of atopic dermatitis in this adult population.

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1. Introduction

Atopic dermatitis (AD), a highly pruritic chronic inflammatory skin disease, has been suggested to mainly affect children (Lan et al., 2009). Consequently many studies have focused on understanding the childhood occurrence of this disease. However, recent studies have shown that the prevalence of an AD among both children and adults has increased substantially over the last few decades, primarily in industrialized countries (Asher et al., 2006; Orfali et al., 2009). Furthermore, the occurrence of an AD among adults has been shown to significantly affect socioeconomic conditions and quality of life (Poole et al., 2010; Wollenberg et al., 2008). To address this increasingly important yet still broadly neglected public health issue, epidemiological studies that investigate the distribution and

prevalence of an AD in adult populations are necessary. The identification of potential risk factors for an AD in adults may also play an important role in the development of early prevention programs and public policymaking.

Although the risk factors for an AD are not fully understood, interactions among genetic, immunological, and environmental factors are known to be involved in the pathogenesis of the disease (Novak, 2009). The prevalence of an AD has increased markedly during the last decades in industrialized countries and urban regions, suggesting that environmental factors play a critical role in its expression (Williams et al., 1999). Most AD patients show sensitivity to environmental allergens, and the most frequent contact allergens affecting these patients are metals (Giordano-Labadie et al., 1999). Some AD cases have improved with a metal-free diet and the elimination of contact with metals (de Cook et al., 1966). These studies suggest that metals may be a major environmental risk factor for an AD.

Among the heavy metals, mercury is known to have profound and complex effects on the immune system (Vas and Monestier, 2008). Mercury exposure has been shown to induce an immune response characterized by the proliferation of T and B lymphocytes, which elevates serum immunoglobulin IgG1 and IgE levels

Abbreviations: AD, atopic dermatitis; OR, odds ratio; CI, confidence interval; BMI, body mass index

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(Schiraldi and Monestier, 2009). Moreover mercury exposure may lead to autoimmune dysfunction and systemic inflammation in affected populations (Gardner et al., 2010).

Mercury is dispersed widely in the environment, and an exposure may be increased by human activities that release the metal into the air, soil, water, and food (Wong and Lye, 2008). An exposure to mercury occurs mainly through the consumption of mercury-contaminated fish, but other foodstuffs (e.g., drinking water, cereals, vegetables, and meat) and dental amalgams also contribute to a limited extent to the overall body burden (Galal-Gorchev, 1993).

Biomonitoring studies have revealed many contributing factors to the body burden of metals, including sex, age, body mass index (BMI), education, and diet. Epidemiological studies have found significant variation in the prevalence of most diseases according to demographic variables and environmental risk factors, including metals. The present study therefore used Korean national survey data to analyze the demographic variation in blood mercury concentrations and AD prevalence in adults. We also attempted to elucidate the association between blood mercury levels and the adult prevalence of an AD in this population sample.

2. Materials and methods

2.1. Study population

This population-based study was conducted between April and June 2005. Participants were recruited from the adult population (≥ 20 years of age) of the Republic of Korea, using stratified random sampling of census blocks. The number of census blocks was determined based on the population of each city, and then 200 census blocks were randomly selected.

2.2. Data collection

Individual subjects from selected census blocks were invited to a public health center in the census block to be interviewed and to give a blood sample. In face-to-face interviews, the study participants were asked their sex, age, education level, cigarette smoking status, alcohol drinking status, income, dietary pattern, and medical history of an AD. Blood specimens were collected by venipuncture, using supplies designed specifically for trace metal measurement. Blood mercury was measured by cold-vapor atomic absorption spectrometry, using a dedicated mercury analyzer (M-6000A; CETAC Technologies, Omaha, NE, USA). The blood mercury analyses were carried out by a laboratory certified by the Korean Ministry of Health and Welfare. The limits of detection and linearity of the standard curve for blood mercury were 0.036 $\mu\text{g/l}$ and 0.999, respectively. For internal quality assurance and control, a standard reference material (Lyphochek[®] Whole Blood Metals Control; Bio-Rad, Hercules, CA, USA) was analyzed. The coefficient of variation was 8.3% for blood mercury.

Height and weight were measured with subjects wearing light clothing and no shoes. BMI was then calculated as weight (kg) divided by the square of height (m^2). The study protocol was approved by the Korean Ministry of Health and Welfare and was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects, as defined by the Helsinki Declaration. The study participants provided written informed consent. Of the selected subjects in the census blocks, 1990 (70%) individuals completed the interview and provided a blood sample.

2.3. Variable definitions

Education was categorized as less than a high school diploma, high school diploma, and college or higher. Cigarette smoking and alcohol drinking statuses were defined as never, occasional, or frequent. The occasional smoking and drinking categories included former smokers and those who did not smoke everyday, and participants who drank less than once per month, respectively. The categories of frequent smoking and drinking were defined as smoking everyday and drinking more than once per month, respectively. Income was calculated by dividing the square root of household size by the monthly household income, according to the Organisation for Economic Co-operation and Development method (OECD, 2009). Income was categorized by quartiles, based on the income of all Korean households in 2005. Self-reported fish or shellfish consumption was categorized as less than 5 times/month, 6–9 times/month, 10–29 times/month, and more than 30 times/month. The criteria of an AD were based on a self-reported history of doctor-diagnosed AD.

2.4. Statistical analysis

We evaluated differences in categorical variables between groups using the Mantel-Haenszel chi-square test, and the differences between two groups in continuous variables were examined using the two-sample *t* test. We calculated geometric means with 95% confidence intervals (CIs) for blood mercury concentration by taking the antilog of the mean of the natural log-transformed values. Based on a normal probability plot, geometric means were used to improve the approximation of a normal distribution. Estimate statements in linear regression model were used to determine the adjusted geometric mean of blood mercury.

We fitted multiple linear regressions of the log-mercury concentrations on the predictor variables. The exponentiated model coefficients represent the proportional change in the arithmetic mean associated with each level of the predictor, relative to a reference level and adjusting for the other predictors in the model. Odds ratios (ORs) with 95% CIs for the prevalence of an AD compared to the reference were calculated using multivariate logistic regression analyses with all of the covariates. AD prevalences were also compared among tertiles of blood mercury concentration using multivariate logistic regression after adjusting for potentially confounding variables. A result was considered to be statistically significant if the 95% CI did not include one. All statistical analyses were conducted using an SAS version 9.1 software (SAS Institute, Inc., Cary, NC, USA).

3. Results

Our study population consisted of 1990 adult Korean subjects; 217 (10.9%) had a history of AD and were placed in the lifetime AD prevalence category, and 176 (8.8%) had been diagnosed with an AD within 1 year of the study and were placed in the 1-year AD prevalence category (Table 1). Lifetime and 1-year AD prevalence rates did not differ significantly according to demographic factors, such as sex, age, BMI, education, cigarette and alcohol consumption, income, and fish or the shellfish consumption. However, blood mercury level was significantly associated with increased lifetime and 1-year prevalences of an AD (Fig. 1). Adjusted geometric mean mercury levels were 3.45 (95% CI, 3.17–3.76) $\mu\text{g/l}$ among respondents having no AD during the lifetime and 4.66 (95% CI, 3.81–5.70) among those having an AD during the lifetime. Moreover adjusted geometric mean mercury levels were higher among participants having AD within recent 1 year: 3.44 (95% CI, 3.16–3.75) among participants without 1-year AD and 4.91 (95% CI, 3.97–6.08) among those with 1-year AD.

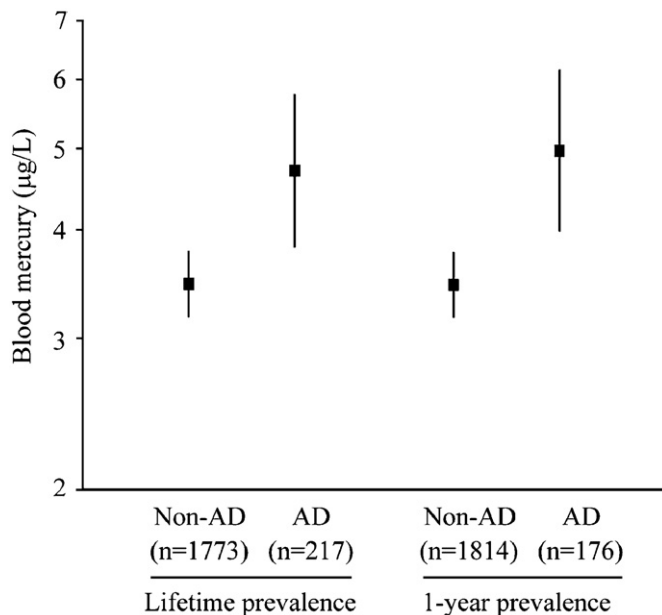
To determine the effects of demographic characteristics on blood mercury level and AD prevalence, multiple and logistic regression analyses were conducted for blood mercury concentration and AD incidence, respectively. All blood mercury values exceeded the minimum detection limit, ranging 0.07–55.94 $\mu\text{g/l}$. The geometric mean blood mercury concentration was 4.34 $\mu\text{g/l}$ (95% CI, 4.21–4.48) and varied according to demographic factors, as shown in Table 2. Blood mercury concentrations were highest in males (5.01 $\mu\text{g/l}$), followed by frequent cigarette smokers (4.99 $\mu\text{g/l}$). Frequent alcohol drinking, increased income, and consumption of fish or shellfish were also associated with an increased blood mercury levels. Furthermore, participants aged 40–59 years had the highest blood mercury concentrations among age groups.

Mercury concentrations were distributed similarly across population subgroups after simultaneously adjusting for predictors in a log-linear regression, with some exceptions. The mercury levels of males, those aged 40–59 years, and among those with frequent alcohol consumption, the highest quartile of an income, and fish or shellfish consumption more than 30 times/month remained significantly higher after an adjustment. However, the mean blood mercury level was no longer significantly associated with cigarette smoking after an adjustment for potential covariates.

Logistic regression analysis was performed to assess the independent influence of demographic variables on the risk of lifetime or 1-year AD prevalence, while controlling for other demographic factors. The parameter estimates were transformed

Table 1Distribution of demographic characteristics by prevalence of atopic dermatitis (AD) among Korean adults ≥ 20 years of age [n(%)].

Characteristics	No. ^a	Lifetime prevalence of an AD			1-Year prevalence of an AD		
		AD (% within group)	No AD (% within group)	p-Value ^b	AD (% within group)	No AD (% within group)	p-Value ^b
Total	1990	217 (100)	1773 (100)		176 (100)	1814 (100)	
Sex				0.098			0.08
Male	995	97 (44.7)	898 (50.6)		77 (43.8)	918 (50.6)	
Female	995	120 (55.3)	875 (49.4)		99 (56.2)	896 (49.4)	
Age (years)				0.421			0.648
20–39	745	86 (39.6)	659 (37.2)		70 (39.8)	675 (37.2)	
40–59	893	96 (44.3)	797 (45.0)		75 (42.6)	818 (45.1)	
≥ 60	351	35 (16.1)	316 (17.8)		31 (16.6)	320 (17.7)	
BMI				0.862			0.859
< 18.5	81	7 (3.2)	74 (4.2)		7 (4.0)	74 (4.1)	
18.5–22.9	718	78 (36.0)	640 (36.4)		60 (34.1)	658 (36.6)	
23–27.4	918	110 (50.7)	808 (45.9)		92 (52.3)	826 (45.9)	
≥ 27.5	259	22 (10.1)	237 (13.5)		17 (9.6)	242 (13.4)	
Education				0.983			0.51
< High school	623	62 (28.6)	561 (31.6)		55 (31.3)	568 (31.3)	
High school	737	92 (42.4)	645 (36.4)		72 (40.9)	665 (36.7)	
> High school	630	63 (29.0)	567 (32.0)		49 (27.8)	581 (32.0)	
Cigarette smoking status				0.568			0.427
Never	1026	114 (53.3)	912 (52.8)		91 (52.6)	935 (52.8)	
Occasional	422	38 (17.7)	384 (22.2)		30 (17.3)	392 (22.2)	
Frequent	494	62 (29.0)	432 (25.0)		52 (30.1)	442 (25.0)	
Alcohol drinking status				0.613			0.853
Never	432	52 (24.0)	380 (22.0)		41 (23.7)	391 (22.1)	
Occasional	473	49 (22.9)	424 (24.5)		39 (22.5)	434 (24.5)	
Frequent	1037	113 (52.8)	924 (53.5)		93 (53.8)	944 (53.4)	
Income (US\$/month)				0.775			0.693
< 490	538	54 (25.5)	484 (27.6)		47 (27.5)	491 (27.3)	
490–875	491	64 (30.2)	427 (24.3)		47 (27.5)	444 (24.7)	
876–1361	435	41 (19.3)	394 (22.4)		34 (19.9)	401 (22.3)	
> 1361	504	53 (25.0)	451 (25.7)		43 (25.1)	461 (25.7)	
Fish or shellfish consumption				0.218			0.405
< 5 Times/month	124	11 (5.9)	113 (7.2)		11 (7.2)	113 (7.1)	
6–9 Times/month	461	42 (22.5)	419 (26.8)		34 (22.2)	427 (26.7)	
10–29 Times/month	638	75 (40.1)	563 (36.1)		59 (38.6)	579 (36.3)	
≥ 30 Times/month	526	59 (31.5)	467 (29.9)		49 (32.0)	477 (29.9)	

^a Totals are not all equal because of missing data.^b p Determined by Mantel-Haenszel chi-square test.**Fig. 1.** Age and sex-adjusted geometric mean blood mercury levels by the prevalence of atopic dermatitis (AD) among Korean adults ≥ 20 years of age. Participants were classified in non-AD and AD groups according to the history of an AD or the 1-year prevalence of an AD. Error bars indicate 95% confidence intervals.

to ORs with 95% CIs. The ORs for lifetime AD prevalence were significantly higher for frequent cigarette smokers (OR=1.93; 95% CI, 1.14–3.27) and significantly lower in males (OR=0.59; 95% CI, 0.36–0.97) than in the reference groups after an adjustment for potential confounding variables. Similarly, the ORs for 1-year AD prevalence were significantly higher for frequent cigarette smokers (OR=2.23; 95% CI, 1.25–3.95) and significantly lower in males (OR=0.50; 95% CI, 0.29–0.86) than in the reference groups after an adjustment. These associations were much stronger than those between lifetime AD prevalence and cigarette smoking or sex. The other demographic variables included in this analysis did not significantly influence the adjusted ORs for lifetime or 1-year AD prevalence.

Table 3 shows the prevalence of an AD according to tertiles of blood mercury concentrations. The risk for lifetime AD increased with an increasing blood mercury level. Participants in the highest tertile (blood mercury ≥ 6.04 µg/l) had a 1.51-fold (95% CI, 1.03–2.21) increased risk of lifetime AD prevalence, compared with those with blood mercury concentrations in the lowest tertile (blood mercury < 3.56 µg/l) after an adjustment for age and sex (model 1, p for trend=0.055). This relationship was continuous and persisted even after an adjustment for cigarette and alcohol consumption, income, and fish or shellfish consumption. These factors were significant covariates determining blood mercury concentration or AD prevalence (model 2), or persisting after an adjustment for all other risk factors (model 3).

Table 2Blood mercury concentrations and adjusted ORs (95% CI) for the prevalence of atopic dermatitis (AD) by demographic characteristics in Korean adults ≥ 20 years of age.

Characteristics	Geometric mean blood mercury [$\mu\text{g/l}$ (95% CI)]	Adjusted proportional change in mean blood mercury [$\mu\text{g/l}$ (95% CI)] ^a	Adjusted OR for lifetime prevalence of AD (95% CI)	Adjusted OR for 1-year prevalence of AD (95% CI) ^b
Total	4.34 (4.21–4.48)	–	–	–
Sex				
Male	5.01 (4.80–5.22)	1.17 (1.06–1.30)*	0.59 (0.36–0.97)*	0.50 (0.29–0.86)*
Female	3.77 (3.61–3.93)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Age (years)				
20–39	4.10 (3.91–4.31)	1.00 (reference)	1.00 (reference)	1.00 (reference)
40–59	4.68 (4.47–4.90)	1.09 (1.01–1.19)*	0.84 (0.58–1.24)	0.81 (0.53–1.25)
≥ 60	4.05 (3.75–4.38)	0.99 (0.87–1.11)	0.92 (0.52–1.63)	0.97 (0.53–1.80)
BMI				
< 18.5	3.74 (3.05–4.60)	1.00 (reference)	1.00 (reference)	1.00 (reference)
18.5–22.9	4.11 (3.92–4.31)	1.10 (0.88–1.38)	1.33 (0.55–3.22)	1.01 (0.41–2.46)
23–27.4	4.60 (4.40–4.81)	1.18 (0.94–1.47)	1.56 (0.64–3.76)	1.32 (0.54–3.12)
≥ 27.5	4.35 (3.95–4.79)	1.13 (0.88–1.43)	1.12 (0.43–2.95)	0.88 (0.33–2.39)
Education				
< High school	4.23 (3.99–4.49)	1.00 (reference)	1.00 (reference)	1.00 (reference)
High school	4.39 (4.18–4.62)	1.06 (0.94–1.19)	1.31 (0.84–2.05)	1.13 (0.69–1.84)
> High school	4.39 (4.17–4.63)	1.08 (0.97–1.21)	1.09 (0.64–1.84)	0.97 (0.54–1.72)
Cigarette smoking status				
Never	3.88 (3.72–4.05)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Occasional	4.85 (4.53–5.19)	1.06 (0.94–1.19)	1.26 (0.73–2.20)	1.44 (0.79–2.64)
Frequent	4.99 (4.70–5.30)	1.08 (0.97–1.21)	1.93 (1.14–3.27)*	2.23 (1.25–3.95)*
Alcohol drinking status				
Never	3.83 (3.58–4.10)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Occasional	3.90 (3.66–4.16)	1.01 (0.92–1.12)	0.82 (0.52–1.28)	0.84 (0.51–1.38)
Frequent	4.81 (4.61–5.01)	1.14 (1.04–1.25)*	0.79 (0.52–1.20)	0.86 (0.55–1.37)
Income (US\$/month)				
< 490	4.05 (3.80–4.31)	1.00 (reference)	1.00 (reference)	1.00 (reference)
490–875	4.21 (4.00–4.50)	1.01 (0.92–1.10)	0.79 (0.52–1.20)	1.03 (0.64–1.64)
876–1361	4.28 (4.00–4.58)	1.04 (0.94–1.14)	0.88 (0.54–1.41)	0.88 (0.53–1.46)
> 1361	4.82 (4.54–5.10)	1.15 (1.05–1.26)*	1.15 (0.73–1.81)	1.13 (0.69–1.83)
Fish or shellfish consumption				
< 5 Times/month	3.85 (3.40–4.37)	1.00 (reference)	1.00 (reference)	1.00 (reference)
6–9 Times/month	4.11 (3.83–4.40)	1.02 (0.89–1.17)	1.00 (0.49–2.03)	0.78 (0.38–1.61)
10–29 Times/month	4.43 (4.19–4.67)	1.09 (0.95–1.24)	1.41 (0.71–2.78)	1.11 (0.56–2.22)
≥ 30 Times/month	4.60 (4.35–4.86)	1.14 (1.01–1.31)*	1.32 (0.66–2.65)	1.13 (0.56–2.30)

^a The exponentiated β -coefficient from log-linear multiple regression that included all covariates in the table.^b ORs adjusted for all covariates in the tables.* $p < 0.05$ Compared with reference.**Table 3**Adjusted ORs (95% CI) for atopic dermatitis (AD), comparing the two highest tertiles with the lowest tertile of blood mercury concentrations in Korean adults ≥ 20 years of age.

	Blood mercury			<i>p</i> For trend
	Tertile 1 (< 3.56 µg/l)	Tertile 2 (3.56–6.04 µg/l)	Tertile 3 (> 6.04 µg/l)	
<i>Lifetime prevalence of an AD</i>				
Model 1	1.00 (reference)	1.03 (0.69–1.53)	1.51 (1.03–2.21)	0.055
Model 2	1.00 (reference)	1.03 (0.69–1.54)	1.50 (1.02–2.21)	0.059
Model 3	1.00 (reference)	1.01 (0.67–1.51)	1.50 (1.02–2.21)	0.057
<i>1-Year prevalence of an AD</i>				
Model 1	1.00 (reference)	1.34 (0.86–2.09)	1.85 (1.20–2.85)	0.019
Model 2	1.00 (reference)	1.34 (0.86–2.10)	1.84 (1.19–2.85)	0.022
Model 3	1.00 (reference)	1.31 (0.84–2.06)	1.82 (1.17–2.83)	0.026

Model 1: adjusted for age and sex. Model 2: adjusted for model 1+cigarette smoking status, alcohol drinking status, income, and fish or shellfish consumption. Model 3: adjusted for model 2+BMI and education.

In addition, the highest tertile of blood mercury concentration was more strongly associated than the lowest tertile with the OR for 1-year AD prevalence (OR=1.85; 95% CI, 1.20–2.85). This association

was unchanged after an adjustment for other potential covariates, including cigarette and alcohol consumptions, income, and fish or shellfish consumption (OR=1.84; 95% CI, 1.19–2.85; p for trend=0.022) and after an adjustment for all eight risk factors (OR=1.82; 95% CI, 1.17–2.83; p for trend=0.026).

4. Discussion

In this population-based study of Korean adults, the lifetime and 1-year prevalences of an AD were 10.9% and 8.8%, respectively. Epidemiological studies have indicated that the prevalence of an AD has increased to affect approximately 2–10% of adults, especially in industrialized countries (Bieber, 2008). Given the differences in genetic and environmental risk factors, the prevalence of an AD may vary widely among countries and by race/ethnicity. A recent study found an 8% dermatologist-diagnosed 1-year AD prevalence among Taiwanese adults (Lan et al., 2009), which was consistent with our prevalence rate of 8.8% among Korean adults.

Our findings demonstrated the variability in blood concentrations of mercury across demographic characteristics. Blood mercury increased most with increased alcohol consumption, income,

and fish or shellfish consumption. A previous study indicated an association between red wine consumption with increased blood mercury concentrations, possibly due to alterations in the rate of alcohol metabolism (Gundacker et al., 2006). However, the degrees to which mercury absorption and excretion rates are affected by alcohol consumption remain unclear. Fish consumption has been identified by many studies as an important variable for an increased total blood mercury levels (Jarup, 2003; Mahaffey et al., 2004; Mozaffarian and Rimm, 2006), and higher income has been shown to be related to blood mercury concentration, because individuals with higher incomes tend to eat more fish (Mahaffey et al., 2009). Our data show that an income level stood alone as a risk factor for an increased blood mercury level after an adjustment for demographic variables, including fish or shellfish consumption. This is consistent with the previous studies, in which higher income groups were at greater risk of mercury exposure (Hightower and Moore, 2003; Mahaffey et al., 2009). Therefore, many lifestyle and environmental factors related to high income levels may contribute to an increased blood mercury levels.

This study also indicated high blood mercury concentrations among males and subjects aged 40–59 years. Previous studies have produced inconsistent results regarding sex differences in blood mercury levels, possibly due to differences in race/ethnicity and lifestyle of the study populations. The elevation of blood mercury level in subjects aged 40–59 years identified in the present study is consistent with biomonitoring data from a population in New York City (McKelvey et al., 2007). These results suggest that males and subjects aged 40–59 years may have more chances of environmental and/or occupational exposure to mercury.

In this study, female gender and cigarette smoking were significant predictors of both lifetime and 1-year AD prevalence. Other epidemiological studies have also shown a significantly higher proportion of females than males in the distribution of an AD by sex (Williams et al., 1999). For example, the prevalence of an AD in Japanese adults aged 20 years or older was 9.3% for females and 5.1% for males (Saeki et al., 2006). Moreover an exposure to environmental tobacco smoke has been postulated as a risk factor for allergies (Kuyucu et al., 2004). While few studies have examined the effects of an active smoking on the risk for an AD among adults, many studies have identified a positive effect of environmental tobacco smoke on allergies and/or AD among children (Böhme et al., 2010; Kerkhof et al., 2003; Krämer et al., 2004). Furthermore, an active smoking is positively associated with eczema on the hands among adults (Thyssen et al., 2010).

After an adjustment for potential covariates, we analyzed the mercury levels of subpopulations with lifetime or 1-year AD. Overall, mercury blood levels were associated with significantly increased AD prevalence in adults. The immunomodulatory effects of mercury compounds are well known; low levels of mercury induce autoimmunity and the generalized activation of the immune system (Schuppe et al., 1998; Vas and Monestier, 2008). As immunological factors contribute to the pathogenesis of an AD (Leung and Bieber, 2003), mercury-triggered immunological reactions may play an important role in the mechanism of this disease.

In this study, we observed a positive association between mercury body burden and the lifetime prevalence of an AD, but much stronger associations between blood mercury and 1-year AD prevalence. As the half-life of mercury in blood is 37 days (Vas and Monestier, 2008) and mercury body burden is significantly correlated with recent AD (Weidinger et al., 2004), an individual's current mercury level will closely reflect the recent incidence of an AD more.

This study is subject to a number of limitations. Because the study used a cross-sectional design, the results only indicate associations and cannot be used to determine causality. The skin barrier is known to be damaged in patients with an AD, thereby

defective epidermal barrier could enhance the penetration of mercury through the skin barrier (Cork et al., 2006; Gattu and Maibach, 2011). Therefore, future studies should focus on whether a causal relationship can be established between mercury levels and the risk of an AD. Additionally, though genetic and immunological factors are important in the pathogenesis of an AD, we were unable to determine how the associations of mercury with an AD may be modified by genetic and immunological factors. In spite of these limitations, this study has several major strengths. To our knowledge, this is the first study to assess the association between mercury concentrations and AD among adults using nationally representative data. The other strength is that this study was able to control for several important confounding variables, including cigarette smoking, alcohol drinking, and fish or shellfish consumption.

The results of this study have important implications for the recommended action level for adult blood mercury. A high blood level of mercury could be one of the most important environmental risk factors for an AD. Our study supports the continuation of efforts to reduce mercury body burden, thereby reducing the risk of an AD in adult populations. To more fully elucidate the detailed etiological factors of an AD, further investigations of genetic and immunological risk factors, as well as other environmental factors, are necessary.

5. Conclusions

In this population-based study, adults with higher mercury body burdens were found to have an increased risk of an AD. These associations were stronger for 1-year AD prevalence than for lifetime prevalence, because an individual's current level of mercury reflects recent AD. Our results suggest the importance of promoting healthy behaviors to minimize the consumption of cigarettes, alcohol, and mercury-contaminated seafood, and the need to evaluate the body burden of mercury that contributes to the incidence of an AD.

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Disclaimers/competing interests declaration

The authors declare they have no competing financial interests.

Ethical consideration

The study protocol was approved by the Korean Ministry of Health and Welfare and was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects, as defined by the Helsinki Declaration. The study participants provided written informed consent.

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