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ORIGINAL ARTICLE

Asthma-Like Symptoms are Increased in the Metabolic Syndrome

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Background. The prevalence of obesity and asthma has been increasing during the last several decades. Obesity has been reported to be associated with asthma. Obesity, especially abdominal obesity, is the main component of the metabolic syndrome. **Objectives.** We thus hypothesized that metabolic syndrome is an important contributing factor for the development of asthma-like symptoms. **Methods.** The Korean Health and Genome Study started in 2001 as an ongoing population-based study of Korean adults 40 to 69 years of age. The prevalence of asthma-like symptoms in the previous 12 months was obtained by a questionnaire, and spirometric testing was conducted. **Results.** Among the 10,038 participants, the data from 9,942 individuals (4,716 men and 5,226 women) was available. Asthma-like symptoms (wheeze [$p = 0.0006$], resting dyspnea [$p = 0.0062$], and post-exercise dyspnea [$p < 0.0001$]) were increased in the subjects of the metabolic syndrome group. Subjects with asthma-like symptoms had a decreased lung function compared to subjects without asthma-like symptoms. Among the components of the metabolic syndrome, abdominal obesity and hypertension were the risk factors for asthma-like symptoms. **Conclusions.** Metabolic syndrome is associated with asthma-like symptoms. Among the components of metabolic syndrome, abdominal obesity and hypertension are the risk factors for asthma-like symptoms.

Keywords asthma-like symptoms, metabolic syndrome, epidemiology, Korea

INTRODUCTION

Asthma is a chronic inflammatory disorder that is associated with airway hyper-responsiveness, and this leads to recurrent episodic symptoms. Asthma is estimated to affect about 300 million individuals worldwide, with the global prevalence of asthma ranging from 1% to 18% of the general population (1). The risk factors for the development of asthma are complex, ranging from genetic traits and environmental factors to multifactorial causes that are interlaced with other disease entities such as gastroesophageal reflux disease (GERD) and obesity. Since the late 1990s, obesity has been reported to be associated with asthma (2–5). Obesity, especially central obesity, is known to be an important component of the metabolic syndrome. The metabolic syndrome is a commonly used term for the clustering of type 2 diabetes mellitus, essential hypertension, dyslipidemia, and central obesity. Although there have been several studies about the association between asthma and obesity, to the best of our knowledge, there is no study concerning the relationship between the metabolic syndrome and asthma or asthma-like symptoms.

This study examines whether the metabolic syndrome is an important contributing factor for the development of asthma or asthma-like symptoms.

MATERIALS AND METHODS

Study Subjects

The Korean Health and Genome Study started in 2001 as an ongoing population-based study of Korean adults 40 to 69 years of age. The participants of the study include residents of an industrialized urban city Ansan, which is 32 km southwest of the capital city, Seoul, and in a rural city, An-sung, which is 100 km south of Seoul. The study procedures were in accordance with institutional guidelines and the procedures were approved by the Institutional Review Board of Korea University Medical Center. Informed consent was obtained from the study participants.

Study enrollment was based on the knowledge about community differences and on the most efficient method for recruiting representative samples of the Korean population. Since telephone use in Ansan is high, enrollment was based on random selection from directorate listings that were made available on compact discs by the local telephone companies. After 10,957 telephone calls, 2,523 men and 2,497 women agreed to participate in a baseline physical examination that included routine assessment of anthropometry, blood pressure, pulmonary function, electrocardiogram (ECG), lipid profiles, and other factors. In Ansong, the sampling was based on telephone, mailing, and door-to-door solicitations within 5 randomly selected regions from a total of 11 regions. After identifying 7,192 eligible subjects, 2,239 men and 2,779 women underwent identical examinations as were done in Ansan. In both Ansan and Ansong, the age and sex

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distributions of those subjects who were examined were comparable with those of the subjects who were not examined.

Asthma-Like Symptoms and Pulmonary Function Testing

The prevalence of asthma-like symptoms in the previous 12 months was obtained by a questionnaire that all the subjects completed. Spirometric testing was conducted by an experienced pulmonary technician through the use of a portable spirometer (Vmax-2130; SensorMedics, Yorba Linda, CA, USA) according to the criteria of the American Thoracic Society (6). The predicted forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) were obtained with using the methods of Morris (7).

Definition of the Metabolic Syndrome

Data were also collected on the factors that were used to define the components of the metabolic syndrome. Metabolic syndrome was diagnosed when ≥ 3 of the following 5 risk factors were present: an elevated blood pressure, a low serum level of high-density lipoprotein cholesterol (HDL-C), an elevated level of serum triglycerides, a high fasting serum glucose level, and abdominal obesity (waist circumference) (8).

Hypertension was diagnosed when the systolic blood pressure was ≥ 130 mmHg or the diastolic blood pressure was ≥ 85 mmHg, or when a study participant was receiving antihypertensive medication. Low HDL-cholesterol was defined when these levels were <40 mg/dL in men and <50 mg/dL in women, based on the blood that was drawn after a 10-hour fast and after precipitation of the other lipoproteins with using heparin-manganese chloride. Based on the same samples, the triglyceride concentrations were determined enzymatically after hydrolyzation with glycerol. Hypertriglyceridemia was defined when the triglyceride concentrations were ≥ 150 mg/dL. Fasting samples were also used to determine the serum glucose based on an enzymatic reaction; High fasting glucose was defined as a glucose level ≥ 110 mg/dL or when a subject was receiving oral hypoglycemic agents or insulin therapy. Abdominal obesity was defined as a waist circumference ≥ 90 cm for men and ≥ 85 cm for women (9). Specifically, the waist circumference was measured at a midpoint between the lower rib margin and the iliac crest in a standing position while the subject was wearing only underwear.

Statistical Analysis

All the data were summarized as mean (SD) for the continuous variables and as the frequency (percentage) for discrete variables. Student's *t* test and the chi-square test were performed to compare baseline characteristics between the metabolic and non-metabolic syndrome groups. The Cochran Mentel and Haenszel test was used to adjust the age factor for comparing the prevalence of asthma-like symptoms between the two groups. Finally, multiple logistic regression analysis evaluated the significant metabolic components that contributed to asthma-like symptoms.

RESULTS

Among the 10,038 participants in the Korean Health and Genome Study, the data from 9,942 individuals (4,716 men

TABLE 1.—Baseline characteristics of the study participants.

Variables	Metabolic syndrome (n = 2730, 27.46%)	Non-metabolic syndrome (n = 7212, 72.54%)	<i>p</i> value
Age, years	55.02 (8.59)	51.04 (8.75)	<0.0001
Male	957 (35.05)	3759 (52.12)	<0.0001
HDL, mg/dL			
Male	37.14 (6.81)	45.24 (10.06)	<0.0001
Female	40.01 (7.02)	48.51 (10.15)	<0.0001
Fasting glucose, mg/dL	95.78 (31.59)	84.30 (15.22)	<0.0001
Triglyceride, mg/dL	229.07 (127.69)	136.86 (81.77)	<0.0001
Waist circumference, cm			
Male	90.58 (6.55)	81.88 (6.87)	<0.0001
Female	88.85 (7.43)	78.16 (9.63)	<0.0001
SBP, mmHg	128.97 (18.60)	112.95 (15.90)	<0.0001
DBP, mmHg	81.38 (11.52)	72.72 (10.57)	<0.0001

Data are presented as mean (SD) or number (%).

and 5,226 women) was available for examining the association between asthma-like symptoms and the metabolic syndrome.

Table 1 shows the general and clinical characteristics of the study participants according to the presence or absence of metabolic syndrome. The mean age was 55.0 years for the subjects with the metabolic syndrome and the mean age was 51.0 years for the subjects without metabolic syndrome. The proportion of males was 35.05% and 52.12% for the 2 groups, respectively. The prevalence of the individual components of the metabolic syndrome was significantly higher in the metabolic syndrome group ($p < 0.0001$).

Among asthma-like symptoms, the prevalence of wheeze, resting dyspnea, and post-exercise dyspnea was significantly higher in the metabolic syndrome group than that in the non-metabolic syndrome group ($p < 0.05$, age adjusted). Yet the prevalence of night cough, dust-induced dyspnea, and a history of asthma treatment was not different between two groups (Table 2).

The FVC (% predicted), FEV₁/FVC (%), FEV₁ (% predicted), and forced expiratory flow during the middle half of the forced vital capacity (FEF_{25–75}) (% predicted) were significantly lower in those patients who had wheeze than in those patients who did not have wheeze in the metabolic syndrome group ($p < 0.0001$). This phenomenon was similar to resting dyspnea and post-exercise dyspnea in the metabolic syndrome group (Table 3).

Among the components of the metabolic syndrome, abdominal obesity and high blood pressure were revealed to be risk factors for asthma-like symptoms with their odds ratios ranging from 1.06 to 2.04 ($p < 0.05$) (Table 4). The rest

TABLE 2.—The prevalence of an affirmative response (%) to the written questions on asthma-like symptoms.

Variables	Metabolic syndrome (n = 2730, 27.46%)	Non-metabolic syndrome (n = 7212, 72.54%)	* <i>p</i> value
Wheeze	304 (11.14)	563 (7.81)	0.0006
Night cough	286 (10.71)	659 (9.29)	0.2291
Resting dyspnea	243 (8.90)	447 (6.20)	0.0062
Post-exercise dyspnea	406 (14.87)	766 (10.62)	<0.0001
Dust-induced dyspnea	233 (8.72)	554 (7.78)	0.5781
History of asthma Tx	87 (3.25)	219 (3.08)	0.8544

Data are presented as number (%). **p* value: age adjusted.

TABLE 3.—The age-adjusted pulmonary function tests according to the presence and absence of asthma-like symptoms in the metabolic syndrome group (n = 2730).

Variables	Present	Absent	p value
Wheezing	304 (11.14)	2426 (88.86)	
FVC, % predicted	100.50 (15.66)	104.50 (15.24)	<0.0001
FEV ₁ /FVC, %	77.78 (8.31)	80.27 (7.06)	<0.0001
FEV ₁ , % predicted	106.55 (19.58)	113.07 (18.01)	<0.0001
FEF _{25–75} , % predicted	88.03 (33.98)	104.20 (33.56)	<0.0001
Resting dyspnea	243 (8.90)	2487 (91.10)	
FVC, % predicted	102.12 (14.89)	104.29 (15.40)	0.0465
FEV ₁ /FVC, %	78.11 (7.60)	80.18 (7.18)	<0.0001
FEV ₁ , % predicted	108.85 (18.81)	112.75 (18.17)	<0.0001
FEF _{25–75} , % predicted	90.61 (33.69)	103.60 (33.78)	<0.0001
Post-exercise dyspnea	406 (14.87)	2324 (85.13)	
FVC, % predicted	102.25 (15.86)	104.40 (15.21)	0.0117
FEV ₁ /FVC, %	79.03 (8.12)	80.18 (7.07)	0.0102
FEV ₁ , % predicted	109.82 (19.69)	112.85 (17.98)	0.0054
FEF _{25–75} , % predicted	96.11 (36.79)	103.59 (33.34)	0.0002

Data are presented as mean (SD) or number (%).

of components (HDL, TG, high glucose) did not show any significant correlation with asthma-like symptoms.

DISCUSSION

The principal finding of our study is that asthma-like symptoms (wheeze, resting dyspnea, and post-exercise dyspnea) were increased in the subjects of the metabolic syndrome group and subjects with asthma-like symptoms had decreased lung function compared to subjects without asthma-like symptoms. Among the components of the metabolic syndrome, abdominal obesity and hypertension were shown to be the risk factors for asthma-like symptoms.

There have been several previous studies that investigated the correlation between obesity and asthma-like symptoms (2–5, 10, 11). In these studies, the body mass index (BMI) usually represented the overall obesity. The components of the metabolic syndrome occur more frequently in the overweight or obese subjects, but this is not merely because of obesity per se. In other words, excessive visceral adiposity (but not simply being overweight) will increase the likelihood that a person will be insulin resistant and subsequently be diagnosed with metabolic syndrome. In this context, abdominal obesity could be particularly useful for identifying the persons who are at an increased risk for metabolic syndrome, which is relevant to insulin resistance. To the best of our knowledge, there has been no study concerned with the

relation between the metabolic syndrome and asthma-like symptoms, and our results firmly support our hypothesis that abdominal obesity and metabolic syndrome are linked to the risk factors of asthma-like symptoms.

Several studies focusing on the relation between obesity and asthma have studied the role of leptin (3, 12–15). According to these reports, leptin was suggested to have an important pro-inflammatory role that is relevant to airway function and the immune response and that leptin might be associated with a variety of other inflammatory markers such as C-reactive protein (CRP), fibrinogen, leukocytosis, and interferon (IFN)- γ . Although the exact role of leptin in asthma has not yet been defined, both asthma and leptin seem to be related with airway inflammation. Furthermore, Guler et al. reported that a significant elevation in serum leptin was observed in asthmatics when compared with healthy children despite that both groups had a similar mean body mass index (12). They suggested that not a merely elevated BMI but increased level of leptin might be important for the development of asthma.

Among the components of the metabolic syndrome, we found that central obesity and hypertension were significantly associated with asthma-like symptoms. Elevated serum leptin levels are commonly observed in obese patients. In addition, the hyperleptinemia and leptin resistance increases the norepinephrine turnover and sympathetic nerve activity in animals and humans (16–18). The renal and sympathetic actions of leptin contribute to the pathogenesis of hypertension, which is also associated with central obesity and metabolic syndrome (19). Further, the subjects in our study who had asthma-like symptoms were also significantly associated with decreased lung functions. In short, hypertension and central obesity, which are related with hyperleptinemia in the patients with metabolic syndrome, may be related with the decreased lung functions in those patients who have asthma-like symptoms.

Several limitations must be considered when interpreting our results. First, the validity of self-reported information is a major concern for those studies that use questionnaires, and this is a typical limitation of most epidemiologic studies. Second, as our study is based on cross-sectional data, a causal relationship between asthma-like symptoms and metabolic syndrome could not be clearly defined.

The purpose of our investigation was to determine the correlation of metabolic syndrome and asthma-like symptoms via leptin as a “common denominator” instead of merely measuring the level of leptin and thus explaining its association with these two diseases. The strong point of the current study rests on the fact that this is relatively large scale study with a total of about 10,000 participants. Moreover, this is the first study that has evaluated the relation between asthma-like symptoms and the metabolic syndrome.

In conclusion, our findings from the Korean Health and Genome Study showed that the metabolic syndrome is associated with asthma-like symptoms. Among the components of metabolic syndrome, abdominal obesity and hypertension are the risk factors for asthma-like symptoms. Our study suggests that the metabolic syndrome might be associated with bronchial asthma. However, further work is needed to confirm our findings.

TABLE 4.—The estimated odds ratios of asthma-like symptoms due to the presence vs. the absence of low HDL-cholesterol, hypertriglyceridemia, high glucose, abdominal obesity, and hypertension.

	Wheezing	Resting dyspnea	Post-exercise dyspnea
HDL	0.99 (0.85–1.15) ^a	0.99 (0.83–1.17)	1.05 (0.92–1.21)
TG	1.11 (0.96–1.30)	1.10 (0.93–1.30)	1.06 (0.93–1.21)
High glucose	1.07 (0.88–1.32)	0.95 (0.75–1.20)	0.92 (0.76–1.11)
Abdominal obesity	1.76 (1.51–2.04)*	1.63 (1.38–1.93)*	1.63 (1.43–1.86)*
HTN	1.24 (1.06–1.46)*	1.27 (1.06–1.52)*	1.34 (1.16–1.54)*

HDL = high-density lipoprotein; TG = triglyceride; HTN = hypertension.

^a95% confidence interval. * $p < 0.05$.

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