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Relationship Between Serum Concentrations of Organochlorine Pesticides and Metabolic Syndrome Among Non-Diabetic Adults

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Objectives: This study was performed to investigate if organochlorine pesticides (OCPs) were associated with metabolic syndrome and insulin resistance among non-diabetes.
Methods: Among subjects who participated in a community-based health survey, 50 non-diabetic subjects with metabolic syndrome and 50 normal controls were selected. Insulin resistance was measured by the homeostasis model assessment (HOMA-IR). Eight OCPs were selected.
Results: After adjusting for confounders except for body mass index (BMI), beta-hexachlorocyclohexane (β-HCH) and heptachlor epoxide were positively associated with metabolic syndrome. Odds ratios across tertiles of β-HCH and heptachlor epoxide were 1.0, 3.2 and 4.4, and 1.0, 4.0 and 6.0, respectively (p for trend = 0.01 and <0.01). After additional adjustment for body mass index (BMI), heptachlor epoxide still showed an increasing trend with adjusted odds ratios of 1.0, 4.1, and 4.6 (p for trend = 0.10). When the five components of metabolic syndrome (with the definition of high fasting glucose ($\geq$100 mg/dL)) were separately analyzed, all components were positively, but not significantly, associated with heptachlor epoxide. As the serum concentration of heptachlor epoxide increased, HOMA-IR increased significantly in subjects with metabolic syndrome even after adjusting for BMI (p value <0.05 and <0.01).
Conclusions: Despite the small sample size, this study suggests that the background exposure to some OCPs may be associated with metabolic syndrome.

Key words: Organochlorine compounds, Environmental pollutants, Persistent organic pollutants, Metabolic syndrome X, Insulin resistance, Obesity
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INTRODUCTION

Persistent organic pollutants (POPs) such as polychlorinated dibenzo-p-dioxins, dibenzofurans, polychlorinated biphenyls, and organochlorine pesticides (OCPs) are stored in the adipose tissues of various living organisms because of their persistence in the environment and highly bioaccumulative nature [1]. Recent epidemiological studies have reported that the background exposure to POPs was strongly associated with type 2 diabetes in the general population [2-4]. Among several subclasses of POPs, OCPs tended to show the strongest association with type 2 diabetes [5,6].

On the other hand, there has been little research on whether the background exposure to POPs is associated with prediabetic conditions. After conducting an extensive literature review, only two studies were found that had been performed on the relationship of POPs with metabolic syndrome or insulin resistance in the U.S. non-diabetic general population [5,7]. Similar to type 2 diabetes, OCPs showed consistent associations with these prediabetic conditions [5,7].

OCPs were introduced in the 1940s and had been widely used for about two decades worldwide [8]. Although most of them have been banned since the 1970s in developed countries because of their environmental persistence and toxicity, some developing countries, especially in Asia, are still using some of them [8]. It has been reported that some OCPs were

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commonly detected in Koreans, although their absolute values were not higher than those of people in developed countries [9].

Metabolic syndrome is a constellation of risk factors related to increased incidence of cardiovascular disease and progression to type 2 diabetes. Although the prevalence of obesity as defined by the World Health Organization (WHO) is relatively low in Asia compared to western countries, metabolic syndrome is growing into a significant public health problem in Asia [10-12]. Recent use of OCPs in Asia may be related to the risk of metabolic syndrome in Asians. This case-control study was conducted to investigate the associations between serum concentrations of OCPs and metabolic syndrome in non-diabetic Koreans, with the hypothesis that serum concentrations of OCPs were higher in those with metabolic syndrome than those without it.

MATERIALS AND METHODS

I. Study Subjects

A community-based health survey was performed from June 2006 to December 2006 in Uljin county, South Korea. Residents aged ≥ 40 were passively invited to participate in the survey through a local newspaper and the boards of a community health service center and local hospital. Among 1,007 participants, there were 267 participants with metabolic syndrome after excluding participants who had diabetes (fasting glucose concentration ≥ 126 mg/dL or under medication). 50 subjects with metabolic syndrome were randomly selected as cases and 50 subjects without any component of metabolic syndrome were randomly selected as controls. Controls were individually matched to cases by age (±2 years) and sex. This study was conducted with the approval from the Institutional Review Board at the Kyungpook National University Hospital.

II. Measurement

Body weight was measured in light clothing and without shoes. Height was measured in a standing position. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist circumference was measured at the midpoint between the lower border of the rib cage and the iliac crest. Systolic and diastolic blood pressures were measured in the sitting position after 5-minute rest. Three blood pressure readings were obtained at 1-minute intervals, and were averaged and used in the analyses.

Blood was drawn after at least 8 hours overnight fasting. Fasting glucose, triglyceride, and high density lipoprotein (HDL) cholesterol were determined by enzymatic methods using ADVIA 1650 (Bayer Inc., New York, USA). Insulin was measured by a radioimmunoassay with a Packard gamma counter (GMI Inc., Minnesota, USA), and insulin resistance was estimated using the homeostasis model assessment (HOMA) method calculated by the following equation: (fasting insulin [mU/L] * fasting glucose [mmol/L] / 22.5).

OCPs were analyzed at the laboratory of the School of Environmental Science and Engineering, POSTECH (Pohang, Korea) using isotope dilution method with JMS-800 (JEOL, Tokyo, Japan) for gas chromatography-high resolution mass spectrometry (GC-HRMS). Analysis was conducted blind to case-control status. For a batch analysis, one procedure blank consisting of purified water and one in-house reference standard consisting of pooled human serum were analyzed for every 10 samples analyzed. The analytic results were reported on both wet-weight basis and lipid-adjusted or lipid-standardized basis. Total lipids were calculated using the formula: Total lipids (mg/dL) = 2.27 ×total cholesterol+triglyceride+62.3. Lipid-standardized concentrations of organochlorine pesticide (OCP) created by dividing each OCP concentration by the total lipid value were used. Limits of detection (LOD) defined as three times signal to noise ratio, and samples <LOD were given a half value of each LOD value.

Although 22 OCPs were measured in this study, eight pesticides for which at least 70% of study subjects had concentrations more than the LOD: beta-hexachlorocyclohexane (β-HCH) (100%), hexachlorobenzene (99%), oxychlordane (87%), trans-nonachlor (100%), heptachlor epoxide (98%), o,p' -DDE: o,p' -dichloro-diphenyl-dichloro-ethylene (o,p' -DDE) (70%), p,p' -dichloro-diphenyl-dichloro-ethylene (p,p' -DDE) (100%) and p,p' -dichloro-diphenyl-trichloro-ethane (p,p' -DDT) (98%) were selected.

III. Statistical Analyses

This study used the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria instead of using the original NCEP ATP III criteria. Modified NCEP ATP III criteria is recommended in the WHO West Pacific Region [13]. Metabolic syndrome was diagnosed on the concomitant presence of at least three of the following five features; waist circumference ≥90 cm (men), ≥80 cm (women); arterial pressure ≥ 130/85 mmHg or under medication; triglyceride ≥150 mg/dL; fasting glucose ≥110 mg/dL; HDL cholesterol <40 mg/dL (men), <50 mg/dL (women).

Serum concentrations of OCPs were categorized into three groups using control group tertile cutoff points, and multiple logistic regression analysis was used to calculate the risk for metabolic syndrome associated with OCPs. Although conditional logistic regression analysis is generally recommended in matched case-control studies, only the results of unconditional logistic regression analysis are shown because those of conditional logistic regression analysis were statistically unstable. In fact, in terms of point estimates, the results of conditional logistic regression showed stronger associations. Associations between OCPs and HOMA-IR were separately examined in case and control groups using Pearson correlation coefficients. Possible confounders were age (continuous), sex, alcohol consumption (continuous), cigarette smoking (continuous), and BMI (continuous). Throughout the paper, two models were presented; first, age, sex, alcohol consumption, and cigarette smoking were adjusted, and second, BMI was additionally adjusted. All data were analyzed using SAS version 9.1 (SAS Inc., Cary, NC, USA).

RESULTS

The demographic and biochemical characteristics of cases and controls are shown in Table 1. Compared with controls, BMI, waist circumference, systolic blood pressure, diastolic blood pressure, triglyceride, fasting plasma glucose, fasting insulin, and HOMA-IR were significantly higher in cases while HDL cholesterol was significantly lower in cases. When serum concentrations of OCPs between cases and controls were compared, serum concentrations of β-HCH, trans-nonachlor, and heptachlor epoxide were significantly higher in cases than in controls (Table 2).

Table 1. General characteristics and clinical variables between subjects with and without metabolic syndrome (percent or mean±standard deviation)

	Control (n=50)	Case (n=50)	p-value*
Men (%)	28.0	28.0	>0.95
Age (yr)	56.5 ± 6.9	56.5 ± 6.9	>0.95
Body massIndex (kg/m^2)	21.7 ± 2.3	25.8 ± 2.6	<0.01
Waist circumference (cm)	75.3 ± 6.9	88.7 ± 6.2	<0.01
Systolic blood pressure (mmHg)	114.9 ± 12.7	137.8 ± 16.0	<0.01
Diastolic blood pressure (mmHg)	70.6 ± 8.6	83.5 ± 9.2	<0.01
Triglyceride (mg/dl)	76.8 ± 26.7	211.7 ± 94.5	<0.01
Fasting plasma glucose (mg/dl)	89.2 ± 8.0	101.9 ± 20.4	<0.01
HDL cholesterol (mg/dl)	53.7 ± 9.2	38.4 ± 5.9	<0.01
Fasting insulin (μU/mL)	6.6 ± 2.5	10.7 ± 5.2	<0.01
HOMA-IR	1.47 ± 0.65	2.77 ± 1.85	<0.01

HDL: high density lipoprotein
HOMA-IR: homeostasis model assessment of insulin resistance
* Chi-square test or independent T-test

Table 2. Concentrations of organochlorine pesticides between subjects with and without metabolic syndrome (mean±standard deviation) (Unit : ng/lipid g)

	Control (n=50)	Case (n=50)	p-value*
Beta-hexachlorocyclohexane	46.1 ± 35.5	61.5 ± 37.6	<0.01
Hexachlorobenzene	20.8 ± 8.6	21.4 ± 11.5	0.77
Oxychlordane	8.0 ± 5.6	9.6 ± 7.5	0.22
Trans-nonachlor	21.7 ± 17.7	31.3 ± 30.0	0.05
Heptachlor epoxide	7.9 ± 7.0	13.2 ± 17.8	<0.01
o,p' -DDE	1.0 ± 0.9	1.2 ± 1.5	0.70
p,p' -DDE	416.3 ± 287.1	491.0 ± 398.7	0.47
p,p' -DDT	19.9 ± 10.5	23.4 ± 14.4	0.30

DDE; p'-dichloro-diphenyl-dichloroethylene
DDT; dichlorodiphenyl-trichloro-ethane
* Independent T-test after the natural logarithm transformation

Among eight OCPs, both β-HCH and heptachlor epoxide were positively and significantly associated with the prevalence of metabolic syndrome after adjusting for age, sex, cigarette smoking, and alcohol consumption (Table 3). Adjusted Odds Ratios (ORs) were 1.0, 3.2 (95% CI=1.0-10.3), and 4.4 (95% CI=1.4-13.5) across tertiles of β-HCH (p for trend =0.01; model Ⅰ). Heptachlor epoxide was also strongly associated with adjusted ORs of 1.0, 4.0 (95% CI=1.2-13.8), and 6.0 (95% CI=1.8-20.2) (p for trend <0.01; model Ⅰ). Although these significances disappeared after additional adjustment for BMI, heptachlor epoxide still showed a positive trend with adjusted ORs of 1.0, 4.1 (95% CI=0.8-21.5), and 4.6 (95% CI=0.9-23.5) (p for

Table 3. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of prevalence of metabolic syndrome by control group tertiles of lipid adjusted organochlorine pesticides

Analytes	Organochlorine pesticide tertiles (n=100)			p-trend
	1st Tertile	2nd Tertile	3rd Tertile	
Beta-hexachlorocyclohexane				
Median (ng/lipid g)	21.4	39.3	66.8	
Cases / Controls	6 / 17	18 / 16	26 / 17	
Model I	Referent	3.2 (1.0 - 10.3)	4.4 (1.4 - 13.5)	0.01
Model II	Referent	1.4 (0.3 - 6.3)	1.6 (0.4 - 7.1)	0.51
Hexachlorobenzene				
Median (ng/lipid g)	13.3	20.6	31.1	
Cases / Controls	25 / 17	10 / 16	15 / 17	
Model I	Referent	0.4 (0.1 - 1.1)	0.6 (0.2 - 1.6)	0.23
Model II	Referent	0.1 (0.0 - 0.6)	0.6 (0.2 - 2.6)	0.29
Oxychlordane				
Median (ng/lipid g)	4.4	7.7	12.6	
Cases / Controls	18 / 17	13 / 16	19 / 17	
Model I	Referent	0.8 (0.3 - 2.3)	1.1 (0.4 - 3.3)	0.82
Model II	Referent	0.8 (0.2 - 3.6)	0.8 (0.2 - 3.6)	0.81
Trans-nonachlor				
Median (ng/lipid g)	9.6	17.9	37.2	
Cases / Controls	14 / 17	16 / 16	20 / 17	
Model I	Referent	1.2 (0.4 - 3.6)	1.6 (0.5 - 4.9)	0.42
Model II	Referent	0.4 (0.1 - 1.7)	0.8 (0.2 - 3.5)	0.81
Heptachlor epoxide				
Median (ng/lipid g)	3.0	5.3	12.7	
Cases / Controls	5 / 17	18 / 16	27 / 17	
Model I	Referent	4.0 (1.2 - 13.8)	6.0 (1.8 - 20.2)	<0.01
Model II	Referent	4.1 (0.8 - 21.5)	4.6 (0.9 - 23.5)	0.10
o,p' -DDE				
Median (ng/lipid g)	0.2	0.9	2.0	
Cases / Controls	23 / 17	14 / 16	13 / 17	
Model I	Referent	0.6 (0.2 - 1.6)	0.5 (0.2 - 1.4)	0.18
Model II	Referent	0.3 (0.1 - 1.4)	0.4 (0.1 - 1.6)	0.15
p,p' -DDE				
Median (ng/lipid g)	161.0	314.6	723.8	
Cases / Controls	16 / 17	15 / 16	19 / 17	
Model I	Referent	0.9 (0.3 - 2.6)	1.1 (0.4 - 3.1)	0.80
Model II	Referent	0.4 (0.1 - 1.8)	0.6 (0.2 - 2.3)	0.48
p,p' -DDT				
Median (ng/lipid g)	10.7	18.0	33.6	
Cases / Controls	18 / 17	12 / 16	20 / 17	
Model I	Referent	0.7 (0.2 - 1.9)	1.2 (0.4 - 3.1)	0.80
Model II	Referent	0.8 (0.2 - 3.1)	1.4 (0.3 - 5.9)	0.64

DDE; p'-dichloro-diphenyl-dichloroethylene
DDT; dichlorodiphenyl-trichloro-ethane
Model I is adjusted for age, sex, alcohol, and smoking
Model II is adjusted for age, sex, alcohol, smoking, and body mass index

trend =0.10). On the other hand, hexachlorobenzene, o,p' -DDE, p,p' -DDE, and trans-nonachlor showed negative or J-shaped patterns. Although they were not statistically significant, each adjusted OR in the 2nd tertile was the lowest and that in the 3rd tertile increased slightly but did not exceed 1.0 (model II). Some OCPs, especially o,p' -DDE, showed negative patterns even though they were nonsignificant.

When the five components of metabolic syndrome were separately analyzed, both β-HCH and heptachlor epoxide tended to be associated with several components of metabolic syndrome. Even though most of the statistical significances disappeared after the additional adjustment for BMI, heptachlor epoxide still showed positive trends with all components of metabolic syndrome (with the modified criterion of high fasting glucose ($\geq$100 mg/dL)(Table 4).

Table 5 shows correlation coefficients between OCPs and HOMA-IR. As serum concentrations of heptachlor epoxide increased, HOMA-IR increased among subjects with metabolic syndrome. Even after adjusting for BMI, heptachlor epoxide still showed a significant

Table 4. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of five components of metabolic syndrome by tertiles of lipid adjusted serum concentrations of beta-hexachlorocyclohexane and heptachlor epoxide

	Organochlorine pesticide tertiles (n=100)			p-trend
	1st Tertile	2nd Tertile	3rd Tertile	
Beta-hexachlorocyclohexane				
Numbers	23	34	43	
Waist circumference (≥90 cm (men), ≥80 cm (women))				
Model Ⅰ	Referent	2.5 (0.8 - 7.9)	2.8 (0.9 - 8.4)	0.08
Model Ⅱ	Referent	0.9 (0.2 - 4.2)	0.7 (0.2 - 3.0)	0.58
High blood pressure (≥130/85 mmHg or under medication)				
Model Ⅰ	Referent	4.8 (1.4 - 16.4)	6.1 (1.9 - 20.0)	<0.01
Model Ⅱ	Referent	2.7 (0.6 - 13.2)	2.9 (0.6 - 13.5)	0.20
High triglyceride (≥150 mg/dL)				
Model Ⅰ	Referent	2.5 (0.8 - 8.1)	2.6 (0.8 - 8.1)	0.13
Model Ⅱ	Referent	0.8 (0.2 - 4.0)	0.7 (0.2 - 3.3)	0.69
High fasting glucose (≥110 mg/dL)				
Model Ⅰ	Referent	7.1 (0.8 - 66.6)	8.2 (0.9 - 71.4)	0.06
Model Ⅱ	Referent	4.8 (0.5 - 46.5)	5.1 (0.6 - 46.2)	0.19
Low HDL cholesterol (<40 mg/dL (men), <50 mg/dL (women))				
Model Ⅰ	Referent	1.4 (0.5 - 4.2)	1.4 (0.5 - 4.0)	0.57
Model Ⅱ	Referent	0.4 (0.1 - 1.9)	0.3 (0.1 - 1.4)	0.16
Heptachlor epoxide				
Numbers	22	34	44	
Waist circumference (≥90 cm (men), ≥80 cm (women))				
Model Ⅰ	Referent	3.0 (0.9 - 9.8)	3.7 (1.2 - 11.7)	0.04
Model Ⅱ	Referent	2.2 (0.4 - 11.2)	1.6 (0.3 - 8.0)	0.68
High blood pressure (≥130/85 mmHg or under medication)				
Model Ⅰ	Referent	3.6 (1.0 - 12.3)	7.3 (2.1 - 24.7)	<0.01
Model Ⅱ	Referent	3.4 (0.7 - 17.8)	6.6 (1.3 - 34.7)	0.03
High triglyceride (≥150 mg/dL)				
Model Ⅰ	Referent	4.8 (1.3 - 18.1)	5.9 (1.6 - 21.8)	0.01
Model Ⅱ	Referent	4.6 (0.9 - 24.6)	3.9 (0.8 - 20.1)	0.18
High fasting glucose* (≥100 mg/dL)				
Model Ⅰ	Referent	3.1 (0.7 - 13.9)	4.9 (1.2 - 20.9)	0.03
Model Ⅱ	Referent	2.7 (0.6 - 12.3)	3.5 (0.8 - 15.3)	0.11
Low HDL cholesterol (<40 mg/dL (men), <50 mg/dL (women))				
Model Ⅰ	Referent	1.8 (0.6 - 5.6)	3.4 (1.1 - 10.5)	0.03
Model Ⅱ	Referent	1.2 (0.3 - 5.0)	1.9 (0.4 - 7.9)	0.34

HDL: high density lipoprotein
Model Ⅰ is adjusted for age, sex, alcohol, and smoking
Model Ⅱ is adjusted for age, sex, alcohol, smoking, and body mass index
* When we analyzed the association between heptachlor epoxide and high fasting glucose, we redefined high fasting glucose as ≥ 100 mg/dL because there was no case in the referent group with the definition of ≥110 mg/dL

relationship. Among those without metabolic syndrome, heptachlor epoxide showed non-significant positive associations with HOMA-IR.

DISCUSSION

In this study, among 8 OCPs, heptachlor epoxide was most consistently associated with both metabolic syndrome and HOMA-IR. The associations of other OCPs with metabolic syndrome were not obvious, especially after adjusting for BMI. However, when the associations of OCPs with insulin resistance were separately examined in cases and controls, heptachlor epoxide was significantly and positively associated with HOMA-IR among subjects with metabolic syndrome even after adjusting for BMI. On the other hand, o,p' -DDE showed negative patterns though they were not statistically significant, suggesting that associations between OCPs and metabolic syndrome might be different depending on specific types of OCPs.

In previous studies which were performed among the U.S. population, among various OCPs, β-HCH, p,p' -DDE, oxychlordane, and trans-nonachlor were examined in relation to diabetes, insulin resistance, and metabolic syndrome [5-7]. Among these 4 OCPs, oxychlordane and trans-nonachlor were most strongly

Table 5. Pearson correlation coefficients between HOMA-IR and log-transformed serum concentrations of organochlorine pesticide

Analytes	Control (n=50)	Case (n=50)
Beta-hexachlorocyclohexane		
Model Ⅰ	0.16	0.22
Model Ⅱ	0.16	0.22
Hexachlorobenzene		
Model Ⅰ	0.13	0.19
Model Ⅱ	0.13	0.20
Oxychlordane		
Model Ⅰ	0.08	0.28
Model Ⅱ	0.08	0.25
Trans-nonachlor		
Model Ⅰ	0.06	0.20
Model Ⅱ	0.06	0.20
Heptachlor epoxide		
Model Ⅰ	0.20	0.36*
Model Ⅱ	0.20	0.32*
o,p' -DDE		
Model Ⅰ	0.08	0.25
Model Ⅱ	0.07	0.22
p,p' -DDE		
Model Ⅰ	-0.01	0.12
Model Ⅱ	-0.01	0.13
p,p' -DDT		
Model Ⅰ	0.05	0.15
Model Ⅱ	0.04	0.10

DDE; p'-dichloro-diphenyl-dichloroethylene
DDT; dichlorodiphenyl-trichloro-ethane
HOMA-IR: homeostasis model assessment of insulin resistance
Model Ⅰ is adjusted for age, sex, alcohol, and smoking
Model Ⅱ is adjusted for age, sex, alcohol, smoking, and body mass index
* p value <0.05

associated with type 2 diabetes and insulin resistance [5,6] while β-HCH showed the strongest association with metabolic syndrome [7]. In this study, subjects with high concentrations of β-HCH showed higher prevalence of metabolic syndrome only before adjusting for BMI. Heptachlor epoxide was not included in previous studies [5-7], because it was detected in less than 60% of study subjects in the U.S. population. Even though it was impossible to directly compare the current finding with those of previous studies, the consistent pattern of association of heptachlor epoxide with metabolic syndrome, each component of metabolic syndrome, and HOMA-IR suggest that heptachlor epoxide may be the most important one in relation to metabolic disturbance in Koreans.

Heptachlor epoxide is the most persistent metabolite of heptachlor which was used extensively in the past (1970s and 1980s) for killing insects in homes, buildings, and on food crops, mainly corn [1,14,15]. At present, humans are exposed to heptachlor and their metabolites through eating fish, dairy products, and fatty meat from animals [14,15]. Though there has been little human study on heptachlor epoxide, one recent prospective cohort study observed that the risk of diabetes increased in relation to using of heptachlor epoxide among pesticide applicators [2]. To our best knowledge, there has been no laboratory study on the associations between heptachlor epoxide and metabolic disturbance such as insulin resistance. However, one animal study reported significant variations of serum lipid levels after oral and intraperitoneal administration of heptachlor epoxide [16]. In relation to other health effects, animals fed heptachlor had enlarged livers, damaged kidney, and neoplasms at various sites [17-19]. Moreover, there is evidence that heptachlor epoxide was associated with infertility and improper development of offspring [20]. In fact, heptachlor belongs to the class of cyclodiene among OCPs [17,19]. Interestingly, both oxychlordane and trans-nonachlor which were strongly associated with diabetes and insulin resistance in the U.S. population, also belongs to the class of cyclodiene. Thus, in this sense, our findings on heptachlor epoxide can be interpreted as similar to those of previous studies.

β-HCH is an isomer of HCH, in which the active insecticidal ingredient is γ-HCH (lindane) [21]. β-HCH is more persistent and more slowly cleared from the body than other isomers, therefore β-HCH is the easiest isomer to detect in humans among the three and may be most likely to affect individual health chronically [21]. Nevertheless, the association between β-HCH and chronic diseases has only been rarely reported. Some Asian developing countries like China and India still use HCH, and the residents are continuously exposed to this contaminant [22].

In this study, BMI played an important role in the association between OCPs and metabolic syndrome, as evidenced by the fact that further adjustment for BMI made most of the associations with metabolic syndrome disappear. Because waist circumference, an abdominal obesity index which is highly correlated with BMI, is one component of metabolic syndrome and BMI itself is strongly related to all metabolic syndrome components, including BMI as a covariate may be an overadjustment in this study. Even though OCPs were associated with metabolic syndrome even after adjusting for BMI in the previous study [7], our sample size is very small compared with that of the previous study which was

performed among subjects ≥700.

The major limitation of this study is the cross-sectional design. The association between lipid soluble toxins and metabolic syndrome or insulin resistance may be explainable by reverse causality. Secondly, some of results came out as not statistically significant despite their strong associations due to the small sample size. Finally, only OCPs were examined in this study. Besides OCPs, other subclasses of POPs such as polychlorinated biphenyls may be as important as OCPs. In addition, drawing conclusions about associations with individual compounds based on epidemiological studies would be difficult because there are considerable correlations between the serum concentrations of organochlorine pesticides.

In summary, it was found that some OCPs such as heptachlor epoxide, oxychlordane, or β-HCH were associated with metabolic syndrome or insulin resistance. Although further prospective studies are needed to confirm these associations, the chronic background exposure to environmental pollutants such as OCPs may be involved in the pathogenesis of metabolic syndrome or insulin resistance.

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