Section A-Research paper

"A CROSS SECTIONAL STUDY TO EVALUATE PULMONARY DYSFUNCTION IN PATIENTS WITH METABOLIC SYNDROME BY PULMONARY FUNCTION TESTS."

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ABSTRACT:

Background: Metabolic syndrome is a combination of various metabolic diseases which further leads to pulmonary dysfunction. The major features of metabolic syndrome includes central obesity, insulin resistance, hypertension, dyslipidaemia, high Triglycerides and low HDL levels. To evaluate this we studied the pulmonary function tests by spirometry in patients with metabolic syndrome and to find relation of spirometric parameters (FVC, FEV1, FEV1/FVC) with metabolic syndrome.

Methods: This was a single centre hospital-based cross-sectional, observational, descriptive study conducted in subjects admitted to the General Medicine Ward of our institute over a period of 18 months from October 2020 to March 2022. Pulmonary function tests were carried out on patients with metabolic syndrome by spirometer and were observed for pulmonary dysfunction.

Results: Mean age was 53.6+ 14.4 years ranging from 22 to 85 years. Mean systolic blood pressure was 132.7 (+17.3) and mean diastolic blood pressure was 80.9 (+9.8) mm of Hg. Mean serum triglyceride level was 255.9 (+142.5). Mean high density lipoprotein was 38.1 (+11.7). Mean fasting blood sugar was 178.2 (+97.5). On pulmonary function test category, majority 45.1% had restrictive pattern. Association between metabolic syndrome component and FEV1, showed that as metabolic syndrome component increases, FEV1 also increases. ('p' = 0.17). Association between metabolic syndrome component and FVC, showed that as metabolic syndrome component increased FVC decreased and shows statistical significance. ('p' = 0.04). Association between metabolic syndrome component and FEV1/FVC showed

that as metabolic syndrome component increased ratio also increased and shows statistical significance. ('p'= 0.0002)

Conclusion: In the present study we observed that increasing components of metabolic syndrome had significantly impaired pulmonary functions. It was observed that, as the components of metabolic syndrome increased, severity of pulmonary dysfunction also increased. To conclude, increasing components of metabolic syndrome have significant impairment of the pulmonary function.

Keywords: *Mets – Metabolic Syndrome, PFT – Pulmonary Function Test, FEV1 – Forced expiratory volume in the first second, FVC – Forced Expiratory Capacity*

INTRODUCTION:

Metabolic syndrome is a combination of various metabolic diseases which further leads to cardiac disorders. The major features of metabolic syndrome includes central obesity, insulin resistance, hypertension, dyslipidaemia, high Triglycerides and low HDL levels. The highest recorded prevalence of metabolic syndrome worldwide is among Native Americans with an age adjusted 53% women and 45% men meeting the criteria of NCEP ATP III. Overweight/obesity, sedentary lifestyle, lipodystrophy, Diabetes mellitus and cardiovascular diseases are all risk factors for metabolic syndrome. 75% subjects of Type2 DM or Impaired glucose tolerance have the metabolic syndrome. Individuals with metabolic syndrome are twice as likely to die of cardiovascular disease as those who do not, and their risk of an acute myocardial infarction or cerebrovascular accident is threefold higher. The exact cause is not known, with insulin resistance being the central cause and etiologic being multifactorial. [1,2] In general with increase in free fatty acid flux to the liver, increased production of ApoB containing triglyceride rich very low density lipoprotein occurs. Hypertriglyceridemia is an excellent marker of insulin resistant condition. The other major lipoprotein disturbance in metabolic syndrome is reduction in HDL cholesterol. [3,4]

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 Type 2 Diabetes Mellitus. Although the link between impaired lung function and cardiovascular events and Type 2 Diabetes Mellitus has been recognized, the association between impaired lung function and MetS has not been comprehensively assessed. [5] As such, there is increasing interest in changes in metabolic syndrome associated with changes in pulmonary function. [6] Recently, it is reported that among the changes in pulmonary function, pulmonary function, deterioration is related to hypertension, type 2 diabetes, low-density lipoprotein cholesterol, overall obesity, abdominal obesity and insulin resistance. 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. [7,9]

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). [10,11] 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. [12] 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. [13,14] Hence, present study was carried out to study the pulmonary function tests by spirometry in subjects with metabolic syndrome and to find relation of spirometric parameters (FVC, FEV1,FEV1/FVC) with components of metabolic syndrome.

Methodology:

Study design: Observational, cross-sectional type of study.

This was a single centre hospital-based cross-sectional, observational study conducted in subjects admitted to the General Medicine Ward and Medical Intensive Care Unit (MICU) of our institute over a period of 18 months from October 2020 to March 2022.

Study Setting: Krishna Hospital, Karad

Study Population: The accessible population of the study included subjects admitted in Krishna Hospital or visiting OPD of Krishna Hospital, Karad and having metabolic syndrome.

Study period: October 2020 to March 2022

Sample: The subjects who fulfilled inclusion criteria were considered as samples.

Inclusion criteria: According to NCEP ATP III: ―Three or more of the following: 1. Central Obesity: Waist circumference >102 cm(>40 inches) in male or >88 cm (>35 inches) in female. 2. Hypertriglyceridemia: Triglycerides ≥ 150 mg/dl (≥ 1.7 mmol/L). 3. Low HDL cholesterol: <40 mg/dl(<1.0 mmol/L) in male or <50 mg/dl(<1.3mmol/L) in female. 4. Hypertension: Blood pressure ≥ 130/85 mm Hg or specific medication. 5. Fasting plasma glucose ≥100 mg/dl(≥ 6.1 mmol/L) or specific medication or previously diagnosed type 2 diabetes mellitus.

Exclusion criteria: 1. Subjects with cardiopulmonary diseases, neuromuscular disorders, musculoskeletal disorders, in postoperative state, any serious systemic illness, endocrine abnormalities (hypothyroidism, cushing's syndrome, etc),individuals below 18 years of age and smokers were excluded from the study. 2. Subjects with proven records of chronic renal disease or history of chronic intake (duration >6 months) of any drug that is known to decrease glomerular filtration rate or with creatine levels ≥ 1.5 mg/dl. 3. Subjects with Cerebrovascular Accident. 4. Subjects who have refused consent to the study.

Ethics Committee approval: The clearance for the study was taken from institutional ethics committee after discussion of the study protocol with committee, patients were included in the study only after they give written informed consent to participate.

Statistical Analysis: Data was collected using a semi-structured pretested questionnaire, data Collected was entered in Microsoft Excel. Data is represented in frequencies and percentages, charts and graphs. Mean and standard deviation of quantitative variables is shown. Appropriate statistical tests are applied using SPSS software version 21 for analysis. Chi square test is used for association and student's t-test is used for comparison wherever applicable. Pearson's Correlation is used to check the correlation between metabolic syndrome component and FVC, FEV1 and FEV1/FVC, where 'r' value denotes the correlation coefficient and p value if less than 0.05 shows significant correlation. Other statistical tests are used as per study requirements. P value < 0.05 is taken as statistical significance.

Observations and Results:

Table 1 shows mean and standard deviation of the study population with metabolic syndrome

In the present study of 113 subjects, the mean age among the males and females were 54.30 (± 14.52) and 51.54 (± 14.11) years respectively and was statistically insignificant ('p' value =0.341).

The mean waist circumference among the males and females were 1004.61 (± 11.17) and 92.56 (± 8.43) cms respectively and was statistically insignificant. ('p' value =0.135).

The mean systolic blood pressure among the males and females were 134.68 (± 15.26) and 129.46 (± 20.94) mmHg respectively and was statistically insignificant. ('p' value =0.087)

The mean diastolic blood pressure among the males and females were 82.04 (± 9.09) and 78.65 (± 11.09) mmHg respectively and was statistically significant. ('p' value=0.002)

The mean serum triglyceride levels among the males and females were 280.91 (± 159.76) and 193.08 (± 62.38) mg/dL respectively and was statistically significant. ('p' value =0.001)

The mean serum high density lipoprotein levels among the males and females were 35.32 (± 11.09) and 44.41 (± 11.30) mg/dL respectively and was statistically significant. ('p' value =0.003)

The mean fasting blood glucose levels among the males and females was 191.99 (± 106.76) and 137.41 (± 39.74) mg/dl respectively and was statistically significant. ('p' value =0.001)

Raised diastolic blood pressure, raised serum triglyceride levels and raised HDL levels were statistically significant in males compared to females ('p' value = 0.002,0.001 and 0.003 respectively)

Table 1: Mean and Standard deviation of the study population with metabolic syndrome

Variables	**Mean (± SD)**		**One-way Annovatest 'P' value**
	Male	**Female**	
Age (years)	54.30 (±14.52)	51.54 (±14.11)	0.341

Waist circumference (cms)	104.61 (±11.17)	92.56 (±8.43)	0.135
Systolic blood presssure (mmHg)	134.68 (±15.26)	129.46 (±20.94)	0.087
Diastolic blood pressure (mmHg)	82.04 (±9.09)	78.65 (±11.09)	0.002
Triglycerides (mg/dL)	280.91 (±159.76)	193.08 (±62.38)	0.001
High density lipoprotein (mg/dL)	35.32 (±11.09)	44.41 (±11.30)	0.003
Fasting blood sugar (mg/dL)	191.99 (±106.76)	137.41 (±39.74)	0.001

Distribution of study population with metabolic syndrome according to pulmonary function tests.

Table 2 and figure 1 shows that of total 48 subjects with 3 metabolic syndrome components 18 subjects had mixed obstructive and restrictive pattern, 3 subjects had normal pulmonary function test, 16 subjects were having obstructive pattern, 11 subjects were having restrictive pattern.

Of total 39 subjects with 4 metabolic syndrome components 4 had mixed obstructive and restrictive pattern, 16 subjects had obstructive pattern, 19 subjects had restrictive pattern.

Of total 26 subjects with 5 metabolic syndrome components 4 subjects had mixed obstructive and restrictive pattern, 3 subjects had obstructive pattern, 19 subjects had restrictive pattern.

Of total 113 subjects, 26(23.1%) were having mixed obstructive and restrictive pattern,

3 subjects (2.7%) had normal pulmonary function test, 35 subjects (30.9%) had obstructive pattern and 49 subjects (43.3%) had restrictive pattern.

As the number of components of metabolic syndrome increased, the pulmonary dysfunction also increased. This relation between pulmonary dysfunction and components of metabolic syndrome in this study population is statistically significant. (X2 = 26.565; DF =6; 'p' value = 0.00017)

Table 2: Distribution of study population with metabolic syndrome according to pulmonary function test

Pulmonary Function Test	**Metabolic Syndrome component**			**Total**	**Percent**
	3	**4**	**5**		

Mixed Obstructive and Restrictivepattern	18(15.9%)	4(3.5%)	4(3.5%)	26	23.1
Normal	3(2.6%)	0(0%)	0(0%)	3	2.7
Obstructive pattern	16(14.1%)	16(14.1%)	3(2.6%)	35	30.9
Restrictive pattern	11(9.7%)	19(16.8%)	19(16.8%)	49	43.3
Total	48(42.4%)	39(34.5%)	26(23%)	113	100

Figure 1: Distribution of study population with metabolic syndrome according to pulmonary function test

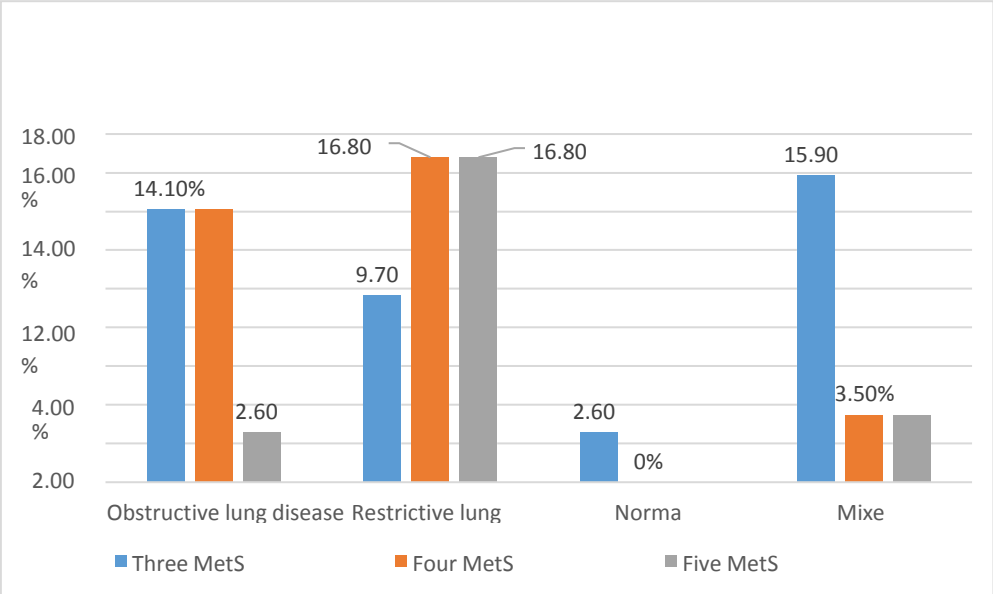


Table 3 and figure 2 shows association between metabolic syndrome components and pulmonary function test.

Metabolic component 3 had mean FEV1 of 2.1 litres, metabolic component 4 had mean FEV1 of 2.3 litres and metabolic component 5 had mean of 2.4litres.

Thus it is observed that as the component of Metabolic syndrome increases the mean for FEV1 also increases.

Association between metabolic syndrome components and FEV1 showed that as MetS component increased FEV1 also increased. As p value is 0.17 shows no statistical significance.

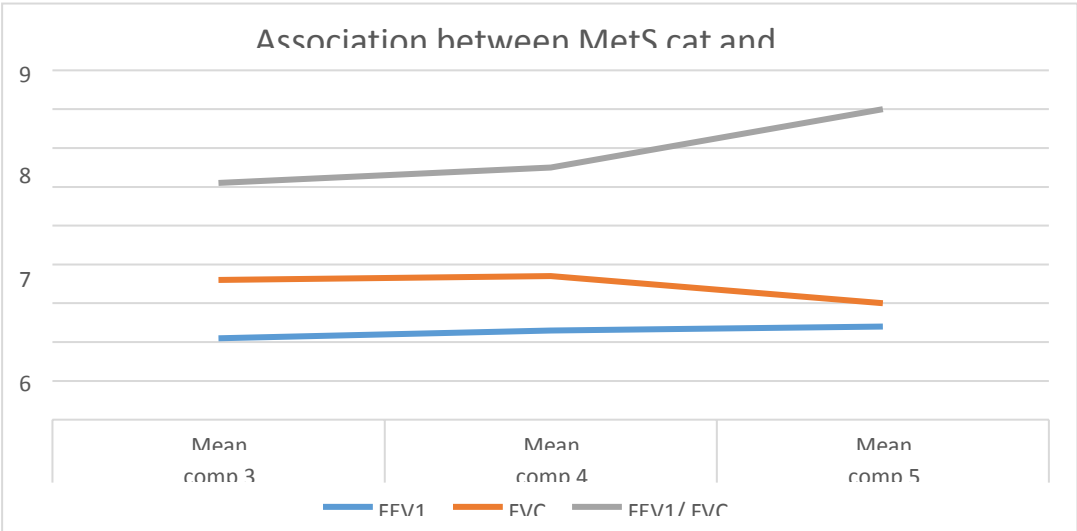
Metabolic component 3 had mean FVC of 3.6 litres, metabolic component 4 had mean FVC of 3.7litres and metabolic component 5 had mean of 3.0 litres.

Association between metabolic syndrome component and FVC showed that as MetS component increased FVC decreased. As p value is 0.04 shows statistical significance.
Metabolic component 3 had mean FEV1/ FVC of 61.2%, metabolic component 4 had mean FEV1/ FVC of 65.9% and metabolic component 5 had mean FEV1/ FVC of 80.5%.
Association between metabolic syndrome component and FEV1/FVC showed that as components of MetS are more from 3 to 5, the mean FEV1/FVC ratio is also higher with 'p' value <0.002.

Table 3: Association between Metabolic Syndrome components and Pulmonary function test

Pulmonary Function Test parameters	**Metabolic syndrome components**						**'p' value**
	3		**4**		**5**		
	Mean	SD(±)	Mean	SD(±)	Mean	SD(±)	
FEV1	2.1	0.8	2.3	0.6	2.4	0.6	0.17
FVC	3.6	1.2	3.7	1.1	3	0.8	0.04
FEV1/ FVC	61.2	18.1	65.9	20.7	80.5	12.33	0.0002

Figure2: Association between metabolic syndrome components and pulmonary function test



DISCUSSION:

There has been increasing incidence of metabolic syndrome (MetS) and pulmonary dysfunction. Recent studies have shown association between the MetS and PFT. We compared our study with other similar studies. The variation amongst various studies can be

attributed to the geographical, cultural and ethnic differences in the subjects with metabolic syndrome taken into consideration.

In the present study, majority of the subjects were in the age group of 40-59 years (54%) followed by age group 60 and above (36%) with the mean age of 53.6(±14.4) years ranging from 22 to 85 years. The distribution according to the gender showed that majority of the subjects were males 76 (67.3%) with females 37 (32.7%). The findings were different from other studies such as Chaudhary SC et al where maximum number of subjects were in 20-39 years of age group (45%) followed by those aged 40-59 year (26%).[5] Mean age of subjects was 39.59(±8.67) years. Study by Sachdeva S et al showed that most of the subjects belonged to age group 60 and above years (n=19) followed by 40- 59 years age group (n=16). [14] The mean age of the subjects was 57.94 (±10.45) years. Prabhu S et al showed that 46% were females and 54% were males. Study by Sachdeva S et al showed that 73.3.% were females. [10] [14] In the present study it was observed that the mean waist circumference in males and females was 104.61 (±11.17) cms and 92.56 (±8.43) cms respectively. In study by Prabhu S et al it was observed that mean waist circumference in males and females was 97.48 (±10.77) cms and 90.22 (±9.37) cms respectively. [10] In present study it was observed that mean systolic blood pressure in males and females was 134.68 (±15.26) and 129.46 (±20.94) mmHg respectively. In study by Prabhu S et al it was observed that mean systolic blood pressure in males and females was 142.65 (+15.11) and 134.43 (±13.33) mmHg respectively.[10] In this study it was observed that 77% subjects had raised systolic blood pressure. In the study by Sachdeva S et al it was observed that mean systolic blood pressure in males and females was 132.71 (±11.45) and 128.68 (±12.34) mmHg respectively. [14]

According to this study 81.7% were having raised systolic blood pressure. The mean diastolic blood pressure in males and females was 82.04 (±9.09) and 78.65 (±11.09) mmHg respectively. In study by Prabhu S et al it was observed that mean diastolic blood pressure in males and females was 80.34 (±12.33) and 76.23 (±10.22) mmHg respectively.[10] In this study it was observed that 70% subjects had raised diastolic blood pressure. In the study by Sachdeva S et al it was observed that mean diastolic blood pressure in males and females was 84.67 (±12.33) and 78.88 (±10.23) mmHg respectively. It was observed that 89% had raised diastolic blood pressure. [14] In the present study it was observed that mean serum triglyceride level in males and females was 280.91 (±159.76) and 193.08 (±62.38) mg/dl respectively. In the study by Prabhu S et al it was observed that mean serum triglyceride level in males and females was 180.10 (±40.31) and 210.30 (±44.40) respectively.[10] In the study by Sachdeva S et al it was observed that mean serum triglyceride level in males and females was 170.30 (±36.31) and 190.45 (±34.67) mg/dl respectively and 58.3% had raised triglyceride levels.[14] The mean high density lipoprotein level in males and females was 35.32 (±11.09) and 44.41 (±11.30) mg/dl respectively. 76.69% had raised high density lipoprotein levels. In the study by Prabhu S et al it was observed that mean high density lipoprotein level in males and females was 38.22 (±11.21) and 42.44 (±12.22) mg/dl respectively. [10] In the study by Sachdeva S et al it was observed that mean high density lipoprotein level in males and females was 36.45 (±10.45) and 46.23 (±16.52) mg/dl respectively and 78% had low high density lipoprotein level.[14] The mean fasting blood sugar level in males and females was 191.99 (±106.76) and 137.41 (±39.74) mg/dl

respectively. Prabhu S et al showed that mean fasting blood sugar level in males and females was 177.45 (±55.67) and 135.45 (±37.34) mg/dl respectively and 26.7% had raised fasting blood sugar levels. [10]

Of the total subjects 42.5% had 3 metabolic syndrome components, 37.2% had 4 metabolic syndrome components and only 20.3% had 5 metabolic syndrome components. In the study by Sachdeva S et al it was observed that 40% (n=24) of the subjects had 4 components positive while 35% (n=21) of the subjects had 3 components positive. 25% (n=15) of the subjects had all 5 components of metabolic syndrome positive. [14] On pulmonary function test, mean FEV1 was 2.2 (+0.7), mean FVC was 3.5 (+1.1) and mean FEV1/FVC was 66.9 (+19.4). On pulmonary function test category,45.1% had restrictive pattern, followed by 30.1% had obstructive pattern, 22.1% had mixed obstructive and restrictive pattern and 2.7% had normal range. In the study by Sachdeva S et al it was observed that 43.3% (n=26) subjects had a restrictive pattern, 33.3% (n=20) of the subjects had a mixed pattern while 16.7% (n=10) of the subjects had a normal picture. Only 6.7% (n=4) of the subjects had an obstructive pattern ($p<0.001$).[14]

In the study by Prabhu S et al it was observed that mean FVC was 84 (±4.592) and mean FEV1 82.7 (±6.47). [10] Association between metabolic syndrome component and pulmonary function test showed that among subjects with restrictive lung disease, majority belonged to metabolic syndrome component 3 and 4 ('p' value = 0.0006) and shows statistical significance. Association between metabolic syndrome component and FEV1 showed that as metabolic syndrome component increased FEV1 also increased and shows no statistical significance. ('p' value = 0.17) Association between metabolic syndrome component and FVC, it was observed that as metabolic syndrome component increased FVC decreased and shows statistical significance. ('p' value = 0.04). Association between metabolic syndrome component and FEV1/FVC, it was observed that as metabolic syndrome component increased, ratio of FEV1/FVC also increased and shows statistical significance ('p' value = 0.0002). Similar findings were observed in study by Chaudhary SC et al. [5] There was a strong linear decrease in FVC and FEV1 as the number of components of metabolic syndrome increased. As the number of metabolic syndrome component increased, subjects had more severe decline in pulmonary function. Bae MS et al showed that all metabolic syndrome components were associated with pulmonary function impairment and more the metabolic syndrome components subjects had, the more severe their pulmonary functions declined.[6]

Our result were in concordance with the study conducted by Bae et al which did not find a correlation of FEV1 and increasing number of components of metabolic syndrome.[6] In the study by Prabhu S et al it was observed that there was a significant impact of fasting blood sugar and waist circumference on decreasing FVC 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.[10] In the study by Sachdeva S et al it was observed that mean value of FEV1 had no correlation with increasing number of components of metabolic syndrome whereas mean value of FVC showed a decreasing trend with increasing number of components of metabolic syndrome. [14] Subjects with 3 metabolic syndrome components had a mean FVC of 1.888 (±0.67). Subjects with 4

metabolic syndrome components had a mean FVC of 1.881 (±0.75). Subjects with 5 metabolic syndrome components had a mean FVC of 1.34 (±0.58). In the study by Chaudhary et al it was observed that subjects with 3 metabolic syndrome components had mean FVC of 2.86 (±0.06). Subjects with 4 metabolic syndrome components had mean FVC of 2.80 (±0.08) and subjects with 5 metabolic syndrome components had mean FVC of 2.78 (±0.09).

Table : Comparison of present study with other studies

Author	**Sample size (n)**	**Study design**	**Interpretation**
Chaudhary SC et al [4]	100	Cross sectional	Study observed that 28% of the male and 46.6% of female subjects showed restrictive pattern and 7% of male and 13.4% of female subjects showed mixed pattern. All MetS components were associated with pulmonary function impairment. As the number of MetS components increases, patients had more severe decline in pulmonary functions.
Bae MS et al [6]	1370	Prospective study	Study observed that all metabolic syndrome components were associated with pulmonary function impairment, and more the metabolic syndrome components subjects had, more severe their pulmonary functions declined.
Prabhu S et al [10]	50	Cross sectiona	Study concluded that there was a significant impact of fasting blood sugar and waist circumference on decreasing FVC in both genders with minimally significant impact of other components of metabolic syndrome on FVC with no effect on FEV1 and indicating a restrictive pattern of pulmonary function derangement.
Sachdeva S et al [14]	60	observational cross sectional study	The mean FVC was significantly higher in males as compared to females. Mean FVC was 2.45 (±0.86) L in males while females had a mean FVC of 1.65 (±0.49) L (p 0.002). Study concluded that patients with metabolic syndrome have significant impairment of the pulmonary function with restrictive pattern being the most common one.
Lin et al[58]	46514	Metanalysis	Study concluded that obesity and metabolic syndrome were associated with impaired lung function in adults.
Makkar et al,	50	Prospective	Study observed that varying derangements in

[59]			the different parameters of pulmonary function tests, suggestive of dominantly restrictive with some obstructive pattern as indicated by significant decline in FVC, peak expiratory flow rate (PEFR) and maximum expiratory flow at 75% (MEF75).
Present study	113	Observational Descriptive Cross sectional study	In this study it was observed that as the components of metabolic syndrome increased, severity of pulmonary dysfunction also increased. Most common pulmonary function test category noticed was restrictive pattern. Increasing components of metabolic syndrome have significant impairment of the pulmonary function.

Conclusion:

In the present study we observed that increasing components of metabolic syndrome had significantly impaired pulmonary functions. Majority of subjects in the present study had three and four metabolic syndrome components. It was observed that, in the present study as the components of metabolic syndrome increased, severity of pulmonary dysfunction also increased. Most common pulmonary function test pattern noticed was restrictive pattern. The increasing prevalence of diabetes, coupled with obesity, dyslipidaemia, hypertension and ultimately metabolic syndrome has put a significant proportion of the population at risk of potential pulmonary dysfunction. Physical activity, dietary modification, weight reduction, control of hypertension and diabetes may halt the progression of complications of metabolic syndrome. To conclude, increasing components of metabolic syndrome have significant impairment of the pulmonary function.

Conflict of interest: None
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