ORIGINAL ARTICLE

Study of Pulmonary Function Test Abnormalities in Metabolic Syndrome

Shyam Chand Chaudhary[1*], Tulika Kumari[2], Kauser Usman[3], Kamal Kumar Sawlani[4], D Himanshu[4], Kamlesh Kumar Gupta[4], Munna Lal Patel[4], Avinash Agarwal[5], Ajay Kumar Verma[6]

Abstract

Introduction: Metabolic Syndrome (MetS) is defined as a constellation of an interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of atherosclerotic cardiovascular disease and T2DM. Although the link between impaired lung function and cardiovascular events and T2DM has been recognized, the association between impaired lung function and MetS has not been comprehensively assessed.

Material and Methods: A cross sectional prevalence study was done in tertiary care hospital in northern India on 100 patients of the age between 25-65 years who fulfilled the IDF criteria for MetS to evaluate pulmonary function test (Spirometry) abnormalities.

Result: Maximum number of patients were in 31-40 years of age group (45%) followed by those aged 41-50 year (26%), <30 years (15%), >50 years (14%). Mean age of patients was 39.59±8.67 year. In this cross-sectional study, patients with Metabolic Syndrome showed significantly lower FVC % predicted (P< 0.001), FEV1 % predicted (P< 0.001) as compared to the group without Metabolic Syndrome. There was a strong linear decrease in FVC and FEV1 % predicted as the number of components of MetS increases. We observed that 28% of the male and 46.6% of female patients showed restrictive ventilatory pattern and 7% of male and 13.4% of female patients showed mixed pattern.

Conclusion: All MetS components were associated with pulmonary function impairment. As the number of MetS components increases, patients had more severe decline in pulmonary functions.

Introduction

South Asia is home to one-quarter of the world's population. It is undergoing an epidemiological transition in the urban and sub urban area which is characterized by a decrease of infectious diseases and an increase in chronic non -infectious ones. This increase is largely due to a marked change in lifestyle, including changes in food consumption patterns.[1] Among non-infectious disease, Metabolic Syndrome is one of the most important one. It is defined as a constellation of an interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of atherosclerotic cardiovascular disease, T2DM.[2]

Impaired lung function is more than a simple reflection of airflow limitation; it may also be a marker of premature death.[3] In a number of recent studies, it was reported that among the changes in pulmonary function, deterioration in pulmonary function is related to hypertension, type 2 diabetes, low-density lipoprotein cholesterol, overall obesity, abdominal obesity and insulin resistance.[4] Among the above listed factors, hypertension, diabetes, and abdominal obesity are included as diagnostic criteria for MetS.[5] Hence it can be inferred that identifying the relationship between MetS and pulmonary function deterioration is meaningful.

Material and Method

Subject

A cross sectional prevalence study was done in tertiary care hospital in northern India on 100 patients of the age between 25-65 years who fulfilled the IDF criteria for Metabolic Syndrome to evaluate pulmonary function test (Spirometry) abnormalities. It was done over a period of 1 year from Sep 2016 to Aug 2017 and patients were enrolled from OPD and those admitted in indoor wards. Patients with cardiac, endocrine, pulmonary, orthopaedic, or neurogenic condition and any systemic or surgical illness were excluded from the study.

Study protocol

The subjects were informed about the study through information sheets, and written consent was obtained from all subjects. The study was approved by Research and Ethical Committee of the institute. Testing was performed in the hospital where a rapid, appropriate response to an emergency was possible, and physician was also available on call whenever any emergency arises. A detailed clinical history and physical examination carried out for every subject. History of presence of risk factors, like smoking, hypertension, dyslipidaemia, diabetes mellitus and presence of any other chronic disease was inquired. The anthropometric characteristics, blood pressure, plasma glucose, and lipid levels, were measured. Metabolic syndrome was defined on the basis of IDF criteria which include waist circumference >90 cm in males, >80 cm in females and two or more of the following, a high triglyceride level (>150mg/dl) or on specific medication, a low high-density lipoprotein-cholesterol (HDL-C) level

[1]Professor, [2]Junior Resident, [3]Professor, [4]Associate Professor, Department of Medicine, [5]Professor, Department of Critical Care Medicine, [6]Assistant Professor, Department of Respiratory Medicine, K.G.M.U., Lucknow, Uttar Pradesh; *Corresponding Author

Received: 02.02.2018; Accepted: 23-07-2018

Table 1: Comparison of biochemical/hematological variables between two groups

Variables	Group I N - 100	Group II N-100	Student 't' test	
	Mean ± SD	Mean ± SD	't'	'p'
Hb (g/100 ml)	11.92 ± 1.28	11.89 ±1.27	0.199	0.842
TLC (cells/cumm)	8255.40 ± 2806.83	8125.9±2800.21	0.327	0.744
DLC (Neutrophil %)	70.69 ± 7.88	70.74 ± 8.14	-0.044	0.965
DLC (Lymphocyte %)	33.09 ± 6.75	33.47 ± 6.52	-0.405	0.686
Platelet (Lacs)	1.95 ± 0.58	9.08 ± 45.34	-1.574	0.117
S. bilirubin (mg%)	0.85 ± 0.47	0.87 ± 1.05	-0.207	0.836
SGOT (U/L)	42.55±31.32	75.31 ± 175.44	-1.836	0.068
SGPT (U/L)	42.32±24.79	90.1 8± 232.58	2.046	0.042
ALP (IU/L)	232.48±84.50	191.89 ± 130.04	2.597	0.010
S. Protein (g/dl)	6.17±0.52	6.27 ± 1.07	0.859	0.392
S. Albumin (g/100 ml)	3.07±0.63	3.31± 0.61	-2.699	0.008
S. Uric acid (mg/dl)	5.547±2.02	5.70± 2.18	0.548	0.584
S. Urea (mg/dl)	35.94±8.08	35.48± 8.27	0.398	0.691
S. Creatinine	1.21±0.35	1.20± 0.35	0.234	0.815

Table 2: Comparison of different variable of Met S between group I, and II

	Group I (N -100)	Group II (N-100)	χ^2	'P' value
Obese	100	21	130.579(df=1)	<0.001
Hypertensive	79	9	99.432(df=1)	<0.001
Fasting bl sugar level (>100 mg/dl)	100	1	196.040(df=1)	<0.001
Hypertriglyceredemia (>150 mg/dl)	88	1	153.234(df=1)	<0.001

Table 3: Comparison of spirometry findings in between two groups

Variables	Group I N-100	Group II N-100	Student 't' test	
	Mean± SD	Mean± SD	't'	'p'
FEV1	69±0.06	71±0.02	10.848	<0.001
FVC	66±0.08	75±0.19	19.919	<0.001
FEV1/FVC	87.02±2.80	78.59±4.46	16.022	<0.001

Table 4: Association of MetS components with spirometry findings among Cases (Group I)

	3 MetS components (N=25)	4 MetS components (N=35)	5 MetS components (N=40)	ANOVA	
	Mean± SD	Mean±SD	Mean±SD	F	P
FEV1	2.49± 0.04	2.42±0.04	2.38±0.08	3.897	<0.001
FVC	2.86± 0.06	2.80±0.08	2.78±0.09	0.866	<0.001
FEV1/FVC	87.11± 2.15	82.17±3.10	80.70±2.74	2.890	<0.001

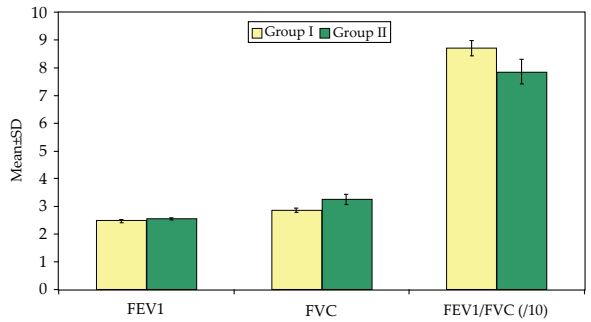

Fig. 1: Comparison of spirometry findings in between two groups

(<40mg/dl for men and <50 mg/dl for women) or on specific medication, high blood pressure (≥130/85 mm Hg) or on specific medication, and a high fasting plasma glucose concentration (>100 mg/dl) or on specific medication or previously diagnosed type 2 DM / Impaired fasting glucose/ impaired glucose tolerance.[5] Subsequently, spirometry was done.

Spirometry

Lung function test was performed in every participant by an experienced technician using an automated flow-sensing spirometer based on American Thoracic Society recommendations.[6] The Spirometry machine used was Med graphics Cardio respiratory diagnostics. Software used was Breeze Suite 7.1.0.32 and database version 521. Patients were instructed to sit up on the chair straight, with feet flat on the floor and legs uncrossed. Before performing the forced expiration, tidal (normal) breaths was taken first, then a deep breath was taken still using the mouthpiece, followed by a further quick, full inspiration. For FVC and FEV_1, the patient takes a deep breath in, as large as possible, and blows out as hard and as fast as possible and keeps going until there is no air left. For VC, the patient takes a deep breath in, as large as possible, and blows steadily for as long as possible until there is no air left. The patient needs to keep blowing until no more air comes out and the volume–time trace reaches a plateau with <50 mL being exhaled in 2 s For FEV_1 and FVC, the best two values should be within 5% or 150 mL of each other, whichever is greater. If FVC is <1.0 L, then the values should be within 100 ml.[7] Patients were instructed not to use bronchodilator on the day of pulmonary function test. If at all possible, at least three and up to a maximum of eight forced expiratory manoeuvres were performed in an effort to meet the American Thoracic Society standards.[6] Values used in the study were the forced vital capacity (FVC), FEV_1, and FEV_1-to-FVC ratio. The highest FVC and FEV_1 value of the three or more tests with acceptable curves was used in the analysis.

Obstructive lung impairment was defined as an FEV_1-to-FVC ratio < 70% and an FVC > 80% of the predicted value. Restrictive lung impairment was defined as an FVC < 80% of the predicted value and an FEV_1-to-FVC ratio > 70%. Mixed lung impairment was defined as a FEV_1-to-FVC ratio < 70% and FVC < 80% of the predicted value. The other was defined as normal lung function.[6,8]

Serum sampling and biochemical analysis

Blood samples were obtained following 12 hours of fasting were immediately centrifuged (3000 rpm) for 10 minutes; the sera were separated and frozen at - 8 ºC until analysis. Fasting blood glucose (FBG), total cholesterol, triglycerides (TG), and high density lipoprotein cholesterol (HDL-C) levels were determined by enzymatic method using commercial available diagnostic kit on fully automated biochemical analyzer. Low density lipoproteins cholesterol (LDL-C) was determined by using Friedewald formula (Friendewald et al., 1972).

Statistical analysis

The statistical analysis was done using SPSS (Statistical package for social science) Version 15.0 statistical analysis software. The values were represented in No (%), Mean±SD. Student's t-test was used while assessing spirometry data. P < 0.05 was considered statistically significant.

Result

A total of 100 patients of Met-S fulfilling the inclusion criteria of the study were enrolled as cases (male-70, female-30, mean age-39.59±8.67) and classified as group I while 100 age gender matched controls (normal

Table 5: Prevalence of ventilatory pattern in metabolic syndrome subjects

	Male (n-70)	Female (n-30)
Normal	35 (50%)	12 (40)
Restrictive	28 (40%)	14 (46.6%)
Mixed	7 (10%)	4 (13.4%)

healthy subjects, male- 66, female-34, mean age-42.81±9.45) were also included in the study and classified as group II.

On comparing the hematological and biochemical variables, statistically significant difference among patients of group I and group II was observed in SGPT, S ALP and S. Albumin levels only. SGPT level of subjects of group II (90.18±232.58 U/l) was found to be significantly higher than that of group I (42.32±24.79 U/L). In the same way ALP level of subjects of group I (232.48±84.50 IU/L) was found to be significantly higher than that of group II (191.89±130.04 IU/L) and mean serum albumin levels of group II (3.31±0.61) were found to be significantly higher than that of group I (3.07±0.63) (Table 1).

Among group I, proportion of subjects with obesity, hypertension, raised fasting blood sugar level, increased triglyceride level, and low HDL level were 100%, 79%, 100%, 88%, 48% respectively. In the same way, among group II proportion of subjects with obesity, hypertension, raised fasting blood sugar level, increased triglyceride level, and low HDL level were 21%, 9%, 1%, 1, 0% respectively. This difference among different variables of MetS between two groups was found to be statistically significant ($p<0.001$) (Table 2).

Metabolic Syndrome and pulmonary function test

The subjects with MetS showed significantly lower FVC % predicted ($P< 0.001$), FEV1% predicted ($P< 0.001$), and significantly higher FEV1/FVC % predicted ratio ($P< 0.001$) as compared to control (Table 3 and Figure 1).

On comparing the FEV1 of group I subjects, a continuous decline in FEV1 with increase of number of metabolic syndrome components was observed i.e. 3 Metabolic Syndrome components (2.49±0.04), 4 Metabolic Syndrome components (2.42±0.04) and 5 Metabolic Syndrome components (2.38±0.08) and this association was found to be statistically significant.

On comparing the FVC of these subjects, a continuous decline in FVC with increase of number of Metabolic Syndrome components was observed i.e. 3 Metabolic Syndrome components (2.86±0.06), 4 Metabolic Syndrome components (2.80 ±0.08) and 5 Metabolic Syndrome components (2.78±0.09) and this association was found to be statistically significant.

In the same way on comparing the FEV1/ FVC of these subjects, a continuous decline in FEV1/FVC with increase of number of metabolic syndrome components was observed i.e. 3 Metabolic Syndrome components (87.11± 2.15), 4 Metabolic Syndrome components (82.17±3.10) and 5 Metabolic Syndrome components (80.70±2.74) and this association was found to be statistically significant (Table 4).

Prevalence of ventilatory pattern in Metabolic Syndrome subjects

Prevalence of normal ventilatory patterns in the study group among male was 50% and restrictive pattern was 28% followed by mixed pattern (7%). In the same way prevalence of normal ventilatory pattern among female was 40% followed by restrictive pattern 46.6% and mixed pattern (13.4%) (Table 5).

Discussion

The present study showed that pulmonary function variables are significantly decreased ($p<0.001$) in subject with Metabolic Syndrome compared to non-metabolic subjects. These finding are similar to those obtained in the studies on Korean non-smoking males (Lim et al., 2010) and Taiwan population (Chen et al., 2014).[9] In addition, another study shows that there was a small, but statistically significant difference in FEV1/FVC between subjects with and without Metabolic Syndrome (van Huisstede et al., 2013). It might support our hypothesis that the presence of Metabolic Syndrome may influence lung function impairment. In addition, abdominal obesity was reported as the most powerful predictor of pulmonary function impairment (Leone et al., 2009).[10] One potential explanation is that increased abdominal obesity directly affects thoracic and diaphragm compliance, which decreases lung function (Salome et al., 2010).[11] In addition, American study found a negative correlation between FEV1/ FVC and waist circumference (Chen et al., 2001).[9] Another study from Australia showed that FVC has negative correlation with male's abdominal obesity (Lazarus et al., 1998a). In a Japanese study, lung function impairment due to hyperglycaemia and abdominal obesity was suggested (Yoshimura et al., 2012).[12] In addition, another Korean study showed that waist circumference, hypertension, hyperglycaemia, and HDL-C sturdily influenced lung function (Choi et al., 2011).[13] Our results were consistent with previous studies.

There are several explanations for the relationship between reduced lung function and Metabolic Syndrome. Metabolic Syndrome is a cluster of disease which comprises of multiple cardiovascular risk factors such as Insulin resistance, dyslipidemia, glucose intolerance, and hypertension, most of which could stem from one cause, visceral obesity. It has been shown that obesity is one of the causes of physiologic impairments in respiratory system. Obesity causes airflow limitation with reduction of both FEV1 and FVC, and reduces lung volumes, especially expiratory reserve volume (ERV), and functional residual capacity (FRC). These changes predispose toward a decrease in peripheral airway diameter, reduction in respiratory system compliance, as well as an increase in oxygen cost of breathing and airway hyperresponsiveness (AHR). Taken together, decrease in retractive forces of the lung parenchyma on the airways at low lung volume in obese people, lead to reduction in airway calibre and increased AHR, which potentially causing detrimental effect on lung function.

There was a significant ($p<0.001$) inverse relationship between the number of components present and pulmonary function. In both males and females, abdominal obesity, high blood pressure, high triglycerides, and low HDL-C were significantly associated with lower FEV1 percent predicted, FVC percent predicted, FEV1/FVC percent predicted (all of the parameters, $p<0.001$). High blood sugar level was significantly associated with lower FEV1 percent predicted.

A study conducted by YU D et al concluded that participants with a greater number of Metabolic Syndrome components were more likely to have reduced lung function, particularly if Type 2 diabetes was present: the predicted value of forced expiratory

volume in 1 s decreased by 5-6% for participants with 2-4 Metabolic syndrome components, and by 9% for those with Type 2 diabetes which is consistent with our finding.[14]

In this cross-sectional study we observed that the prevalence of normal ventilatory patterns in the study group among male was 50% and restrictive pattern was 28% followed by mixed pattern (7%). In the same way prevalence of normal ventilatory pattern among female was 40% followed by restrictive pattern46.6% and mixed pattern (13.4%). The results of this study were similar to those reported from population-based studies (Lim et al., 2010; Nakajima et al., 2008).[15]

Conclusion

Our study proposed that 53% of the MetS patients had spirometry abnormality in the form of Restrictive (42%), and mixed pattern (11%). None of the patients had obstructive pattern. Change in FEV1, FVC was inversely proportional to each component of MetS, and also there was a strong linear decrease in FVC percent predicted, FEV1 percentage predicted as the number of components of Metabolic Syndrome increases.

References

1. Institute for Health Metrics and Evaluation. The Global Burden of Disease: Generating Evidence, Guiding Policy—South Asia Regional Edition. Seattle, WA: Institute for Health Metrics and Evaluation, University of Washington and Human Development Network, The World Bank; 2013.
2. Wang J, Ruotsalainen S, Moilanen L, et al. The metabolic syndrome predicts cardiovascular mortality: a 13-year follow-up study in elderly non-diabetic Finns. *Eur Heart J* 2007; 28:857-64.
3. Young RP, Hopkins R, Eaton TE. Forced expiratory volume in one second: not just a lung function test but a marker of premature death from all causes. *Eur Respir J* 2007; 30:616–622.
4. Lin WY, Yao CA, Wang HC, et al. Impaired lung function is associated with obesity and metabolic syndrome in adults. *Obesity (Silver Spring)* 2006; 14:1654–1661.
5. International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome, 2005. www.idf.org
6. American Thoracic Society: standardization of spirometry. *Respir Crit Care Med* 2014; 189:17-18.
7. Moore VC. Spirometry: step by step. *Breath* 2012; 8:232-240.
8. Evans, SE, Scanlon, PD. Current practice in pulmonary function testing. *Mayo Clin Proc* 2003; 78:758–763.
9. Chen Y, Rennie D, Cormier YF, et alWaist circumference is associated with pulmonary function in normal-weight, overweight, and obese subjects. *Am J Clin Nutr* 2007; 85:35–39.
10. Leone N, Courbon D, Thomas F, et al. Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. *Am J Respir Crit Care Med* 2015; 179:509–516.
11. Salome CM, King GG, Berend N. Physiology of obesity and effects on lung function. *J Appl Physiol* 2010; 108:206–211.
12. Yoshimura C, Oga T, Chin K, et al. Relationships of decreased lung function with metabolic syndrome and obstructive sleep apnea in Japanese males. *Intern Med* 2012; 51:2291.
13. Choi HK, Ford ES, Li C, et al. Prevalence of the metabolic syndrome in patients with gout: the Third National Health and Nutrition Examination Survey. *Arthritis Rheum* 2007; 57:109-15.
14. Yu D, Simmons D. Association between lung capacity measurements and abnormal glucose metabolism: findings from the Crossroads study. *Diabet Med* 2014; 31:595–599.
15. Nakajima H, Kubouchi Y, Muneyuki T, et al. A possible association between suspected restrictive pattern as assessed by ordinary pulmonary function test and the metabolic syndrome. *Chest* 2008; 134:712-718.