

How to Cite:

Kunti, R., Togiti, R. K., Kiran, D., & Sravanthi, T. C. (2021). Pulmonary function tests in people with metabolic syndrome: A cross sectional observational study in a tertiary care hospital Telangana India. *International Journal of Health Sciences*, 6(S8), 1986–1995.
<https://doi.org/10.53730/ijhs.v6nS8.12544>

Pulmonary function tests in people with metabolic syndrome: A cross sectional observational study in a tertiary care hospital Telangana India

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Abstract---Background: Metabolic syndrome is a cluster of cardio-metabolic risk factors characterized by abdominal obesity, insulin resistance, and chronic systemic inflammation. Objectives: i)To assess pulmonary function in people with metabolic syndrome ii)To assess whether each component of metabolic syndrome affects pulmonary function indices. Methodology: After a detailed history and physical examination, subjects underwent investigations like fasting lipid profile, fasting blood sugars, electrocardiogram, chest x-ray, pulmonary function tests, 2D echocardiography. Results:In both groups majority had normal pulmonary function tests. In metabolic syndrome group, most common abnormal PFT reported was mild restriction. The pattern of pulmonary function tests is mild restriction in metabolic syndrome subjects. In the overall study group, hypertension, fasting glucose, body mass index, waist circumference have significant negative correlation with both FEV1 and FVC and triglycerides have significant negative correlation with FVC whereas

total cholesterol has significant negative correlation with FEV1. Only HDL-c has strong positive correlation with FVC. Conclusion: The findings in this study highlight the notion that FVC and FEV1 are inversely associated with the accumulation of metabolic syndrome components and also independently associated with each component of metabolic syndrome.

Keywords---metabolic syndrome, forced expiratory volume, abdominal obesity.

Introduction

Metabolic syndrome is a common metabolic disorder that may result from the increasing prevalence of obesity. Metabolic syndrome is a cluster of cardio-metabolic risk factors characterized by abdominal obesity, insulin resistance, and chronic systemic inflammation¹. Positive associations with lung function impairment have been reported for components of the metabolic syndrome, such as hypertension², type 2 diabetes mellitus^{3,4}, low-density lipoprotein cholesterol⁵, and overall obesity⁶. In recent large cohort studies, it has been shown that there is also a relationship between lung function impairment and the metabolic syndrome⁷. The mechanisms underlying the relationship between impaired lung function and the metabolic syndrome are unclear. The chronic low-grade systemic inflammation that is associated with obesity might explain this relationship.

As the obese population increases, the incidence of metabolic syndrome is also increasing. There has been a recent report on the relationship between the diagnostic criteria of metabolic syndrome or changes in the pulmonary function and cardiovascular mortality and total mortality⁸. As such, there is increasing interest in changes in metabolic syndrome associated with changes in pulmonary function. In a number of recent studies, it was reported that the deterioration in pulmonary function is related to hypertension, type 2 diabetes, low-density lipoprotein cholesterol, overall obesity, abdominal obesity and insulin resistance⁹. Among the above listed factors, hypertension, diabetes, and abdominal obesity are included as diagnostic criteria for metabolic syndrome, hence it can be inferred that identifying the relationship between metabolic syndrome and pulmonary function deterioration is meaningful. As such, this study will look into the relationship based on the changes in metabolic syndrome diagnostic criteria and pulmonary function indices, like forced expiratory volume for 1 second (FEV₁), forced vital capacity (FVC), and FEV₁/FVC ratio.

Materials and Methods

This study titled "Pulmonary Function Tests in People with Metabolic Syndrome: A Cross Sectional observational study in a tertiary care hospital Telangana India" was carried out during the period of from december 2013 to march 2015. The study was conducted on 132 subjects admitted during the above period in Osmania medical college and hospital, Hyderabad, India with an aim to evaluate Pulmonary Function Tests in People with Metabolic Syndrome.

Inclusion Criteria

Age above 18 years who fits in criteria of metabolic syndrome given below. Under current guidelines, revised in 2005 by the National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA), metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions

1. Fasting glucose ≥ 100 mg/dL (or receiving drug therapy for hyperglycemia)
2. Blood pressure $\geq 130/85$ mm Hg (or receiving drug therapy for hypertension)
3. Triglycerides ≥ 150 mg/dL (or receiving drug therapy for hypertriglyceridemia)
4. HDL-C < 40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced HDL-C)
5. Waist circumference ≥ 102 cm (40 in) in men or ≥ 88 cm (35 in) in women; if Asian American, ≥ 90 cm (35 in) in men or ≥ 80 cm (32 in) in women (The international diabetes federation [IDF] criteria allow the use of a body mass index [BMI] > 30 kg/m² in lieu of the waist circumference criterion.)

Exclusion Criteria

1. Previous history of lung disease
2. Signs and symptoms of respiratory infections at the time of test
3. History of being admitted during past six months with respiratory symptoms
4. History of cardiovascular illness

Ethics

This study was approved by the Institutional Ethics Committee OMC, Hyderabad. An informed written consent was taken from all the patients involved in the study after explaining regarding the study.

Study Procedure

In this study, total number of subjects is $n=132$. The number of persons in metabolic syndrome group $n = 65$, number of persons in control group $n = 67$. The purpose of the study was explained to the patient and informed consent was obtained. After a detailed history and physical examination, subjects underwent investigations like fasting lipid profile, fasting blood sugars, electrocardiogram, chest x-ray, pulmonary function tests, 2D echocardiography {if necessary}

Results

In this study, majority of the patients belonged to age group between 51 -60 ($n=26$ in metabolic syndrome group and $n= 21$ in control groups), majority of the patients were male ($n=43(66\%)$ in metabolic syndrome group and $n=50(75\%)$ in control groups), Most of them were smokers in both groups. The number of smokers in metabolic syndrome group is $n=39(60\%)$ and number of smokers in control group is $n=49(73\%)$, In this study, majority of them are non-alcoholics in both groups.

The number of alcoholics in metabolic syndrome group is n=18(27.7%) and in control group is n=27(40.3%), Systolic blood pressure in most of the patients belonging to metabolic syndrome group measured in between 140-159 mm Hg(n=31) and in control groups between 120-139 mm Hg(n=32) In this study, diastolic blood pressure in most of the patients belonging to metabolic syndrome group measured in between 90-99 mm Hg(n=24) followed by 80-89mm Hg(n=23) and in control groups between 80-89 mm Hg(n=28) followed by 60-79mm Hg(n=27) In this study, majority of the persons in metabolic syndrome group were obese (27.5-29.9)(n=21) and in control group were overweight (23-24.9)(n=31) In this study, in majority of male persons in metabolic syndrome group the measured waist circumference is between 101-110cms (n=15).In majority of female persons with metabolic syndrome, the measured waist circumference is between 81-90 cms (n=12). In majority of male persons in control group the measured waist circumference is between 81-90cms (n=38).

PARAMETERS	Mean Value
Age	59.7 +/- 11
Male Sex	43(66%)
Waist circumference(cms)	94.1 +/- 7.6
Triglycerides(mg/dL)	150.6 +/- 48.4
HDL-c(mg/dL)	32.6 +/- 5.3
Fasting Blood Glucose(mg/dL)	27.9 +/- 2.5
Systolic BP(mm Hg)	143.6 +/- 23.2
Diastolic BP(mm Hg)	88.7 +/- 10.5

Table:1 Various parametrs and their mean value in metabolic syndrome

In female persons with metabolic syndrome, the measured waist circumference is between 71-80 cms (n=7) majority of persons in metabolic syndrome measured fasting blood sugars is between 150-199mg/dL (n=22) and in control group is <100 mg/dL(n=46). In majority of persons belonging to metabolic syndrome group the measured total cholesterol is between 150-199mg/dL,200-249mg/dL (n=27 in both clusters) and in controls it is in 150-199 mg/dL(n=32). In this study, in majority of persons in metabolic syndrome and control groups, the measured triglycerides fell in the range of 100-149 mg/dL (n=25 and n=48 respectively). In this study, in both groups majority had normal pulmonary function tests (n=26 in metabolic syndrome, n=61 in control group).In metabolic syndrome group, most common abnormal pulmonary function test reported was mild restriction (n=26).

Discussion

The number of metabolic syndrome patients included in this study is 65 when compared with Rogliani et al¹⁰ (n=119) and Chen et al¹¹ (n=8602).

Age distribution

PARAMETERS	Mean Value	Rogliani et al ¹⁰
Age	59.7 +/- 11	60.1 +/- 11.6
Male Sex	43(66%)	132(56%)
Waist circumference(cms)	94.1 +/- 7.6	101.46 +/- 11.80
Triglycerides(mg/dL)	150.6 +/- 48.4	159.75 +/- 141.40

HDL-c(mg/dL)	32.6 +/- 5.3	48.53 +/- 14.11
Fasting Blood Glucose(mg/dL)	27.9 +/- 2.5	102.38 +/- 18.81
Systolic BP(mm Hg)	143.6 +/- 23.2	168
Diastolic BP(mm Hg)	88.7 +/- 10.5	70

The mean age of subjects in my study is 59.7 +/- 11 years when compared with Rogliani et al which are 60.1 +/- 11.6 years and Chen et al which is 41.9 +/- 10.7 years.

The findings of this study fits well with the recent documentation that the prevalence of MS is independently associated with restrictive lung impairment. A cross-sectional study of 159 consecutive nondiabetic elderly persons attending two social centres showed that restrictive, but not obstructive, respiratory pattern was associated with MS, at least in older people, and did not only reflect a limitation of ventilation due to visceral obesity. In fact, restriction was an independent correlate of MS, also after adjustment for waist circumference and body mass index (BMI). Lin et al.⁹ demonstrated an association between MS and restrictive lung impairment also after adjustment for age, gender, BMI, smoking, alcohol drinking, and physical activity.

Recently, Nakajima et al¹² confirmed that impaired restrictive pulmonary function might be associated with metabolic disorders and MS and documented a severity dependent association in an apparently healthy population. A study by Leone et al⁷ found that abdominal obesity was positively related to both obstructive and restrictive ventilatory patterns, regardless of BMI. In this study BMI, waist circumference, hypertension, fasting blood glucose have strong negative correlation with FVC and are significantly associated with restrictive ventilatory pattern. In this study the strongest negative predictors for FVC are body mass index, waist circumference, fasting blood glucose in this study and the strongest positive predictor for FVC is HDL-c ($p < 0.001$).

Only two cross-sectional population-based studies conducted in Asians⁹ have assessed the relationship between lung function impairment and metabolic syndrome. In accordance with this study findings, both reported metabolic syndrome to be significantly associated with the restrictive ventilatory pattern, but not with the obstructive pattern. A similar finding was obtained in a small study of elderly patients by Fimognari et al¹³. However, in these previous studies, the association between lung function impairment and each individual component of the syndrome was not tested independently of the others.

In the current study, WC has significant ($p = 0.02$) negative relation with FEV1 compared with Rogliani et al where it had positive relation which was not significant. Triglycerides had negative correlation with FEV1 but was not significant in the current study whereas there was significant positive correlation with FEV1 in the study by Rogliani et al ($p = 0.04$). HDL-c had positive correlation with FEV1 but was not significant in the current study whereas there was a significant negative correlation with FEV1 in the study by Rogliani et al ($p = 0.0003$).

In the current study, WC has significant ($p < 0.0001$) strong negative relation with FVC compared with Rogliani et al where it had positive relation which was not significant. Triglycerides had significant ($p = 1.3$) negative correlation with FVC in the current study whereas there was significant positive correlation with FVC in the study by Rogliani et al ($p = 0.03$). HDL-c had strong positive significant ($p < 0.0001$) correlation with FVC in the current study whereas there was a significant negative correlation with FEV1 in the study by Rogliani et al ($p < 0.0001$). FBS had a strong significant negative correlation with FEV1 in the current study ($p < 0.0001$) when compared with Rogliani et al which had insignificant negative correlation had a significant negative correlation with FEV1 in the current study ($p = 0.008$) when compared with Rogliani et al which had insignificant negative correlation.

Triglycerides had positive correlation with FEV1/FVC but was not significant in the current study whereas there was a positive correlation with FEV1/FVC in the study by Rogliani et al which was not significant. HDL-c had negative correlation with FEV1/FVC but was not significant in the current study whereas there was a positive correlation with FEV1/FVC in the study by Rogliani et al which was not significant. FBS had negative correlation with FEV1/FVC which was not significant in both the studies.

In a study by Chen et al findings indicated that both FEV1 and FVC were lower in proportion to the number of metabolic syndrome components the patients had. Notably, individual components of abdominal obesity, low HDL-C, high triglycerides, and high blood pressure were significantly associated with decreasing FVC and FEV1 in both males and females.

Lung Function Impairment and Abdominal Obesity

This study reports a significant negative relation of abdominal obesity with FVC. No previous study has investigated the independent relationship between lung function impairment and abdominal obesity as part of metabolic syndrome. Nevertheless, an inverse relationship between abdominal obesity and lung function has been reported in a few studies, mostly cross-sectional, of middle-aged subjects. This study found that abdominal obesity was strongly associated with lung function impairment, independently of the other two components and major risk factors, including BMI. Similar estimates of the relationship between lung function impairment and metabolic syndrome were obtained if the AHA/NHLBI¹ definition was replaced by the IDF definition, which identifies abdominal obesity as the core component of the syndrome. This association may result from the mechanical effects of truncal obesity and/or the metabolic effects of adipose tissue.

This study observed that the abdominal obesity component was strongly and inversely related to restrictive ventilatory patterns, suggesting a role for mechanisms unrelated to lung volumes. WC is correlated with both subcutaneous adipose tissue and intraabdominal adipose tissue, but it is a better predictor of intraabdominal adipose tissue (deleterious fat deposition) than BMI.

Lung Function Impairment and Diabetes

Lung function impairment, including restrictive ventilatory defect in particular, has been reported to be associated with developing high risk of diabetes in a study by Ford et al³. However, other studies have reported diabetes to be frequently comorbid with chronic obstructive pulmonary disease or faster lung function decline in diabetic individuals than in other subjects⁴. In this study fasting blood glucose is negatively related to FEV1 and FVC parameters and this relation was statistically significant. This is in accordance with previous studies.

SH Shah et al¹⁴ showed that all the pulmonary parameters, that is, FVC, FEV1, FEF25, FEF50, FEF75, FEF25–75, FEF0.2–1.2, and PEFR were significantly reduced except FEV1/FVC in patients of type 2 DM as compared with the healthy controls. Some of the prospective and cross sectional studies have shown low vital capacity or restrictive pattern in type 2 DM. Meta-analysis by van den Borst, *et al*¹⁵ showed that DM is associated with statistically significant, impaired pulmonary function in a restrictive pattern. Moreover, these results were irrespective of body mass index (BMI), smoking, diabetes duration, and HbA1c levels.

Davis, *et al*¹⁶ conducted a study in Western Australia in large number of patients of type 2 DM. They found that VC, FVC, FEV1, and PEFR decreased at an average of between 1.1% and 3.1% of predicted values/year in type 2 DM patients. Ehrlich, *et al*¹⁷ showed that patients with type 2 DM were at increased risk of several pulmonary condition like - asthma, Chronic Obstructive Pulmonary Disease (COPD), fibrosis, and pneumonia. Few studies have mentioned that no significant differences were observed in patients of type 2 DM. Probably the small sample size is the reason behind these findings.

In the study by Weynand¹⁸ *et al* it was found that alveolar epithelium, endothelium capillary, and basal laminae were thickened in lungs on electron microscopy, when compared with the controls. In addition, the thickening of basal laminae was of the same magnitude in lung and kidney. Diabetic microangiopathy might be existing in the pulmonary vascular bed. Moreover, reduced pulmonary capillary blood volume was found, favoring the evidence of microangiopathy. This could lead to redistribution of the pulmonary circulation, resulting in well ventilated areas to become underperfused.

Ljubic¹⁹ *et al* showed that diabetes could lead to the development of pulmonary complications due to collagen and elastin changes. Another theory suggested that increased nonenzymatic glycation of proteins and peptides of the extracellular matrix at chronic high circulating glucose levels may also have an important role in the pathological changes of the lungs in DM patients. Meo et al²⁰ in their studies on Saudi diabetic patients showed significant reduction in FVC, FEV1, and PEF, as compared to their matched controls. They also showed a strong association with a dose-effect response of duration of disease and decreased pulmonary function impairment in their diabetic patients.

Asanuma et al²¹ also reported that FVC and FEV1 were reduced in Japanese diabetic subjects compared to control subjects. The major finding of AS Agarwal et al was a significant reduction in diffusing capacity in type-2 DM patients with microangiopathy as compared to those without microangiopathy and healthy controls. There was a significant correlation of DL/VA percent predicted with microalbuminuria, and with retinopathy. In this study, majority of persons in metabolic syndrome measured fasting blood sugars is between 150-199mg/dL (n=22) and in control group is <100 mg/dL(n=46) and there is significant negative correlation of FBG with FVC and FEV1 parameters resulting in predominant mild restrictive ventilator pattern.

Conclusion

From the results it can be concluded that 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. In this study significant number of persons with metabolic syndrome had mild restrictive pattern of pulmonary function tests even though they were asymptomatic. More importance is to be given to lifestyle modifications like exercise, diet to decrease the incidence of metabolic syndrome.

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