

## Familial aggregation of the metabolic syndrome in Korean families with adolescents

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Received 31 December 2004; received in revised form 2 July 2005; accepted 18 July 2005

Available online 26 August 2005

### Abstract

We investigated the familial aggregation of the metabolic syndrome in Korean families with adolescents. In a cross-sectional observational study, the body mass index, waist circumference, blood pressure, fasting glucose, serum triglyceride, HDL-cholesterol, total cholesterol and fasting insulin concentrations, and homeostasis model assessment (HOMA) score, were examined in each individual in 132 Korean nuclear families. Most variables of the metabolic syndrome in offspring were significantly correlated with those of parents. Compared with sons, daughters had more significant difference for the metabolic parameters according to clustering of risk factors of their parents. Especially, daughters showed higher correlations with their parents for waist circumference, with their mothers for fasting glucose and HDL-cholesterol, and with their fathers for fasting insulin than sons. Compared with children whose parents did not have the metabolic syndrome, the odds ratios in children with at least one parent with the metabolic syndrome were 4.1 (1.6–10.6) for overweight, 3.6 (1.3–10.2) for abdominal obesity, 5.0 (2.0–12.3) for high triglycerides, and 4.8 (1.1–21.0) for the metabolic syndrome. We also observed significant correlations in variables of the metabolic syndrome between siblings and between spouses. In Korean families with adolescents, there is a familial aggregation of the metabolic syndrome, with daughters resembling their parents more than sons. These findings may have significant implications for clinical interventions directed at adolescents at high risk for the metabolic syndrome.

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**Keywords:** Metabolic syndrome; Familial aggregation; Adolescents; Korean

### 1. Introduction

The metabolic syndrome is a constellation of hypertension, impaired glucose tolerance, dyslipidemia, and abdominal obesity and is associated with an increased risk of total and cardiovascular mortality in adults [1,2]. Genetic as well as environmental influences have been implicated in obesity and several cardiovascular risk factors [3,4], and it was recently suggested that the metabolic syndrome may originate in utero [5].

Tracking of cardiovascular disease from childhood to adulthood suggests that early detection of individuals at risk,

along with family-based intervention programs, may have long-term benefits for the prevention of cardiovascular risks [6,7]. Family is one of the most important factors affecting metabolic risk factors in children, in that family displays an interaction between genetic and shared environmental factors [8,9]. Childhood and adolescent overweight has been increasing in Asian countries due to urbanization and economic development [10]. Over the past 10 years, the rates of overweight among Korean children and adolescents aged 5–20 years have doubled [11], which may ultimately cause an increase in adverse cardiovascular outcomes. The prevalence of the metabolic syndrome is high among obese children and adolescents, and increases with increasing obesity [12,13].

An association between parental metabolic disorders and components of the metabolic syndrome in their offspring

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has been observed [3,4]. Most of these studies, however, measured parental history of metabolic disease rather than directly testing components of the metabolic syndrome. Furthermore, no study to date has examined the familial aggregation of metabolic syndrome in Asian countries. In general, Asians have a high prevalence rate of cardiovascular diseases and the metabolic syndrome, even at lower body mass index [14,15]. We therefore sought to evaluate the incidence of familial aggregation of components of the metabolic syndrome, as well as familial influence, on the presence of metabolic syndrome in Korean nuclear families with adolescents.

## 2. Methods

### 2.1. Recruitment of subjects

Study participants included biological families with adolescent children recruited at the Asan Medical Center between July 2001 and February 2002. The study was approved by the Institutional Review Board of Asan Medical Center, and informed consent was obtained. The majority of adolescents resided with their parents in family households in or near Seoul, Korea. Exclusion criteria included obesity secondary to hypothyroidism or Cushing's disease, severe debilitating diseases, or cancer. In addition, women who were pregnant or lactating were excluded. Subjects were also excluded from participation if they had been treated with any anti-obesity agent or insulin, or if they had lost more than 10% of their normal weight during the previous 6 months. The study population was composed of 132 families with adolescent children. There were 487 subjects in total: 128 fathers, 130 mothers, 132 first siblings, 92 second siblings, and 5 third siblings.

### 2.2. Anthropometric measurements

Height and weight were measured by an automatic height–weight scale to the nearest 0.1 cm and 0.1 kg, respectively. Body mass index (BMI) was calculated by dividing weight (kg) by height squared ( $m^2$ ). Body fat and total body fat mass were determined by bioimpedance analysis (Inbody 3.0, Biospace, Korea) [16]. Using a non-elastic tape measure, waist circumference was measured at the end of a normal expiration at the midpoint between the lower border of the rib cage and the iliac crest [17]. The definition of overweight in parents was  $BMI \geq 25 \text{ kg}/m^2$ , as defined by the World Health Organization (WHO) guidelines for adult obesity [17]. Overweight adolescents were classified according to the international cut off points for BMI for overweight by sex between 2 and 18 years calculated to pass through a BMI of  $25 \text{ kg}/m^2$  at age 18 years, based on six nationally representative cross-sectional samples [18].

### 2.3. Measurements of metabolic risk factors

The components of the metabolic syndrome (systolic blood pressure, diastolic blood pressure, and serum fasting plasma glucose, triglycerides, and HDL-cholesterol concentrations), as well as other metabolic variables (serum concentrations of total cholesterol and fasting insulin, and homeostasis model assessment score), were measured in all subjects.

Blood pressure was measured with a mercury sphygmomanometer with the individual in a sitting position and after 10 min of rest. Study subjects refrained from smoking or ingesting caffeine during the 30 min preceding the measurement. Cuff size was selected according to the arm circumference of each participant. Blood samples were obtained from each subject after a 12-h overnight fast by evacuation from an antecubital vein into vacutainer tubes. Fasting plasma glucose concentration was measured by a glucose oxidase method, and total cholesterol and triglycerides levels were measured by enzymatic procedures using an autoanalyzer (Hitachi-747, Japan). The HDL-cholesterol fraction was measured enzymatically after precipitation of apo-B containing lipoproteins with  $MnCl_2$ . Fasting insulin concentration was measured by radioimmunoassay (Dianabott, Japan). Homeostasis model assessment (HOMA) score, an estimate of insulin resistance, was calculated as fasting serum insulin ( $\mu\text{U}/mL$ )  $\times$  fasting plasma glucose ( $mmol/L$ )/22.5 [19].

### 2.4. Definition of the metabolic syndrome

Metabolic syndrome in parents was defined according to criteria modified from those of the NCEP ATP III [20]. The criteria for high blood pressure, high fasting glucose, high triglyceride, and low HDL-cholesterol were adopted from the reference values of the NCEP ATP III [20]. The reference values for abdominal obesity, however, were taken from the Asia–Pacific guidelines for obesity [21]. Parents having three or more of the following criteria were defined as having the metabolic syndrome: blood pressure  $\geq 130/\geq 85 \text{ mmHg}$ ; fasting glucose  $\geq 6.05 \text{ mmol}/L$  (110 mg/dL); serum triglycerides  $\geq 1.65 \text{ mmol}/L$  (150 mg/dL); HDL-cholesterol  $< 1.05 \text{ mmol}/L$  (40 mg/dL) in men or  $< 1.30 \text{ mmol}/L$  (50 mg/dL) in women; waist circumference  $> 90 \text{ cm}$  in men or  $> 80 \text{ cm}$  in women.

In adolescents aged 11–19 years, elevated systolic or diastolic blood pressure was defined as a value at or above the 90th percentile for age, sex, and height recommended by the updated Task Force Report on the diagnosis and management of hypertension in childhood [22]. The reference value for elevated fasting glucose was 110 mg/dL or higher ( $\geq 6.1 \text{ mmol}/L$ ) [23]. Criteria for triglycerides ( $\geq 110 \text{ mg}/dL$  or  $\geq 1.24 \text{ mmol}/L$ ) and HDL-cholesterol ( $\leq 40 \text{ mg}/dL$  or  $\leq 1.03 \text{ mmol}/L$ ) were adopted from published reference values [24,25]. Abdominal obesity was defined as a value at or above the 90th percentile for age and sex from representative national data of Korean adolescents [26]. Children

having three or more of the following criteria were defined as having the metabolic syndrome: blood pressure  $\geq 90$  percentile; fasting glucose  $\geq 6.05$  mmol/L (110 mg/dL); serum triglycerides  $\geq 1.24$  mmol/L (110 mg/dL); HDL-cholesterol  $< 1.05$  mmol/L (40 mg/dL); waist circumference  $\geq 90$  percentile.

2.5. Statistical analysis

Descriptive data were expressed as mean values with standard deviations for continuous variables. The analysis of variance with Tukey’s test was used to compare differences of variables in offspring according to the number of components of the metabolic syndrome among parents. Logistic regression analysis was performed to examine the risks of the metabolic syndrome and overweight in children according to the status of the metabolic syndrome of parents. The odds ratios (OR) are presented together with their 95% confidence intervals (CI).

The degree of familial aggregation was evaluated by an intraclass correlation coefficient ( $r$ ) after adjusting for age and sex. The intraclass correlations in nuclear families were estimated using the maximum likelihood variance component technique for unequal family sizes in a random-effect model [27]. Since the relationship between age and metabolic risk factors may vary between men and women, as well as between parents and offspring, the regression model was built separately in parents and children by sex, and a  $z$ -transformation was used to standardize the regression residuals by generation and sex.

$$r = \frac{S_A^2}{S_A^2 + S_W^2}$$

where  $S_A^2$  is the sample estimate of  $\rho_A^2$ , the component of variance due to among-family effects;  $S_W^2$  is the sample estimate of  $\rho_W^2$ , the component of variance due to within-family effects [27]. The statistical significance of  $r$  was tested using the standard method for comparing the calculated  $F$  to  $F_0$ , the tabulated value of the  $F$ -distribution with  $k - 1$  and  $N - k$  degrees of freedom at the 0.05 level of significance, where  $k$  is the number of families and  $N$  is the total number of observations included in the respective analyses. We also applied  $Z$ -test to analyze gender difference of offspring in correlation coefficients between parents. All analyses were two-tailed and a  $p$ -value  $< 0.05$  was considered statistically significant. Statistics were performed using SAS 8.0.

3. Results

3.1. Basic characteristics of family members

The basic characteristics of the parents and their children are presented in Table 1. The mean age of the children was 13.3 years, and the mean parental age was 43.6 years for fathers and 40.9 years for mothers. The prevalence of the metabolic syndrome was 13.3% for fathers and 10.0% for mothers, compared with 10.3% for sons and 1.9% for daughters.

3.2. Anthropometric measurements and metabolic variables of offspring according to the number of components of the metabolic syndrome in parents

Anthropometric measurements and metabolic variables of offspring according to the number of components of

Table 1  
Basic characteristics and metabolic variables of 487 family members

	Mean $\pm$ S.D.			
	Fathers (128)	Mothers (130)	Sons (126)	Daughters (103)
Age (years)	43.6 $\pm$ 4.3	40.9 $\pm$ 3.8	13.3 $\pm$ 3.3	13.3 $\pm$ 3.5
BMI (kg/m <sup>2</sup> )	25.1 $\pm$ 2.9	24.0 $\pm$ 3.3	22.8 $\pm$ 5.0	21.3 $\pm$ 4.5
Waist circumference (cm)	87.4 $\pm$ 7.3	77.8 $\pm$ 7.4	78.4 $\pm$ 13.3	71.3 $\pm$ 11.2
Systolic blood pressure (mmHg)	122.0 $\pm$ 13.5	114.4 $\pm$ 11.5	114.6 $\pm$ 13.7	109.0 $\pm$ 11.0
Diastolic blood pressure (mmHg)	80.0 $\pm$ 12.6	69.9 $\pm$ 10.1	66.2 $\pm$ 11.6	64.7 $\pm$ 9.6
Fasting glucose (mg/dL)	93.9 $\pm$ 16.0	87.5 $\pm$ 8.4	85.3 $\pm$ 6.6	83.6 $\pm$ 5.8
Total cholesterol (mg/dL)	200.7 $\pm$ 31.6	183.7 $\pm$ 30.0	172.2 $\pm$ 32.5	174.6 $\pm$ 30.9
Triglyceride (mg/dL)	156.9 $\pm$ 106.4	96.5 $\pm$ 53.2	97.3 $\pm$ 60.9	93.8 $\pm$ 48.4
HDL-cholesterol (mg/dL)	50.4 $\pm$ 11.5	54.0 $\pm$ 12.4	53.9 $\pm$ 13.1	55.5 $\pm$ 12.2
Fasting insulin ( $\mu$ IU/mL)	8.7 $\pm$ 6.4	8.3 $\pm$ 5.2	14.2 $\pm$ 12.3	11.9 $\pm$ 7.6
HOMA score	1.81 $\pm$ 1.40	1.63 $\pm$ 1.08	2.71 $\pm$ 2.52	2.21 $\pm$ 1.44
	No. (%)			
Overweight	63 (49.2)	42 (32.3)	68 (54.0)	38 (37.0)
Abdominal obesity	40 (31.3)	47 (36.2)	46 (43.8)	24 (28.6)
High blood pressure	28 (21.9)	8 (6.2)	21 (19.6)	8 (9.1)
High fasting glucose	12 (9.4)	3 (2.3)	0 (0.0)	0 (0.0)
High triglyceride	49 (38.3)	20 (15.4)	39 (31.0)	22 (21.4)
Low HDL-cholesterol	19 (14.8)	50 (38.5)	15 (11.9)	5 (4.9)
Metabolic syndrome	17 (13.3)	13 (10.0)	13 (10.3)	2 (1.9)

Data are presented as mean and standard deviations.

Table 2

Anthropometric measurements and metabolic variables of offspring according to the number of components of the metabolic syndrome in fathers

	Number of components of the metabolic syndrome in fathers		
	0	1	≥2
<b>Sons (n)</b>	35	31	30
Age (years)	13.1 ± 3.3	13.1 ± 3.2	12.4 ± 3.5
BMI (kg/m <sup>2</sup> )	20.9 ± 5.2	23.3 ± 5.5	23.1 ± 5.4
Body fat (%)	20.4 ± 7.4	24.9 ± 9.7	25.0 ± 9.7
Waist circumference (cm)	74.3 ± 14.3	79.2 ± 13.8	78.4 ± 14.0
Systolic blood pressure (mmHg)	113.4 ± 15.4	115.3 ± 14.5	113.2 ± 14.4
Diastolic blood pressure (mmHg)	65.7 ± 12.2	66.4 ± 12.5	65.7 ± 12.4
Fasting glucose (mg/dL)	84.5 ± 5.6	85.2 ± 6.5	86.8 ± 7.5
Total cholesterol (mg/dL)	169.4 ± 34.1	174.2 ± 29.3	172.3 ± 30.3
Triglyceride (mg/dL)	89.9 ± 50.2	94.6 ± 72.6	102.2 ± 50.3
HDL-cholesterol (mg/dL)	56.9 ± 15.2	55.5 ± 13.5	52.1 ± 12.6
Fasting insulin (μIU/mL)	14.0 ± 14.5	13.4 ± 7.0	15.8 ± 17.1
HOMA score	2.6 ± 2.9	2.5 ± 1.4	3.1 ± 3.6
<b>Daughters (n)</b>	27	30	26
Age (years)	12.8 ± 3.9	12.9 ± 3.8	13.6 ± 3.0
BMI (kg/m <sup>2</sup> )*	19.6 ± 4.2 <sup>b</sup>	21.6 ± 4.2 <sup>b,a</sup>	23.0 ± 4.7 <sup>a</sup>
Body fat (%)*	25.4 ± 7.9 <sup>*</sup>	29.5 ± 7.4 <sup>b,a</sup>	30.8 ± 6.9 <sup>a</sup>
Waist circumference (cm)*	67.2 ± 10.6 <sup>b</sup>	71.3 ± 10.7 <sup>b,a</sup>	76.5 ± 12.5 <sup>a</sup>
Systolic blood pressure (mmHg)*	106.3 ± 10.1 <sup>b</sup>	106.1 ± 11.4 <sup>b</sup>	116.9 ± 10.3 <sup>a</sup>
Diastolic blood pressure (mmHg)	62.9 ± 8.1	63.8 ± 8.5	68.0 ± 13.1
Fasting glucose (mg/dL)	84.7 ± 6.1	82.8 ± 5.6	84.3 ± 5.8
Total cholesterol (mg/dL)	169.4 ± 34.1	174.2 ± 29.3	172.3 ± 30.3
Triglyceride (mg/dL)*	89.9 ± 50.2 <sup>b</sup>	94.6 ± 72.6 <sup>b,a</sup>	102.2 ± 50.3 <sup>a</sup>
HDL-cholesterol (mg/dL)	56.7 ± 9.3	56.9 ± 13.3	54.7 ± 13.7
Fasting insulin (μIU/mL)	11.9 ± 8.2	11.5 ± 7.1	12.8 ± 8.4
HOMA score	2.2 ± 1.6	2.2 ± 1.4	2.4 ± 1.5

Body fat was measured in 96 sons and 83 daughters among offspring.

\*  $p < 0.05$  by ANOVA with Tukey's test. Means in the same row with different superscript letters (a and b) are significantly different.

the metabolic syndrome in fathers and mothers are presented in Tables 2 and 3. We did not observe any significant relationships between anthropometric measurements and metabolic variables in sons and the number of components of the metabolic syndrome in parents. In daughters, however, anthropometric measurements and variables associated with the metabolic syndrome and insulin resistance increased according to the number of components of the metabolic syndrome in parents.

### 3.3. Adjusted intraclass correlation coefficients of components of the metabolic syndrome and other metabolic variables among family members

The intraclass correlations of components of the metabolic syndrome and other metabolic variables adjusted for age and sex in the six combinations of nuclear family members are shown in Table 4. Compared with sons, daughters showed higher correlations with their parents for waist circumference, with their mothers for fasting glucose and HDL-cholesterol, and with their fathers for fasting insulin than sons. However, fathers showed a higher correlation with their children for systolic blood pressure than did mothers. For fasting glucose concentration, the only significant correlation was between mothers and daughters. The correlations between siblings for all metabolic variables

were highly significant. Between spouses, correlations for blood pressure, fasting insulin, and HOMA score were significant.

### 3.4. Odds ratios and 95% confidence intervals for overweight and the metabolic syndrome in offspring with respect to the status of metabolic syndrome of parents

Table 5 shows the odds ratios for overweight and the metabolic syndrome of offspring based on the status of the metabolic syndrome of parents. Compared with children whose parents did not have the metabolic syndrome, the odds ratios in children with at least one parent with the metabolic syndrome were 4.1 (1.6–10.6) for overweight, 3.6 (1.3–10.2) for abdominal obesity, 5.0 (2.0–12.3) for high triglycerides, and 4.8 (1.1–21.0) for the metabolic syndrome.

## 4. Discussion

We have shown here that the risk of the metabolic syndrome in children was highly correlated with parental status of components of the metabolic syndrome. Our data demonstrated that the metabolic syndrome has familial components and point towards the influence of genes and shared environment in the etiology of the metabolic syndrome.

Table 3

Anthropometric measurements and metabolic variables of offspring according to the number of components of the metabolic syndrome in mothers

	Number of components of the metabolic syndrome in mothers		
	0	1	≥2
<b>Sons (n)</b>	36	35	25
Age (years)	12.6 ± 3.3	13.5 ± 3.1	12.1 ± 3.2
BMI (kg/m <sup>2</sup> )	21.2 ± 5.4	22.8 ± 5.3	23.6 ± 5.5
Body fat (%)	22.0 ± 9.1	22.4 ± 8.5	26.6 ± 9.4
Waist circumference (cm)	73.9 ± 13.3	78.6 ± 14.9	80.3 ± 13.5
Systolic blood pressure (mmHg)	114.1 ± 12.8	115.9 ± 17.6	111.1 ± 12.9
Diastolic blood pressure (mmHg)	65.9 ± 10.9	67.9 ± 13.9	63.9 ± 11.7
Fasting glucose (mg/dL)	86.1 ± 6.3	84.8 ± 6.8	85.9 ± 7.5
Total cholesterol (mg/dL)	173.8 ± 29.7	164.9 ± 29.1	175.1 ± 36.3
Triglyceride (mg/dL)	97.8 ± 71.9	94.8 ± 56.2	91.6 ± 34.2
HDL-cholesterol (mg/dL)	57.1 ± 13.8	53.1 ± 12.9	51.6 ± 13.2
Fasting insulin (μIU/mL)	13.1 ± 9.0	14.3 ± 10.3	16.4 ± 20.9
HOMA score	2.5 ± 1.7	2.7 ± 1.8	3.3 ± 4.5
<b>Daughters (n)</b>	37	24	22
Age (years)	12.1 ± 3.2	14.3 ± 3.8	13.2 ± 3.7
BMI (kg/m <sup>2</sup> )*	20.3 ± 4.0 <sup>b</sup>	20.5 ± 3.8 <sup>b</sup>	24.1 ± 5.1 <sup>a</sup>
Body fat (%)*	27.0 ± 6.4 <sup>b</sup>	26.9 ± 8.1 <sup>b</sup>	33.1 ± 7.4 <sup>a</sup>
Waist circumference (cm)*	68.6 ± 10.1 <sup>b</sup>	69.0 ± 9.3 <sup>b</sup>	78.4 ± 14.3 <sup>a</sup>
Systolic blood pressure (mmHg)	110.0 ± 11.3	108.2 ± 11.8	108.5 ± 13.4
Diastolic blood pressure (mmHg)	65.1 ± 9.2	64.8 ± 9.8	64.0 ± 12.4
Fasting glucose (mg/dL)	84.2 ± 6.4	83.7 ± 5.7	82.5 ± 5.2
Total cholesterol (mg/dL)	182.8 ± 28.3	172.5 ± 34.0	169.0 ± 27.8
Triglyceride (mg/dL)*	89.1 ± 39.4 <sup>b</sup>	76.4 ± 45.0 <sup>b,a</sup>	108.9 ± 54.4 <sup>a</sup>
HDL-cholesterol (mg/dL)*	61.9 ± 12.7 <sup>b</sup>	56.3 ± 10.4 <sup>b</sup>	47.6 ± 7.6 <sup>a</sup>
Fasting insulin (μIU/mL)*	10.9 ± 7.3 <sup>b</sup>	10.2 ± 5.9 <sup>b</sup>	16.7 ± 9.1 <sup>a</sup>
HOMA score*	2.1 ± 1.5 <sup>b</sup>	1.9 ± 1.1 <sup>b</sup>	3.1 ± 1.7 <sup>a</sup>

Body fat was measured in 96 sons and 83 daughters among offspring.

\*  $p < 0.05$  by ANOVA with Tukey's test. Means in the same row with different superscript letters (a and b) are significant different.

As familial transmission is a risk factor for obesity [28,29], it is important to evaluate familial factors to identify strategies for the prevention and management of the metabolic syndrome. In particular, we observed gender differences in correlations between parents and offspring. Daughters showed higher correlations with their parents for waist circumference, with their mothers for fasting glucose and HDL-cholesterol, and with their fathers for fasting insulin than sons. However, fathers showed a higher correlation with their children for systolic blood pressure than did mothers. Conversely, for systolic blood pressure, sons showed a significantly higher correlation

with their parents than did daughters. These results are in agreement with previous factor analysis results showing that blood pressure is not closely linked to the other components of the metabolic syndrome [30].

The intraclass correlation for fasting blood glucose between mothers and daughters was the only significant correlation among any of the parent-offspring matched pairs. Although the reasons for this correlation are not clear, these findings are in agreement with studies showing excess maternal transmission of type 2 diabetes [31,32]. Thus, the correlation we observed may represent a genetic effect that is

Table 4

Adjusted intraclass correlation coefficients of components of the metabolic syndrome and other metabolic variables among family members

	Fathers–mothers	Fathers–sons	Fathers–daughters	Mothers–sons	Mothers–daughters	All offspring
Waist circumference <sup>‡</sup>	0.12	0.06	0.37 <sup>†</sup>	0.21*	0.46 <sup>†</sup>	0.34 <sup>†</sup>
Systolic blood pressure	0.21*	0.27*	0.27*	0.18	0.13	0.30 <sup>†</sup>
Diastolic blood pressure	0.21*	0.23*	0.23*	0.24*	0.29*	0.37 <sup>†</sup>
Fasting glucose <sup>§</sup>	−0.05	0.14	0.09	0.16	0.27*	0.49 <sup>†</sup>
Total cholesterol	0.13	0.40 <sup>†</sup>	0.45 <sup>†</sup>	0.37 <sup>†</sup>	0.31 <sup>†</sup>	0.38 <sup>†</sup>
Triglyceride	−0.00	0.03	0.20	−0.04	0.13	0.21*
HDL-cholesterol <sup>§</sup>	0.13	0.37 <sup>†</sup>	0.29*	0.41 <sup>†</sup>	0.65 <sup>†</sup>	0.34 <sup>†</sup>
Fasting insulin <sup>  </sup>	0.38 <sup>†</sup>	0.21*	0.59 <sup>†</sup>	0.33 <sup>†</sup>	0.48 <sup>†</sup>	0.43 <sup>†</sup>
HOMA score	0.30 <sup>†</sup>	0.36 <sup>†</sup>	0.47 <sup>†</sup>	0.31 <sup>†</sup>	0.47 <sup>†</sup>	0.47 <sup>†</sup>

Daughters had higher correlation coefficients with their parents (<sup>‡</sup> $p < 0.05$ ), with mothers (<sup>§</sup> $p < 0.05$ ), and with fathers (<sup>||</sup> $p < 0.05$ ) than did sons by Z-test.\*  $p < 0.05$ .<sup>†</sup>  $p < 0.005$  by intraclass correlation analysis after adjustment for age and sex.

Table 5

Logistic regression analysis with overweight or the metabolic syndrome of offspring as the dependent variable and the status of the metabolic syndrome of parents as the independent variable

	Status of metabolic syndrome	
	Fathers (–) and mothers (–) <sup>a</sup>	Fathers (+) or mothers (+) <sup>b</sup>
	OR	OR (95% CI)
Overweight	1.0	4.1 (1.6–10.6)
Abdominal obesity	1.0	3.6 (1.3–10.2)
High blood pressure	1.0	1.9 (0.6–5.7)
High fasting glucose	1.0	–
High triglyceride	1.0	5.0 (2.0–12.3)
Low HDL-cholesterol	1.0	0.4 (0.1–3.0)
Metabolic syndrome	1.0	4.8 (1.1–21.0)

<sup>a</sup> Number of offspring:  $N = 172$ .

<sup>b</sup> Number of offspring:  $N = 43$ .

expressed or transmitted differently between the sexes, or it may be a sex-specific environmental effect.

The correlations between siblings for all metabolic variables were highly significant. All children recruited into this study were the biological offspring of their parents and shared the same family environment, thus sharing genetic and environmental or behavioral factors. Of particular interest was our finding of non-zero correlations for blood pressure and insulin resistance between spouses. Since spouses are not related by blood, any correlation of these metabolic variables likely reflects the environmental factors to which the couples are exposed.

Compared with children whose parents did not have the metabolic syndrome, the odds ratio for the metabolic syndrome in children having at least one parent with the metabolic syndrome was 4.8 (1.1–21.0). These results indicate that biomarkers for an increased risk of cardiovascular disease are already present in these children. We could not analyze gender differences in the relationship between the occurrence of the metabolic syndrome in parents and children, because the numbers of individuals were insufficient for statistical analysis. We observed a significant increase in odds ratios for overweight, abdominal obesity, and high triglyceride among offspring. In contrast, we found that the odds ratios for high blood pressure, high blood glucose, and low HDL-cholesterol were not significant. These findings suggest that the phenotype of overweight or abdominal obesity appears in adolescence prior to the appearance of the phenotype of hypertension, type 2 diabetes, or low HDL-cholesterol in adulthood. These findings are consistent with the report that the offspring of diabetic parents display excess body fat, beginning in childhood, as well as accelerated progression of adverse risk profile characteristics of the insulin resistance syndrome from childhood to young adulthood [33].

This study has several potential limitations. First, because the study sample was recruited in urban areas and consisted of a high proportion of overweight subjects, we cannot claim that our sample was a representative national sample. Second, we did not account for the variability of morphology

probably due to sexual maturation in adolescents. Third, the fact that very few girls and overall few people in this study showed the metabolic syndrome might decrease the power of the study. The last limitation was our use of arbitrary criteria for the metabolic syndrome in adolescents and adults. Because criteria of the metabolic syndrome have never been formally defined in children or adolescents, we used criteria previously established for adolescents [12]. Among other criteria for the metabolic syndrome for adults [20,34,35], we used the criteria specified by NCEP ATP III which was easier to apply to study subjects.

In conclusion, we have shown here that, in Korean nuclear families, there are familial aggregations for the metabolic syndrome, as well as gender differences in familial correlations of phenotypes of the metabolic syndrome in adolescent children with daughters being more likely than sons to be affected by parental metabolic risk factors. Further studies are necessary to investigate specific genetic and environmental factors related to the metabolic syndrome in this population.

## Acknowledgements

This work was supported by Grant No. R04-2001-00020 from the Korea Science & Engineering Foundation and Grant 2004 from the Korean Society of the Study of Obesity.

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