Original Article

Metabolic syndrome in Korean adolescents and young adult offspring and their parents

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Background and Objectives: Studies have investigated the associations between parental metabolic syndrome (MetS) and offspring MetS. This study aimed to uncover parental-offspring associations for MetS and its components according to offspring sex and age. **Methods and Study Design:** A cross-sectional study in 1,403 fathers, 1,451 mothers, and 1,532 offspring (340 male and 404 female offspring aged 10-18 years; 283 male and 505 female offspring aged 19-25 years) using the Korea National Health and Nutrition Examination Survey data between 2010 and 2013. **Results:** All categorized MetS components in fathers and mothers were significantly associated with the same components in male offspring, while high waist circumference, high triglycerides, and low high-density lipoprotein in fathers and mothers were associated with the same components in female offspring. The number of categorized MetS components which were significantly associated between parent-offspring pairs was greater in offspring aged 19-25 years than in those aged 10-18 years. All categorized MetS components were significantly associated between father-male offspring aged 19-25 years pairs, but not in other parent-offspring pairs. The MetS *per se* in fathers and mothers was significantly associated with that in male offspring aged 10-18 years. **Conclusions:** There were differential associations according to offspring sex and age group and parent's sex with respect to parental-offspring associations for MetS and its individual components. The associations for MetS and its components were stronger in young adult versus adolescent offspring, in male offspring versus female offspring.

Key Words: metabolic syndrome, offspring, parent, sex, age

INTRODUCTION

Metabolic syndrome (MetS) is a constellation of cardiovascular risk factors and an important health issue in adolescents and early adulthood because this condition can result in increased risk of metabolic syndrome, type 2 diabetes mellitus, and cardiovascular disease later in life.[1-3] Familial factors have been considered as a risk factor for MetS, including genetic and environmental factors shared among family members. Studies on familial influence have reported a degree of heritability for MetS and its components,[4,5] an association between parental history of diabetes and MetS in adolescents,[6] and intra-familial associations for cardio metabolic risk factors.[7,8] However, few studies have directly examined the association between parental MetS and offspring MetS in adult offspring[9,10] and adolescent offspring.[11] In those studies, there were differential associations according to parental relation and sex of the adult offspring[9,10] and an increased risk of adolescent MetS with parental MetS.[11] However, whether the parental-offspring associations for MetS and its components differ according to the age of the offspring remains unclear.

This study aimed to uncover the associations between parental-offspring pairs for MetS and its components according to the offspring age groups and sex using data from the Korea National Health and Nutrition Examination Survey (KNHANES).

MATERIALS ANDMETHODS

Study population

Subjects were drawn from a representative sample of the civilian, non-institutionalized Korean population included in the KNHANES as performed by the Korean Ministry of Health and Welfare during 2010-2013.[12,13] Among a total of 27,930 participants included in this study, there were 1,274 families including 1,782 adolescents and young adult offspring. Data pertaining to MetS status in the 1,403 fathers, 1,451 mothers, and 1,532 offspring (340 male and 404 female offspring aged 10-18 years; 283 male and 505 female offspring aged 19-25 years) were used. The KNHANES was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Institutional Review Board of the Korean Center for Disease Control and Prevention. Written in-

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formed consent was obtained from all participants.

Definition of metabolic syndrome

Body mass index (BMI) was calculated as weight (kg)/height (m^2) and measured according to standard procedures. Waist circumference (WC) was measured in the standing position at the narrowest region between the lower margin of the rib cage and the iliac crest. Blood pressure (BP) was assessed manually using a standard mercury sphygmomanometer under standard conditions. Venous blood samples were collected from each subject after a 12-h overnight fast. The levels of high-density lipoprotein (HDL) cholesterol, triglycerides (TG), and fasting plasma glucose (FPG) were measured using an automatic analyzer (Automatic Chemistry Analyzer 7600, Hitachi, Tokyo, Japan).

The definition of MetS was adapted from the International Diabetes Federation (IDF).[14] According to the International Diabetes Federation definition, an individual must have central obesity plus any two of the other four additional components. The five MetS component criteria were as follows: WC ≥90 cm in males aged >16 years, ≥80 cm in females aged >16 years or ≥ the age-specific and the sex-specific 90th percentile for Korean children and adolescent offspring aged 10-16 years;[15,16] BP ≥130/85 mmHg or a history of hypertension; FPG ≥5.6 mmol/L or a history of diabetes mellitus; TG ≥1.7 mmol/L; and HDL <1.03 mmol/L in offspring aged 10-16 years and males aged >16 years or <1.29 mmol/L in females aged >16 years.[14,17] Obesity was defined as a BMI ≥25 kg/m^2 for parents and offspring aged 19-25 years.[18] Overweight was defined as a BMI ≥ the age-specific and the sex-specific 95th percentile for offspring aged 10-18 years.[16,19] Medical history of hypertension and diabetes was assessed using a standardized questionnaire.

Statistical analyses

All analyses were separately conducted by sex and age group (10-18 years and 19-25 years) of the offspring. The chi-square test or t-test was respectively applied to compare categorical variables or continuous variables in the offspring according to sex and age group. The same analyses were conducted to compare between the father and the mother. The mixed linear model was used for the associations between individual MetS components or BMI in offspring and the same MetS component or BMI in the father (or mother) after adjusting for the age of the offspring, father, and mother, the same MetS component in the mother (or father), and the intra-familial correlation. The generalized estimating equation was applied for the associations between MetS *per se* or categorized MetS components in the offspring and the same component in the father (or mother) after adjusting for the age of the offspring, father, and mother, the same variable in the mother (or father), and the intra-familial correlation. The IBM SPSS Statistics software version 21.0.0.0 (IBM, Armonk, NY, USA) was used for analyses.

RESULTS

The prevalence of MetS was not significantly different in offspring according to sex (2.4% in male offspring vs 1.3% in female offspring), while it was significantly different according to offspring age group (1.0% in offspring aged 10-18 years vs. 2.4% in those aged 19-25 years, p=0.036) and parent's sex (20.7% for fathers vs. 16.1% for mothers, p=0.001). There were significant differences in high BP, high TG level, and low HDL level according to the offspring sex, high BP and low HDL level according to offspring age group, and all categorized MetS components according to parent's sex (Table 1).

Table 2 shows the relationships between the MetS component in the father (or the mother) and the same component in the offspring after adjusting for the age of parents and offspring, the intra-familial correlation, and the same MetS component in the mother (or the father). When stratified by offspring sex, WC, glucose level, and HDL level in parents were consistently associated with the same MetS component in the offspring regardless of offspring sex. When further stratified by offspring age group and sex, WC and HDL level in parents were consistently associated with the same component in the offspring regardless of offspring age group and sex. All MetS components were significantly associated between male offspring aged 10-18 years-mother pairs, female offspring aged 19-25 years-father pairs, and female offspring aged 19-25 years-mother pairs.

As shown in Table 3, the associations of categorized MetS components and MetS *per se* in the father (or the mother) with the same variable in the offspring were specific according to the offspring sex and age group and parent's sex. When stratified by offspring sex, all categorized MetS criteria in fathers and mothers were significantly associated with the same criteria in male offspring, while high WC, high TG levels, and low HDL levels were associated between parent-female offspring pairs. When further stratified by offspring age group, all categorized MetS components in fathers and mothers were significantly associated with the same components in male offspring, while high WC, high TG, and low HDL in fathers and mothers were associated with the same components in female offspring. The number of categorized MetS components which were significantly associated between parent-offspring pairs was greater in offspring aged 19-25 years than in those aged 10-18 years. All categorized MetS components were significantly associated between father-male offspring aged 19-25 years pairs, but not in other parent-offspring pairs. The MetS *per se* in fathers and mothers was significantly associated with that in male offspring aged 10-18 years.

DISCUSSION

From this cross-sectional study conducted in a representative sample from the Korean population, the number of offspring who satisfied the criteria of MetS was small. Although some non-significant findings may be related to the lack of power of the statistical analyses, current findings suggest that the associations for the MetS and its components between parents and the offspring were specific to offspring sex and age group and parent's sex. First of all, the associations tended to be stronger in male offspring than in female offspring. In addition, the associations tended to be stronger in offspring aged 19-25 years than in those aged 10-18 years. The associations for all categorized MetS components were found only between

Table 1. Characteristics of offspring and parents

	Offspring sex			Offspring age group			Parents		
	Men (n=744)	Women (n=788)	*p*	10-18 years (n=623)	19-25 years (n=909)	*p*	Father (n=1,403)	Mother (n=1,451)	*p*
Age (y)	18.2±4.8	18.9±4.6	0.002	13.6±2.5	22.1±2.1	<0.001	49.6 (5.5)	46.4 (5.4)	<0.001
Metabolic syndrome	18 (2.4)	10 (1.3)	0.093	6 (1.0)	22 (2.4)	0.036	291 (20.7)	233 (16.1)	0.001
Obesity/overweight	136 (18.3)	88 (11.2)	<0.001	42 (6.7)	182 (20.0)	<0.001	463 (39.4)	435 (30.0)	0.082
High waist	87 (11.7)	74 (9.4)	0.157	56 (9.0)	105 (11.6)	0.108	399 (28.4)	548 (37.8)	<0.001
High blood pressure	90 (12.1)	10 (1.3)	<0.001	25 (4.0)	75 (8.3)	0.001	617 (44.2)	332 (22.9)	<0.001
High glucose	37 (5.0)	28 (3.6)	0.168	30 (4.8)	35 (3.9)	0.357	561 (40.0)	297 (20.5)	<0.001
High triglycerides	81 (10.9)	55 (7.0)	0.007	55 (8.8)	81 (8.9)	0.955	664 (47.3)	253(17.4)	<0.001
Low HDL	80 (10.8)	146 (18.5)	<0.001	66 (10.6)	160 (17.6)	<0.001	359 (25.6)	513 (35.4)	<0.001

HDL: high density lipoprotein cholesterol.
The values were n (%) or mean±SD.
Metabolic syndrome was defined by the criteria of the International Diabetes Federation.
Overweight was defined as a BMI ≥ the age-specific and the sex-specific 95th percentile of BMI for offspring aged 10-18 years.
p-value using chi-square test or *t*-test.

Table 2. Change of MetS component in offspring estimated by 1 unit change of the same MetS component in parent

	All offspring		Offspring aged 10-18 y		Offspring aged 19-25 y	
	Men	Women	Men	Women	Men	Women
Father						
BMI (1 kg/m^2)	0.23 (0.14, 0.32)*	0.33 (0.25, 0.42)*	0.25 (0.12, 0.38)*	0.33 (0.20, 0.45)*	0.20 (0.07, 0.32)*	0.27 (0.15, 0.38)*
WC (1 cm)	0.22 (0.14, 0.31)*	0.25 (0.18, 0.32)*	0.24 (0.12, 0.36)*	0.26 (0.15, 0.38)*	0.19 (0.07, 0.31)*	0.26 (0.17, 0.36)*
SBP (1 mmHg)	0.10 (0.05, 0.16)*	0.05 (0.01, 0.10)*	0.06 (-0.03, 0.14)	0.04 (-0.05, 0.12)	0.15 (0.08, 0.22)*	0.06 (0.01, 0.11)*
DBP (1 mmHg)	0.12 (0.06, 0.19)*	0.05 (-0.01, 0.10)	0.05 (-0.04, 0.14)	-0.01 (-0.11, 0.08)	0.21 (0.12, 0.30)*	0.09 (0.03, 0.16)*
Glucose (1 mmol/L)	0.04 (0.01, 0.06)*	0.05 (0.02, 0.07)*	0.01 (-0.02, 0.04)	0.05 (0.02, 0.09)*	0.06 (0.02, 0.09)*	0.04 (0.01, 0.07)*
TG (1 mmol/L)	0.08 (0.01, 0.15)*	0.07 (0.04, 0.10)*	0.05 (-0.01, 0.11)	0.09 (0.03, 0.15)*	0.09 (-0.02, 0.20)	0.05 (0.01, 0.09)*
HDL (1 mmol/L)	0.25 (0.17, 0.32)*	0.26 (0.19, 0.33)*	0.21 (0.10, 0.33)*	0.33 (0.22, 0.44)*	0.25 (0.15, 0.34)*	0.22 (0.13, 0.31)*
Mother						
BMI (1 kg/m^2)	0.29 (0.20, 0.38)*	0.19 (0.12, 0.26)*	0.33 (0.19, 0.46)*	0.08 (-0.03, 0.19)	0.35 (0.23, 0.46)*	0.24 (0.15, 0.34)*
WC (1 cm)	0.30 (0.22, 0.39)*	0.18 (0.12, 0.25)*	0.36 (0.22, 0.49)*	0.16 (0.05, 0.27)*	0.27 (0.15, 0.39)*	0.19 (0.11, 0.27)*
SBP (1 mmHg)	0.14 (0.08, 0.19)*	0.06 (0.02, 0.10)*	0.21 (0.12, 0.30)*	0.03 (-0.06, 0.11)	0.07 (0.01, 0.14)*	0.08 (0.03, 0.13)*
DBP (1 mmHg)	0.17 (0.10, 0.25)*	0.08 (0.03, 0.13)*	0.21 (0.11, 0.32)*	0.10 (-0.01, 0.20)	0.13 (0.04, 0.23)*	0.08 (0.02, 0.15)*
Glucose (1 mmol/L)	0.09 (0.06, 0.12)*	0.05 (0.03, 0.07)*	0.08 (0.03, 0.14)*	0.01 (-0.05, 0.05)	0.09 (0.06, 0.13)*	0.07 (0.04, 0.10)*
TG (1 mmol/L)	0.11 (-0.01, 0.23)	0.11 (0.04, 0.17)*	0.12 (0.04, 0.20)*	0.19 (0.05, 0.32)*	0.10 (-0.12, 0.31)	0.08 (0.01, 0.14)*
HDL (1 mmol/L)	0.22 (0.15, 0.29)*	0.17 (0.10, 0.23)*	0.24 (0.15, 0.33)*	0.12 (0.02. 0.22)*	0.23 (0.13, 0.32)*	0.20 (0.11, 0.29)*

MetS: metabolic syndrome; BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglycerides; HDL: high density lipoprotein cholesterol.
The values were represented as the estimate (95% confidence interval) after adjusting for fixed effects (ages of offspring, father, and mother, the same MetS component of other parent) and a random effect (family relation) using the mixed linear model.
*p<0.05.

Table 3. Odds ratio for MetS *per se* or individual MetS component in offspring according to the same MetS component in each parent

	All offspring		Offspring aged 10-18 y		Offspring aged 19-25 y	
	Men	Women	Men	Women	Men	Women
Father						
Obesity/overweight	1.68 (1.10, 2.57)*	2.78 (1.68, 4.62)*	2.72 (0.98, 7.52)	4.66 (1.30, 16.70)*	1.53 (0.95, 2.47)	2.50 (1.42, 4.41)*
MetS	2.89 (1.08, 7.73)*	NA	11.7 (1.02, 134.43)*	NA	1.84 (0.56, 6.04)	NA
High waist	2.57 (1.54, 4.29)*	2.09 (1.22, 3.59)*	4.97 (1.83, 13.54)*	2.31 (0.99, 5.41)	2.04 (1.09, 3.83)*	2.01 (1.01, 4.02)*
High blood pressure	2.15 (1.32, 3.48)*	1.92 (0.54, 6.79)	2.63 (0.97, 7.11)	0.73 (0.05, 10.01)	2.10 (1.20, 3.66)*	3.05 (0.50, 18.56)
High glucose	2.88 (1.37, 6.05)*	2.38 (0.97, 5.80)	1.77 (0.59, 5.33)	3.45 (0.96, 12.44)	4.54 (1.47, 14.04)*	1.60 (0.45, 5.71)
High triglycerides	2.71 (2.59, 4.64)*	2.76 (1.43, 5.30)*	2.16 (0.92, 5.04)	1.88 (0.75, 4.74)	3.46 (1.68, 7.10)*	4.20 (1.57, 11.26)*
Low HDL	3.28 (1.96, 5.48)*	2.63 (1.73, 4.00)*	4.05 (1.90, 8.62)*	3.34 (1.48, 7.56)*	2.96 (1.45, 6.02)*	2.60 (1.59, 4.25)*
Mother						
Obesity/overweight	2.13 (1.39, 3.28)*	2.20 (1.33, 3.63)*	2.52 (1.00, 6.33)*	1.77 (0.51, 6.21)	1.95 (1.20, 3.16)*	2.20 (1.25, 3.89)*
MetS	2.60 (0.94, 7.19)	3.39 (0.81, 14.23)	6.18 (1.06, 36.19)*	NA	2.07 (0.66, 6.51)	3.29 (0.77, 14.05)
High waist	1.98 (1.20, 3.27)*	1.96 (1.16, 3.29)*	1.15 (0.45, 2.94)	1.23 (0.48, 3.14)	2.45 (0.33, 4.51)	2.48 (1.26, 4.89)*
High blood pressure	1.95 (1.17, 3.27)*	0.72 (0.15, 3.33)	3.91 (1.44, 10.65)*	NA	1.53 (0.85, 2.75)	1.11 (0.21, 5.87)
High glucose	2.15 (1.01, 4.56)*	2.84 (1.23, 6.56)*	2.99 (0.90, 9.95)	0.92 (0.19, 4.33)	1.77 (0.68, 4.63)	7.89 (2.26, 27.61)*
High triglycerides	4.65 (2.68, 8.06)*	2.17 (1.05, 4.50)*	2.46 (0.91, 6.67)	3.40 (1.16, 9.99)*	6.20 (3.11, 12.34)*	1.54 (0.54, 4.38)
Low HDL	2.14 (1.29, 3.54)*	1.70 (1.12, 2.56)*	1.66 (0.79, 3.49)	1.69 (0.71, 4.01)	2.73 (1.34, 5.57)*	1.69 (1.06, 2.71)*

MetS: metabolic syndrome; HDL: high density lipoprotein cholesterol; NA: not applicable.
Values were represented as odds ratio (95% confidence interval) by generalized estimating equation after adjusting for age of offspring and parents, the same MetS component of other parent, and correlation within family relation.
*$p<0.05$.

the father-male offspring aged 19-25 years pairs, while the associations for all MetS components (as continuous variables) were found between the mother-male offspring aged 10-18 years pairs, the father-female offspring aged 19-25 years pairs, and the mother-female offspring aged 19-25 years pairs. Paternal and maternal MetS were associated with that in male offspring aged 10-18 years.

The differential associations according to offspring sex and parent's sex with respect to the MetS components were suggested in the FeLs Longitudinal Study. In this study conducted for the offspring aged 18-35 years, there were significant associations for MetS classification between male offspring and both the mothers and fathers, but a weaker association between female offspring and mothers. The authors of this study also reported differential associations between the MetS in fathers and mothers and the MetS components in the offspring according to offspring sex.[9] However, they did not present findings for the associations for the same MetS components between parent-offspring pairs. The differential associations according to the parent's sex were also found for the parent-offspring associations in the Framingham Heart Study. In contrast to the current findings of paternal-male offspring associations for MetS, in the Framingham Heart Study performed in the offspring aged 21 years or older, maternal MetS, rather than paternal MetS, was more influential on the occurrence of female offspring with MetS.[10] Several factors such as the differences in age of the offspring, study design, adjusted confounding factors, the definition of MetS, and ethnicity may contribute to those differential associations of the father and mother with their offspring across the various studies.

The reasons behind the differences in offspring age group and sex for those parent-offspring associations are not clear. It is likely that the findings of the stronger parental-offspring associations in offspring aged 19-25 years may be explained by the long-term sharing of the integrated effects of genetic and environmental factors compared to adolescent offspring although genetic and environmental factors shared between parent-offspring pairs could not be dissected in the present study. The higher prevalence of some criteria of MetS components in older offspring and male offspring than in younger offspring and female offspring may partially explain the differences. Further studies are necessary to clarify the influence of offspring age and sex on these associations.

There are several limitations to be noted. As there is lack of information about the biologic parent-offspring relations, some relations may not have been classified as biological kinship. Inclusion of non-biological parental-offspring pairs may attenuate the strength of associations because they cannot contribute genetic factors to the phenotypic relationship. Although there were parental-offspring associations for MetS, the causal relationship cannot be inferred from this cross-sectional study design. As sibling effects, socioeconomic status, dietary factors, physical activity, and other health behaviors of individuals were not taken into account in the analyses, the associations could contain residual effects of those factors. Given those limitations, the present findings extend previous knowledge about parental-offspring associations of MetS *per se* and its individual criteria in a representative population-based sample.

In conclusion, there were differential associations according to offspring sex and age group and parent's sex with respect to parental-offspring associations for MetS and its individual components. The associations were stronger in male offspring than in female offspring and in young adult offspring than in adolescent offspring.

AUTHOR DISCLOSURES

No competing conflict of interest exist.

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