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Association between risk factors of metabolic syndrome with lung function

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Abstract--Introduction: Increased evidence suggests that metabolic syndrome (MetS) is correlated with lung function impairment. This study aimed to explore the associations between MetS risk factors and the lung function. Material and Method: This is a prospective, observational, descriptive study conducted among patients attending at Tertiary care teaching hospital over a period of 1 year. Inclusion criteria: Either gender above the age of 18 years who fulfilled the International Diabetes Federation (IDF) criteria for Metabolic Syndrome to evaluate pulmonary function test (Spirometry) abnormalities. Results: A total of 60 participants (41 males) were included in the study. The characteristics of the eligible subjects stratified by gender and the presence of metabolic syndrome. The BMI, SBP, DBP, waist circumference was statically significant between male and female (all of the parameters, $p < 0.05$). Fasting Blood glucose, Total Cholesterol, Serum triglycerides, CRP, serum uric acid, and serum total bilirubin statically significant between male and female (all of the parameters, $p < 0.05$). Pulmonary function tests, such as FEV1, FEV1 % predicted, FVC, FVC1 % predicted and FEV1/FVC ratio were statically significant among male and female. Conclusion: Our findings highlight the FVC and FEV1 are inversely associated with the accumulation of metabolic syndrome components and also independently associated with each component of metabolic

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syndrome. Therefore, this relationship might receive more attention and even urge action to be taken on metabolic components in the context of poor pulmonary function.

Keywords---metabolic syndrome, forced expiratory volume, forced vital capacity.

Introduction

Metabolic syndrome (MetS) increases significantly along with obesity has become a pandemic. Studies have shown that Indian seem to have a higher risk to develop MetS at a given level of obesity. [1] MetS, characterized by clustering of abdominal obesity, hypertension, insulin resistance and dyslipidemia has been implicated as the contributing factors to the development of cardiovascular diseases and type 2 diabetes. [2, 3] On the other hand, recent studies showed that impaired pulmonary function is associated with all-cause and cardiovascular mortality, [4] correlated with smoking and the components of MetS including obesity, [5] type 2 diabetes, [6] and insulin resistance. [7]

As the components of MetS share partially overlapping pathophysiological mechanisms of common metabolic pathways, giving the MetS a significant potential for predicting lung function. Positive relationships between impaired lung function and MetS have been shown in cross-sectional studies. [8] Similar associations between the components of the MetS with lung function impairment have also been reported in large cohort studies. [9] Furthermore, dyslipidemia has been observed as a biomarker of abnormal lung function, [10] obesity was inversely related to lung function, [11] and fasting serum insulin levels were also negatively correlated with lung function. Recent studies have provided evidence indicating that MetS predicted a steeper FEV₁ decline over time [12] and was associated with a restrictive ventilator pattern in patients with the high waist circumference (WC). [13]

The results of previous studies conducted in Italy, Tai-wan and Japan all suggested that MetS was independently associated with restrictive pattern of impaired pulmonary function. [14] The findings of other reports were also congruent, revealing that restrictive lung disease (RLD) was related with MetS. [15] A cross-sectional study with a small sample size reported that a restrictive, but not an obstructive, respiratory pattern was associated with MetS and insulin resistance in elderly people. [16] One study with a large sample size from nationwide health screening centers in Taiwan also demonstrated that obesity and MetS were associated with restrictive lung impairment. [17] Another study that measured the spirometry parameters and MetS in healthy Korean adults without overt impaired lung function also showed an inverse relationship between lung function and MetS. [18]

Abdominal obesity was a major factor that determined the association between MetS and pulmonary function impairment. A study on physiology of obesity and its effects on pulmonary function has suggested that central obesity is more likely to affect pulmonary volumes, even without direct effects on pulmonary

obstruction. [19] However, large-scale study in Indian are scarce; therefore, the aims of the current study were to explore the associations of MetS components with the lung function and to compare differences between genders and age in an adult population.

Material and Methods

This is a prospective, observational, descriptive study conducted among patients attending at Tertiary care teaching hospital over a period of 1 year.

Inclusion criteria

Either gender above the age of 18 years who fulfilled the International Diabetes Federation (IDF) criteria for Metabolic Syndrome to evaluate pulmonary function test (Spirometry) abnormalities.

Exclusion criteria

The subjects who reported a clinical history on cardiovascular disease (myocardial infarct, angina pectoris) and pulmonary disease (asthma, chronic obstructive pulmonary disease) or cancer, were excluded based on their survey answers. Those with no pulmonary function test results or body measurements (waist circumference, height) were also excluded.

Measurements

1) Survey

Prior to conducting the general health examination, patients' consent was attained to conduct a survey. The patients were asked to record specifically their past clinical history, the types of drugs they are taking, their alcohol and smoking history, and physical activity level, etc. Those who found it difficult to fill out the survey were assisted by nurses. As for physical activity level, subjects were classified into 1) light activity: walking for less than 2 hours a day, working in an office, or working as a housewife with little household chores, 2) medium level activity: walking for 2-4 hours a day, working in manufacturing or service industry, or working as a housewife with a lot of household chores, 3) hard activity: working in agriculture, fishery, civil engineering or construction industry, 4) severe activity: athletes, or those who transport wood or engage in farming work during farming season.

2) Physical measurement

Waist circumference was measured from the center point of the last rib and iliac spine. Height and weight were measured while wearing light clothing (health examination gown). For obesity level, body mass index (BMI) was used, which is the value attained by dividing the body weight (kg) against the height (m²), to classify the subjects into obese (BMI \geq 25 kg/m²), overweight (23 kg/m² \leq BMI < 25 kg/m²) and normal weight (BMI < 23 kg/m²) groups. With the blood test, triglyceride, high-density lipoprotein cholesterol (HDL-C), and fasting blood sugar were measured. Blood pressure was measured using an automatic sphygmomanometer after taking over 5 minutes of rest.

3) Pulmonary function test

Pulmonary function was measured between 8 AM and 12 PM using a spirometer. Subject was in a seated position, and the measurement was taken by an experienced nurse. To reduce any variance in measurement by the person taking the measurement the same nurse measured everyone. The values measured were FEV₁, FVC, and FEV₁/FVC.

Definition of Metabolic Syndrome

Metabolic syndrome, based on the Asia criteria of the American Heart Association/National Heart, Lung, and Blood Institute, [20] is diagnosed when 3 out of the following 5 categories are satisfied: 1) blood pressure of systolic blood pressure \geq 130 mm Hg or diastolic blood pressure \geq 85 mm Hg, or is taking a hypertension drug, 2) fasting blood sugar \geq 100 mg/dL, or is taking a diabetes drug, 3) triglyceride \geq 150 mg/dL, or is taking a dyslipidemia drug, 4) low HDL-C (male $<$ 40 mg/dL, female $<$ 50 mg/dL), or is taking a dyslipidemia drug, or 5) the waist circumference applied is male \geq 90 cm, female \geq 80 cm. Also, female waist circumference of over 85 cm was also applied based on the Korean Society for the Study of Obesity. [21]

Pathology

Liver biopsies were performed all patients according to the severity of the clinical disease after the patients had given consent. All liver biopsy specimens were examined by a pathologist. Scoring of necroinflammation and fibrosis was performed using criteria devised by Brunt et al [12,13]. Non-alcoholic steatohepatitis (NASH) was diagnosed according to liver histology indicating steatosis (mild: $<$ 33% of lobules, moderate: 33%-66% of lobules and severe: $>$ 66% of lobules) with (1) Ballooning degeneration of hepatocytes/mallory bodies; (2) Necro-inflammation (lobular or portal); (3) Fibrosis (perisinusoidal, periportal and/or bridging).

Statistical Analysis

The data was shown as mean \pm standard deviation. For the difference in variables among the groups, Student t-test and x²-test were used. This data was analyzed by using SPSS version 25.0.

Result

A total of 60 participants (41 males) were included in the study. The characteristics of the eligible subjects stratified by gender and the presence of metabolic syndrome.

Table 1: Characteristics of participants between male and female subjects

Variables	Male (n = 41) Mean \pm SD	Female (n = 19) Mean \pm SD	P-value
Age (years)	43.23 \pm 12.52	34.24 \pm 12.81	$<$ 0.05
BMI (kg/m ²)	33.33 \pm 4.16	28.21 \pm 6.91	$<$ 0.05
SBP (mmHg)	139.53 \pm 14.82	132.10 \pm 18.34	$<$ 0.05

DBP (mmHg)	89.27 ±14.36	85.19 ±13.61	<0.05
Waist circumference (cm)	108.37 ±12.26	91.36 ±15.43	<0.05

SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

The BMI, SBP, DBP, waist circumference was statically significant between male and female (all of the parameters, $p < 0.05$).

Table 2: Biochemical of participants between male and female subjects

Biochemical Parameters	Male (n = 41) Mean±SD	Female (n = 19) Mean±SD	P-value
Fasting Blood Glucose (mg/dL)	103.8 ± 9.3	101.4 ± 8.6	<0.05
Total Cholesterol (mg/dL)	188.3 ± 19.3	178.2 ± 18.2	<0.05
Serum Triglycerides (mg/dL)	174.27 ±15.19	161.39 ±19.69	<0.05
HDL-C (mg/dL)	49.37 ±7.71	42.61 ±5.45	<0.05
C-reactive protein (mg/dL)	0.45 ±0.02	0.54 ±0.09	<0.05
Serum uric acid (mg/dL)	5.38 ±0.96	4.26 ±0.81	<0.05
Serum total bilirubin (mg/dL)	0.67 ±0.19	0.33 ±0.14	<0.05

HDL-C, high-density lipoprotein cholesterol; CRP, C-reactive protein.

In table 2, Fasting Blood glucose, Total Cholesterol, Serum triglycerides, CRP, serum uric acid, and serum total bilirubin statically significant between male and female (all of the parameters, $p < 0.05$).

Table 3: Pulmonary Function test of participants between male and female subjects.

PFT	Male (n = 41) Mean±SD	Female (n = 19) Mean±SD	P-value
FEV1 (L)	2.27±0.34	2.01 ±0.33	<0.05
FEV1 % predicted	4.25±0.39	3.68 ±0.24	<0.05
FVC (L)	2.74±0.10	2.23 ±0.17	<0.05
FVC % predicted	5.21±0.36	4.56 ±0.28	<0.05
FEV1/FVC	81.98±9.18	89.77 ±8.12	<0.05

FEV1, forced expiratory volume in 1; FVC, forced vital capacity.

In table 3, pulmonary function tests, such as FEV1, FEV1 % predicted, FVC, FVC1 % predicted and FEV1/FVC ratio were statically significant among male and female.

Table 4: Liver histology according to the presence of metabolic syndrome cases (%)

Liver histology	Male n = 41 (%)	Female n = 19 (%)
Fatty infiltration		
Mild	23 (56.0)	13 (68.4)
Moderate	16 (39.0)	7 (36.8)
Severe	2 (4.8)	1 (5.2)
Necro-inflammation		
Mild	13 (31.7)	5 (26.3)
Moderate	27 (65.8)	12 (63.1)

Severe	1 (2.4)	2 (10.5)
Fibrosis		
Absent	21 (51.2)	9 (47.3)
Perisinusoidal/pericellular	11 (26.8)	6 (31.5)
Periportal	5 (12.1)	3 (15.7)
Bridging	4 (9.7)	1 (5.2)

Discussion

The current analysis indicated a high prevalence of metabolic syndrome, and it was noteworthy that in both men and women, individual composition of abdominal obesity, low HDL-C, and high blood pressure was significantly associated with decreasing FVC and FEV1.

When we independently predicted FVC, FEV1 and FEV1/FVC ratio for each metabolic component, we found that after adjusting for age and family income group, WC was one of the MetS components associated with the decrease of FVC and FEV1 in males. This was consistent with some studies.^[22] At present, it was believed that central obesity (abdominal obesity) was the source of common metabolic diseases and cardiovascular diseases in adults, such as hyperglycemia, hypertension, and dyslipidemia and so on, and was the core component of MetS.^[23] Most of the current data support the link between MetS and impaired lung function mainly through abdominal obesity. WC, as one of the indicators of abdominal obesity, was related to the deterioration of lung function.^[24] Central obesity may affect the mechanical performance of the ventilator because it limits the expansion of the diaphragm. The gender difference may be related to the respiratory movement and fat distribution of the chest wall and abdominal wall, and have different effects on the lung function of women and men.^[25]

Furthermore, MetS is characterized by systemic inflammation, and endothelial dysfunction caused by this systemic inflammation leads to impaired organ system function.^[26] Notably, our study found that males smoke more than females, and that long-term exposure to cigarette smoke causes systemic inflammation. Thus, in active smokers with MetS, since it comes from two sources, visceral fat and lung exposure to cigarette smoke, it may increase systemic inflammation. This may lead to increased endothelial dysfunction and a rapid decline in lung function.^[27]

It was worth noting that an important component in our study was HDL-C, and its increase was significantly correlated with decreased FVC and FEV1 in all participants. Consistent with this observation, a representative of sample study found that low HDL-C were associated with impaired lung function. A small case-control study reported that HDL levels in the COPD group were significantly lower than those in the control group (49.4% vs 61%).^[28] A small population study in Mexico observed that subjects with normal or elevated high-density lipoprotein cholesterol had lower FVC than subjects with low-density lipoprotein cholesterol.^[29]

The pathophysiological role of this link is unknown. Usually chronic inflammation accelerates atherosclerosis in part by altering HDL and its ability to promote

reverse cholesterol transport. [30] Since this lipoprotein has anti-fungal, anti-inflammatory, antioxidant and even anti-apoptotic functions, we hope that its high value will have a beneficial effect on lung function. But in recent years, the role of high density lipoprotein cholesterol as an atherosclerotic protective agent is changing. [31]

In fact, it has been recognized that their ability to get inflammation and mobilize cholesterol is severely affected by the oxidation of HDL-related proteins, and even this dysfunctional HDL may have a pro-inflammatory effect. This new approach to the physiology of high-density lipoprotein cholesterol may partly explain our finding that subjects with high cholesterol have a smaller lung volume. [32] At the same time, a genetic and molecular study reported two polymorphisms in apolipoprotein M (APOM)-related genes associated with decreased lung function in two ethnic groups (African-American and European-American). APOM is a kind of lipoprotein associated with high density lipoprotein cholesterol. The change of its gene expression will change the quality and function of high density lipoprotein cholesterol. In fact, the same study found that high levels of high-density lipoprotein cholesterol were associated with a decrease in the FEV1/FVC ratio. [33]

Conclusion

Our findings highlight the FVC and FEV1 are inversely associated with the accumulation of metabolic syndrome components and also independently associated with each component of metabolic syndrome. Therefore, this relationship might receive more attention and even urge action to be taken on metabolic components in the context of poor pulmonary function.

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