

## Original Research Article

# A study of correlation of pulmonary function test in patients with metabolic syndrome with different components of metabolic syndrome

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## ABSTRACT

**Background:** The increasing incidence of metabolic syndrome has been on the rise especially in urban population and leading to increased risk of cardiovascular disease (CVD) and diabetes mellitus. It has been associated with impairment of pulmonary functions. However, there is limited data regarding the association with individual components of metabolic syndrome and overall effect on components of pulmonary functions.

**Methods:** This is a cross sectional study consisting of 50 subjects with metabolic syndrome. All the subjects underwent pulmonary function tests and the association between different components of metabolic syndrome and pulmonary function were examined using unpaired t-test and Pearson's partial correlation coefficient. This data was analysed by using statistical package for the social sciences (SPSS) version 12.0.

**Results:** In females, moderate negative significant correlation was seen between forced vital capacity (FVC) and systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood sugar (FBS), triglyceride (TG), waist circumference (WC) and body mass index (BMI) whereas positive weak non-significant correlation was seen between FVC and high density lipoprotein cholesterol (HDL), while no such relation was found with forced expiratory volume in one second (FEV1). In males, negative, moderate significant correlation was seen between FVC and FBS whereas strong, positive, significant correlation was seen between FVC and WC; between FVC and BMI. Negative, moderate, significant correlation was seen between FEV1 and WC; between FEV1 and BMI.

**Conclusions:** Our study concluded that there was a significant impact of FBS and WC on decreasing FVC on both genders with minimally significant impact of other components of metabolic syndrome on FVC with no effect on FEV1 hence indicating a restrictive pattern of pulmonary function derangement. Hence, further studies with larger sample size is needed to confirm whether there are direct or indirect mechanisms through which insulin resistance could affect pulmonary function.

**Keywords:** Metabolic syndrome, Pulmonary function test, Forced vital capacity, Obesity, Insulin resistance

## INTRODUCTION

The metabolic syndrome (also known as syndrome X) consists of a constellation of metabolic abnormalities that includes abdominal obesity, insulin resistance, dyslipidaemia and hypertension which lead to increased risk of cardiovascular disease (CVD) and diabetes mellitus.<sup>1</sup>

Insulin resistance and metabolic abnormalities have previously been reported to be associated with impaired pulmonary function in the form of either restrictive or obstructive pattern.<sup>2</sup>

Obesity causes airflow limitation with reduction of both forced expiratory volume in one second (FEV1) and forced vital capacity (FVC), and reduces lung volumes, especially expiratory reserve volume (ERV), and functional residual

capacity (FRC). These changes predispose towards a decrease in peripheral airway diameter, reduction in respiratory system compliance and an increase in work breathing and airway hyper responsiveness (AHR).<sup>3</sup>

Reduced FVC is also a marker for increased mortality in asymptomatic adults or individuals with metabolic syndrome. Abdominal obesity is considered the core of the pathophysiology of metabolic syndrome although definitive pathway and the exact pathophysiological mechanism needs further evaluation. One potential explanation is that increased abdominal obesity directly affects thoracic and diaphragm compliance, which impairs lung function.<sup>4</sup>

Also, lower serum low density lipoprotein cholesterol (HDL-C) level serves as a predictor for the decline of lung function, mainly due to its pleiotropic properties, including antioxidative function. Higher high-sensitivity C-reactive protein (hs-CRP) levels in these individuals imply that inflammation might be an early event in the decline of pulmonary function.<sup>5</sup> Hence, more studies with larger sample size are needed to establish definitive association between the type of pulmonary function impairment and its association with the different components of metabolic syndrome.

The objective of this study is to study and correlate the interpretations of PFT with different components of metabolic syndrome.

## METHODS

### *Source of study*

The study was conducted on patients presenting to the outpatient department in hospitals attached to Bangalore Medical College and Research Institute during the study period from July 2019 to March 2020. Ethical clearance was obtained from the institution prior to enrolling subjects for study. The study design was a cross sectional study including 50 subjects between 18 to 65 years of age with metabolic syndrome who were willing to give consent. Written and informed consents were taken before enrolling for the study. A detailed evaluation was done by history taking which included, occupation complaints if any, presence of past illnesses or current co morbidities, habits including smoking, alcoholism, and drugs, intake of medications and history of previous surgeries. Patients with the following exclusion criteria were excluded from the study:

### *Exclusion criteria*

Patients not willing to give an informed consent; re-existing cardiac disease (myocardial infarction, angina, rheumatic heart disease); pre-existing pulmonary disease like bronchial asthma, chronic obstructive pulmonary disease, obstructive sleep apnea, pneumoconiosis; neuromuscular disorders; lower respiratory tract infection;

critically ill patients (shock, septicemia, multiorgan dysfunction); chest or abdominal pain of any cause; oral or facial pain exacerbated by a mouthpiece; stress incontinence; dementia or confusional state; smokers; and patients with active TB were excluded from the study.

## Measurements

### *Definition of metabolic syndrome*

Metabolic syndrome, based on the Asia criteria of the American heart association/national heart, lung, and blood institute, is diagnosed when 3 out of the following 5 categories are satisfied: blood pressure of systolic blood pressure (SBP)  $\geq 130$  mm Hg or diastolic blood pressure (DBP)  $\geq 85$  mm Hg, or is on an anti-hypertensive drug; fasting blood sugar (FBS)  $\geq 100$  mg/dl, or is on diabetic medication; triglyceride (TG)  $\geq 150$  mg/dl, or is on lipid lowering agents; low HDL-C (male  $< 40$  mg/dl, female  $< 50$  mg/dl), or is on lipid lowering agents; or the waist circumference applied is male  $\geq 90$  cm, female  $\geq 80$  cm.<sup>6</sup>

### *Pulmonary function test*

Pulmonary function was measured using a spirometer (Vitalograph spirometer). Subject was in a seated position, and the measurement was taken by an experienced respiratory technician. To reduce any variance in measurement by the person taking the measurement the same nurse measured everyone. The values measured were FEV1, FVC, FEV1/FVC.

### *Physical measurement*

Waist circumference was measured from the centre point of the last rib and iliac spine. With the morning fasting blood sample, triglyceride, high-density lipoprotein cholesterol (HDL-C), and fasting blood sugar were measured. Blood pressure was measured using a manual sphygmomanometer after taking over 5 minutes of rest in sitting posture.

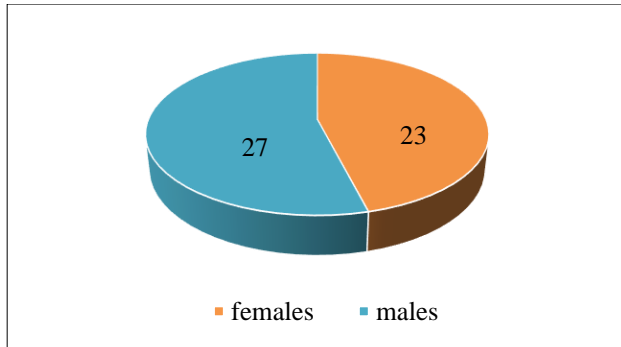
### *Statistical analysis*

The data was shown as mean  $\pm$  standard deviation. For the difference in variables among the groups, unpaired t-test was used. For the relationship between each of the metabolic syndrome components and pulmonary function test variables, Pearson's partial correlation coefficient was used, separately for male and female subjects. This data was analysed by using statistical package for the social sciences (SPSS) version 12.0.

## RESULTS

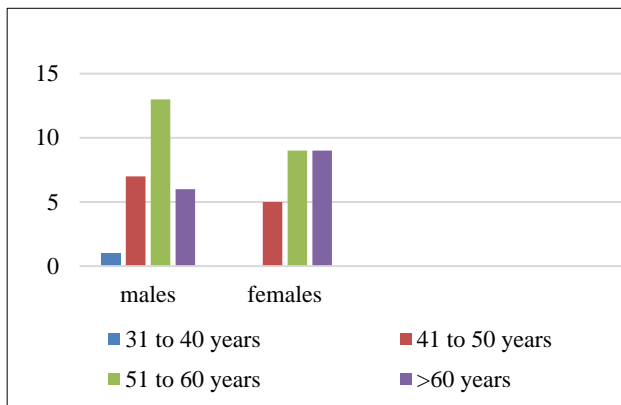
### *Age and gender distribution*

The study comprised a total of 23 (46%) females and 27 (54%) males (Figure 1).



**Figure 1: Gender distribution.**

The lowest age was 38 years and the highest being 65 years. It was found that the mean age of males was higher ( $57.22 \pm 7.434$ ) as compared to females ( $53.30 \pm 7.715$ ) (Figure 2). There was no statistically significant difference between males and females in terms of age.



**Figure 2: Age distribution among males and females.**

#### *Gender distribution with different components of metabolic syndrome*

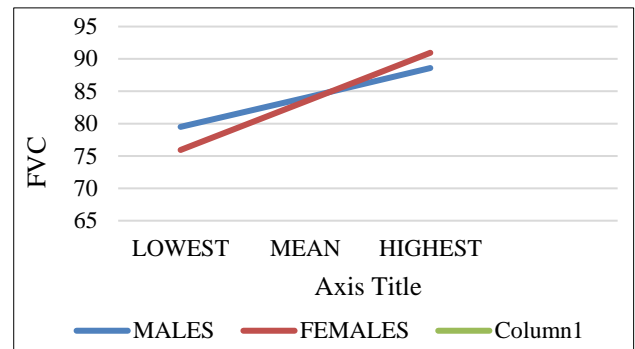
Mean SBP ( $142.65 \pm 15.608$ ), DBP ( $88.70 \pm 6.924$ ), FBS ( $107.35 \pm 15.816$ ), TG ( $180.35 \pm 28.453$ ), HDL cholesterol ( $38.22 \pm 3.861$ ), mean WC ( $97.48 \pm 8.35$ ), BMI ( $33.75 \pm 3.38$ ) were higher in females as compared to males.

Unpaired t test was applied to compare the characteristics between males and females. Statistically no significant difference was seen between males and females (Table 1).

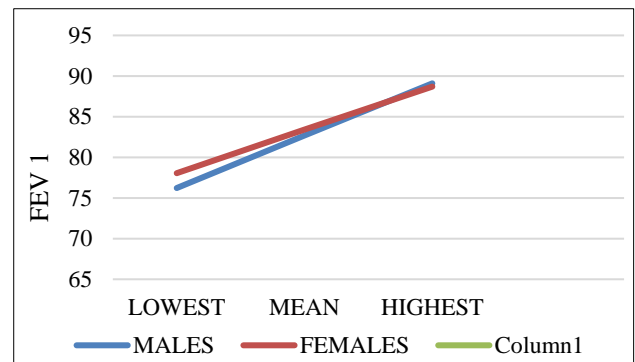
#### *Gender distribution with pulmonary function test*

Mean pre-FVC (%) ( $84 \pm 4.592$ ), pre-FEV1 (%) ( $82.7 \pm 6.47$ ) was higher in males as compared to females (Figures 3 and 4). However, there was no statistically significant difference between the two genders (Table 1).

Table 1 shows the comparison of the characteristics between males and females using unpaired t test.



**Figure 3: FVC distribution between genders.**



**Figure 4: FEV1 distribution between genders.**

**Table 1: Comparison of the characteristics between males and females using unpaired t test.**

Variables	Males		Females		P value
	Mean	SD	Mean	SD	
Age (years)	57.22	7.434	53.30	7.715	0.07
SBP (mm/Hg)	142.65	15.608	142.11	16.032	0.90
DBP (mm/Hg)	88.70	6.924	87.48	5.612	0.49
FBS (mg/dl)	107.35	15.816	102.41	14.023	0.24
TG (mg/dl)	180.35	28.453	174.26	25.305	0.42
HDL C (mg/dl)	38.22	3.861	37.89	4.108	0.77
WC (cm)	94.96	7.462	97.48	8.355	0.26
BMI (kg/m <sup>2</sup> )	32.026	3.553	33.756	3.384	0.08
Pre- FVC (%)	84.00	4.592	83.44	7.506	0.75
Pre-FEV1 (%)	82.70	6.477	83.41	5.358	0.67

**Relationship between diagnostic criteria for metabolic syndrome and pulmonary function****Systolic blood pressure**

There was a statistically significant difference with respect to FVC (%) between groups based on SBP (less than or more than 100) in males' group, females' group and overall ( $p \leq 0.05$ ). Negative, weak non-significant correlation was seen between FEV1 and SBP in females. A weak, negative significant correlation was seen between FEV1 and SBP in males.

**Diastolic blood pressure**

A statistically significant difference was observed with respect to FVC (%) between groups based on DBP (less than or more than 80) in female group and overall ( $p \leq 0.05$ ). Negative, weak non-significant correlation was seen between FEV1 and DBP in females. A weak, negative significant correlation was seen between FEV1 and DBP in males.

**Waist circumference**

Strong, negative, significant correlation was seen between FVC and WC in males whereas, moderate negative significant correlation was seen between FVC and WC in

females. A negative, weak non-significant correlation was seen between FEV1 and WC in females while Negative, moderate, significant correlation was seen between FEV1 and WC in males.

**Fasting blood sugar**

In both males and females, moderate negative significant correlation was seen between FVC and FBS. Whereas there was no significant difference seen with any of the groups with respect to FEV1.

**Triglycerides**

In females, moderate negative significant correlation was seen between FVC and TG. And there was no significant correlation seen between these in males. There was no significant correlation seen between TG and FEV1. Overall, there was a negative significant correlation between TG and FVC.

**HDL-C**

In females, weak positive non-significant correlation was seen between FVC and HDL-C and weak non-significant correlation was seen between FEV1 and HDL-C. No significant correlation was found in males either in terms of FVC or FEV1 (Tables 2 and 3).

**Table 2: Comparison of different components of metabolic syndrome using unpaired t test.**

Variables	Females				Males				Total			
	FVC (%)		FEV1 (%)		FVC (%)		FEV1 (%)		FVC (%)		FEV1 (%)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
<b>SBP (mm/Hg)</b>												
>130	82.53*	4.34	81.8	6.668	81.85*	7.962	82.6	5.888	82.14*	6.58	82.26	6.152
<130	86.75*	3.919	84.38	6.163	88*	3.266	85.71	2.498	87.33*	3.559	85	4.706
<b>DBP (mm/Hg)</b>												
>80	80.85*	2.34	80	9.037	77	14.72	82	6.976	79.45*	8.49	80.73	8.039
<80	85.375*	4.703	83.88	4.897	84.57	5.307	83.65	5.184	84.90*	5.02	83.74	5.004
<b>FBS (mg/dl)</b>												
>100	81.76*	3.632	81.62	8.037	81.6	7.689	82.6	6.706	81.68	6.043	82.14	7.23
<100	86.9*	4.175	84.1	3.542	85.75	6.89	84.42	2.937	86.27	5.717	84.27	3.15
<b>TG (mg/dl)</b>												
>150	83.61	4.353	82.57	6.75	88	7.071	84	2.828	83.56	6.438	83.19	6.2
<150	83.5	8.052	83.77	5.723	83.2	5.07	81.8	3.271	84.57	5.563	82.43	3.101
<b>HDL C (mg/dl)</b>												
>40	84.33	4.093	85.89	4.457	84.75	4.425	81.75	2.5	84.46	4.013	84.62	4.331
<40	83.79	5.026	80.64	6.868	83.22	7.971	83.7	5.7	83.43	6.93	82.54	6.257
<b>WC (cm)</b>												
>80	84	4.592	82.7	6.477	-	-	-	-	84	4.592	82.7	6.477
<80	-	-	-	-	-	-	-	-	-	-	-	-
>90	-	-	-	-	87	2.16	84.25	1.258	82.83	7.952	83.26	5.794
<90	-	-	-	-	82.83	7.952	83.26	5.794	87	2.16	84.25	1.258
<b>BMI (kg/m<sup>2</sup>)</b>												
>23.5	84	4.592	82.7	6.477	83.44	7.506	83.41	5.358	83.7	6.28	83.08	5.848
<23.5	-	-	-	-	-	-	-	-	-	-	-	-

Continued.

**Table 3: Pearson's correlation between FVC (%) and FEV1 (%) with clinical parameters.**

Variables	Females		Males		Total	
	r value	P value	r value	P value	r value	P value
<b>FVC (%)</b>						
SBP	-0.52	0.011*	-0.19	0.33	-0.29	0.038*
DBP	-0.52	0.01*	-0.19	0.33	-0.29	0.035*
FBS	-0.63	0.001*	-0.47	0.011*	-0.49	0.00*
TG	-0.52	0.01*	-0.32	0.09	-0.37	0.007*
HDL C	0.036	0.87	0.18	0.36	0.13	0.35
WC	-0.562	0.005*	-0.72	0.00*	-0.66	0.00*
BMI	-0.567	0.005*	-0.65	0.00*	-0.59	0.00*
<b>FEV1 (%)</b>						
SBP	-0.33	0.12	-0.24	0.22	-0.28	0.04*
DBP	-0.34	0.1	-0.04	0.81	-0.21	0.12
FBS	0.016	0.94	-0.22	0.25	-0.1	0.46
TG	0	0.99	-0.033	0.86	-0.023	0.87
HDL C	0.25	0.23	-0.04	0.83	0.1	0.48
WC	-0.24	0.25	-0.52	0.005*	-0.37	0.008*
BMI	-0.28	0.18	-0.51	0.006*	-0.36	0.009*

\*Significant.

***Relationship between body mass index and pulmonary function test***

In females, moderate negative significant correlation was seen between FVC and BMI while a negative, weak non-significant correlation was seen between FEV1 and BMI. In males, a strong, negative, significant correlation was seen between FVC and BMI whereas a moderately, significant negative correlation was seen between FEV1 and BMI.

Overall, a strong negative correlation was seen in both groups in terms of FEV1 and FVC.

***Overall gender differences in the relationship between pulmonary function test and components of metabolic syndrome***

In females, FVC showed significant decrease with respect to elevated FBS levels whereas there was no significant difference seen with any of the other components with respect to FEV1. In females, moderate negative significant correlation was seen between FVC and SBP, DBP, FBS, TG, WC and BMI whereas positive weak non-significant correlation was seen between FVC and HDLC, while no such relation was found with FEV1.

In males, negative, moderate significant correlation was seen between FVC and FBS whereas strong, positive, significant correlation was seen between FVC and WC; between FVC and BMI. Negative, moderate, significant correlation was seen between FEV1 and WC; between FEV1 and BMI.

Overall, weak, negative significant correlation was seen between FVC and SBP, DBP, TG; between FEV1 and SBP, DBP, WC, BMI. Moderate negative significant

correlation was seen between FVC and FBS, BMI. Moderate negative significant correlation was seen between FVC and WC.

Table 2 shows the comparison of the comparison of different components of metabolic syndrome in terms of pulmonary function tests using unpaired t test.

**DISCUSSION**

According to ICMR-INDIAB study 2015, prevalence rate of obesity and central obesity in India varies from 11.8-31.3% and 16.9-36.3% respectively.<sup>7</sup> The rising prevalence overweight and obesity in India has a direct correlation with the increasing prevalence of obesity-related co-morbidities like hypertension, the metabolic syndrome, dyslipidaemia, type 2 diabetes mellitus (T2DM) and cardiovascular disease. These comorbidities have been associated positively with lung function impairment.<sup>8</sup> Amongst the respiratory conditions, obesity has been known to cause obstructive sleep apnoea, Pickwickian syndrome, hypoventilation syndrome and bronchial syndrome.<sup>9</sup> Excess fat accumulation in the abdominal cavity and on the chest wall affects chest mechanics, increasing the work of breathing, reducing lung volumes, leading to straining of respiratory muscles, impaired gas exchange and reducing exercise tolerance.<sup>10</sup> Several large prospective studies have shown that lung function impairment was predictive of increased cardiovascular morbidity and mortality, independent of smoking.<sup>11</sup>

Our study aimed to find the significance of different components of metabolic syndrome in lung function alterations. Amongst the previous studies, Leone et al showed that both males and females showed reverse-correlation between all diagnostic components of



metabolic syndrome and pulmonary functions.<sup>12</sup> In our study, we found out that FBS and waist circumference had a significant effect on decreasing FVC and not FEV1. Lung function impairment, including restrictive ventilatory defect, in particular, has been reported to be associated with developing high risk of diabetes.<sup>13</sup> Also, whether there is an association between conditions associated with insulin resistance like fatty liver, non-alcoholic hepatic steatosis needs to be studied further. Since diabetes mellitus and pre diabetes is a systemic pro inflammatory state, an indirect pathogenetic mechanism for lung function impairment can be possible.

Khan et al showed that FVC and FEV1 and waist circumference and hip circumference had negative correlation for men, whereas for women, only FVC had correlation and FEV1 showed no correlation.<sup>14</sup> In our study, a strong, negative, significant correlation was observed between FVC and WC in males whereas, moderate negative significant correlation was seen between FVC and WC in females. Sutherland et al used X-ray absorptiometry to study the effect of abdominal obesity on pulmonary function. It was hypothesised that abdominal obesity may directly reduce the lung compliance by exerting mechanical effect on diaphragm and lung volume.<sup>15</sup> Moreover, obesity by itself is a pro inflammatory state due to release of adipocytokines which could further worsen the underlying respiratory compromise.<sup>16</sup> The definitive mechanism for the decrease in lung volume is poorly studied and needs further evaluation.

There was a weak association between lung function impairment and glucose–blood pressure that was more closely related to impaired glycemic control. Both impaired glucose metabolism and blood pressure homeostasis have insulin resistance in common.<sup>17</sup> In our study, there was a moderate negative significant correlation was seen between FVC and FBS in both males and females. Whereas, there was no significant difference seen with any of the groups with respect to FEV1. These results were consistent with the results of Leone et al as previously mentioned.

Although BMI has not been included as a component of metabolic syndrome, studies previously have shown negative associations between BMI and lung functions. In a longitudinal study conducted by Bottai et al, the extent of FVC loss tended to be higher among those who, at baseline, reported greater BMI values.<sup>18</sup> Males experienced larger losses than females which was consistent with our study where males had a stronger association as compared to females for FVC. However, no significant association was seen with FEV1. Studies have found that respiratory function improved with weight loss or waist-to-hip ratio, in morbidly obese patients 1 year after bariatric surgery.<sup>19</sup> So, further studies are needed to confirm the same and to initiate early intervention in metabolic syndrome to decrease cardio-respiratory morbidities in metabolic syndrome.

## Limitations

A small sample size is a major limitation of our study. Hence, further studies with larger sample size in Asian population is needed.

## CONCLUSION

We found a positive independent relationship between lung function impairment and metabolic syndrome in both sexes, predominantly in subjects with high fasting blood sugar levels. Insulin resistance could likely be a predominant contributing factor. Further studies are required to study the underlying mechanisms behind this and to establish whether reversal of metabolic syndrome and insulin resistance will lead to reversal of the lung function impairment.

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