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EFFECTS OF METABOLIC SYNDROME ON PULMONARY FUNCTION TESTS

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Abstract

Background: Metabolic syndrome (MetS) is a cluster of cardiovascular risk factors associated with obesity, hypertension, dyslipidemia, and insulin resistance. These factors have been implicated in the development of respiratory impairments, although the exact mechanisms remain incompletely understood. This study aimed to investigate the influence of MetS and its components on pulmonary function.

Methods: This cross-sectional study included 100 women with MetS (mean age= 52.34±8.56) and 50 age-matched healthy controls (mean age= 48.62 ± 10.48). Anthropometric measurements, blood pressure, and metabolic parameters were assessed according to standard protocols. Pulmonary function tests were conducted to evaluate ventilatory patterns. Statistical analyses were performed using independent t-tests, analysis of variance (ANOVA), and chi-square tests.

Results: Significant differences were observed in socio-demographic characteristics between the MetS and control groups, with a higher prevalence of restrictive and obstructive ventilatory patterns in the MetS group. Pulmonary function variables, including forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and FEV1/FVC ratio, were significantly lower in the MetS group compared to controls. Waist circumference, fasting blood glucose, and insulin resistance were associated with impaired pulmonary function in individuals with MetS.

Conclusion: This study highlights the impact of MetS and its components on pulmonary function in women, with a notable prevalence of ventilatory abnormalities in MetS patients. These findings underscore the importance of addressing metabolic health in the management of respiratory impairments and suggest the need for further longitudinal studies to elucidate the underlying mechanisms and implications for cardiovascular health.

Keywords: *Metabolic syndrome;Pulmonary functions;Insulin resistance; Prevalence*

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INTRODUCTION

Metabolic syndrome is a collection of cardiovascular risk factors that are linked to obesity, high blood pressure, high blood sugar, and abnormal lipid levels [1]. Obesity is well recognized as the primary component that contributes to the development of an inflammatory response barrier, which can lead to meconium accumulation for respiration, deposition of lipids, and excessive growth of smooth muscle in the airways. Ultimately, this might result in a decrease in functional capacity. The occurrence of metabolic syndrome in women is affected by factors such as the number of pregnancies, gestational diabetes, pre-eclampsia, and menopause [4]. The clinical condition [5] is associated with low income. There is evidence suggesting that the occurrence of intravascular atherosclerotic blockage in metabolic syndrome is linked to its components [6].

Pulmonary performance is impaired in both obstructive and restrictive ways, and this impairment is linked to various clinical disorders including chronic lung illness, obesity, diarrhea, hypertension, heart disease, and menopause in women [7,8]. The exact mechanisms of dysfunction have not been fully elucidated. However, obesity appears to be the risk factor that initiates the changes. This is due to the activation of an inflammatory response [9,10] and the influence of arterial hypertension on respiratory function. Arterial hypertension remodels the left ventricle, which can impair vascular flow for pulmonary gas exchange, particularly in women [7]. In the field of pulmonary function, the negative effects of metabolic syndrome are caused by bronchial hyperreactivity [11,12], which results in airway obstruction, decreased functional residual capacity (FRC), and subsequent alterations in ventilation perfusion (V/Q) ratio. This leads to a decrease in tidal volume at the base of the lungs, making them more susceptible to alveolar collapse and reducing tissue oxygenation [9]. Obesity leads to mechanical alterations that contribute to a restrictive breathing pattern. These alterations are associated with a decrease in the diaphragm's ability to expand during respiration, as well as a decline in the recruitment of certain fibers. The clinical implications include decreased strength and endurance of respiratory muscles, leading to muscle fatigue [13], and in severe cases, abrupt respiratory failure.

The components of the metabolic syndrome may impact lung function, however there are unresolved matters that need clarification, such as the most common kind of ventilatory dysfunction and the mechanisms via which changes in lung function occur. The objective of this study was to assess the influence of metabolic syndrome and its components on the pulmonary function.

MATERIALS AND METHODS

This cross-sectional study was conducted in a tertiary care hospital of eastern India. The patients aged between 25-65 years, were randomly selected from the outpatient clinic and diabetes center of Department of General Medicine, of our institute . 100 patients (mean age= 52.34±8.56), with MetS who fulfilled the National Cholesterol, Education Program, Adult Treatment Panel-III (NCEP ATP-III, 2001) criteria were included in the study group (MetS

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group). Age and sex matched 50 healthy volunteers (mean age= 48.62 ± 10.48) who had no features of MetS were included in the control group (Non-MetS). Patients with history of respiratory disease, malignancy, smokers, alcoholics, congestive cardiac failure, pregnant women, and liver disease, were excluded from this study. Trained interviewers, using a structured questionnaire, interviewed all the participants to obtain the information on socio-demographic characteristics, physical activity, smoking, alcohol drinking habits, dietary characteristics, personal and family history of diseases, and hospitalization. Anthropometric measurements and blood pressure measurements were obtained after complete physical examination. Blood pressure (BP) was measured using a mercury sphygmomanometer with over the right arm with the patient lying supine. Weight and height were measured using a daily calibrated digital scale and stadimeter with subject wearing light clothing and no shoes and body mass index (BMI) was also calculated by using Quetlet index (MacKay, 2010) (weight/height^2- kg/m^2). Waist circumference (WC) was measured on bare skin during mid respiration at the narrowest indentation between the 10th rib and iliac crest to the nearest 0.1cm while the patient was standing. Informed consent was obtained from all the participants prior to start the study.

Definition of metabolic syndrome (MetS)

The MetS was diagnosed according to the National Cholesterol Education Program's Adult Treatment Panel-III (NCEP ATP-III) criteria when more than three of the following five components were present: waist circumference (WC) > 102 cms in men and 88 cms in women, blood pressure (BP) >130/85 mmHg or on antihypertensive medications, fasting plasma glucose (FBG) > 110 mg/dL or on anti-diabetic medications, fasting triglycerides (TG) > 150 mg/dl, HDL-C < 40 mg/dL in males and <50 mg/dL in females.

Statistical analysis

Baseline characteristics of the participants were expressed in mean ± SD. Independent Student independent *t*-test was used to compare differences in baseline characteristics between the study group and the control group. Analysis of variance (ANOVA) with post hoc analysis according to Tukey (HSD) was used to compare data among ventilatory pattern subgroups. Chi-square test and Fischer's exact chi Square test were used for the comparison of qualitative data. P< 0.05 were considered statistically significant.

RESULT

The comparison of socio-demographic variables between non-Metabolic Syndrome (Non-Mets) control group (n=50) and the Metabolic Syndrome (MetS) study group (n=100) revealed significant differences in several aspects. In terms of sex distribution, males constituted a higher proportion in the Non-Mets group (64%) compared to the MetS group (44%), with a statistically significant chi-square value of 9.128 and a p-value of 0.003. Regarding dietary habits, the majority of participants in both groups were vegetarian, with no significant difference observed.

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Similarly, no significant difference was found in lifestyle habits, although a trend towards sedentary lifestyle was noted in both groups. However, a significant difference was observed in education level, with a higher proportion of illiterate individuals in the MetS group (45%) compared to the Non-Mets group (34%), indicating a potential association between lower education levels and metabolic syndrome. Additionally, the pattern of pulmonary functions showed a significant difference between the groups, with a higher prevalence of restrictive and obstructive patterns in the MetS group compared to the Non-Mets group. These findings suggest distinct socio-demographic characteristics between individuals with and without metabolic syndrome, emphasizing the importance of addressing these factors in understanding and managing metabolic disorders.

Table 1: Comparison of Socio-demographic variables between Non-Mets and MetS subjects

Socio-demographic Variables		Non-Mets control group (n=50)	Metabolic study group (n=100)	Chi Square Value	**P-Value**
Sex	Male	32 (64%)	44 (44%)	9.128*	**0.003**
	female	18 (36%)	56 (56%)		
Dietary habits	Vegetarian	46 (92%)	91 (91%)	0.22	**0.883**
	Non-Veg.	4(8%)	9(9%)		
Life style	Sedentary	42 (84%)	90 (90%)	3.021	**0.082**
	Non sed.	8 (16%)	10 (10%)		
Education level	Illiterate	17 (34%)	45 (45%)	57.62*	**< 0.001**
	Literate	33 (66%)	55 (55%)		
Ventilatory pattern of pulmonary functions	Normal	49(98%)	50(50%)	65.513*	**< 0.001**
	Restrictive	1(2%)	33(33%)		
	Obstructive	0	13(13%)		
	Mixed	0	4(4%)		

Two sided P value is > 0.05, considered not significant. The row/column association is not statistically significant and P value is < 0.05, considered significant. The row/column variables are significantly associated.

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Table 1 illustrates a comparison of socio-demographic variables between the Non-Metabolic Syndrome (Non-Mets) control group and the Metabolic Syndrome (MetS) study group. In terms of sex distribution, there were significantly more males in the Non-Mets group (64%) compared to the MetS group (44%) ($\chi2$= 9.128, p= 0.003). Dietary habits, categorized as vegetarian or non-vegetarian, showed no significant difference between the two groups ($\chi2$= 0.22, p= 0.883). Regarding lifestyle, there was a higher prevalence of sedentary behavior in both groups, with no statistically significant difference observed ($\chi2$= 3.021, p= 0.082). Education level exhibited a significant difference between the two groups, with a higher proportion of illiterate individuals in the MetS group (45%) compared to the Non-Mets group (34%) ($\chi2$= 57.62, p < 0.001). Additionally, the study identified a significant difference in the pattern of pulmonary functions between the groups, with a higher prevalence of restrictive patterns in the MetS group (33%) compared to the Non-Mets group (2%) ($\chi2$= 65.513, p < 0.001).

Table 2 presents a comparison of baseline characteristics of the study population between the Non-Mets and MetS groups. The MetS group exhibited significantly older age (52.34 ± 8.56 years) compared to the Non-Mets group (48.62 ± 10.48 years) (t = -3.280, p < 0.01). Additionally, the MetS group had lower height (157.59 ± 9.

Table 2: Comparison of base line characteristics of the study population

Anthropometry variables	**Non-Mets (Mean ± SD)**	**Mets (Mean ± SD)**	**t -Value**	**P- Value (2-tailed)**
Age (Years)	48.62 ± 10.48	52.34 ± 8.56	-3.280	**<0.01**
Height (CM)	164 ± 7.24	157.59 ± 9.27	6.686	**< 0.001**
Weight (Kg)	74 ± 8.44	76.99 ± 13.92	-1.970	**<.050**
BMI (Kg/Sq.M)	27.48 ± 2.56	30.74 ± 5.08	-6.037	**< 0.001**
WC (CM)	94.1 ± 6.99	100.51 ± 10.78	-5.746	**< 0.001**
HC (CM)	95.2 ± 6.97	99.52 ± 10.28	-3.783	**< 0.001**
Systolic BP (mmHg)	122.72±6.49	145.15±15.72	-13.684	**<0.001**
Diastolic BP (mmHg)	81.02±3.73	92.52±11.02	-9.940	**<0.001**
FBG (mg/dL)	85.17±12.19	135.02±35.102	-13.780	**< 0.001**
TG (mg/dL)	136.48±48.29	168.89±66.25	-4.348	**< 0.001**
HDL-C (mg/dL)	48.67±4.94	46.86±5.51	4.301	**< 0.001**
HOMA-IR	**3.12 ±1.91**	**8.87 ±6.95**	**-8.101**	**< 0.001**

Table 3 compares pulmonary function variables between the Non-Metabolic Syndrome (Non-Mets) and Metabolic Syndrome (MetS) groups. The mean values with standard deviations (SD)

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are provided for each variable. For forced vital capacity (FVC) as a percentage of predicted value, the Non-Mets group exhibited a significantly higher mean value (94.15 ± 6.19) compared to the MetS group (77.48 ± 14.06). This difference was statistically significant with a t-value of 11.312 and a p-value less than 0.001. Similarly, for forced expiratory volume in one second (FEV1) as a percentage of predicted value, the Non-Mets group had a significantly higher mean value (103.29 ± 7.14) compared to the MetS group (81.71 ± 15.10), with a t-value of 13.542 and a p-value less than 0.001.

The ratio of FEV1 to FVC as a percentage of predicted value was also significantly higher in the Non-Mets group (109.84 ± 4.53) compared to the MetS group (104.91 ± 13.79), with a t-value of 3.478 and a p-value less than 0.001. Additionally, the forced expiratory flow between 25% and 75% of FVC (FEF 25-75) as a percentage of predicted value was significantly higher in the Non-Mets group (101.52 ± 16.04) compared to the MetS group (75.37 ± 23.32), with a t-value of 10.77 and a p-value less than 0.001. These results suggest significant differences in pulmonary function variables between individuals with and without metabolic syndrome, indicating potential implications of metabolic health on lung function.

Table 3: Comparison of pulmonary functions variables between Non-MetS and MetS groups

Pulmonary functions variables	Non-Mets (Mean ± SD)	Mets (Mean ± SD)	t -Value	P- Value (2-tailed)
FVC - % Pred Pre	94.15±6.19	77.48±14.06	11.312	< 0.001
FEV1- % Pred Pre	103.29±7.14	81.71±15.10	13.542	< 0.001
FEV1/FVC- % Pred Pre	109.84±4.53	104.91±13.79	3.478	< 0.001
FEF 25-75 -% Pred Pre	101.52±16.04	75.37±23.32	10.77	< 0.001

All data expressed as mean ± standard deviation<0.05 is statistically significance. %Pred Pre, %Predicted Pretest; FVC, Force Vital capacity; FEV1, Force Expiratory volume in 1 second; FEV1/FVCF ratio; EF25%-75%, Middle of Force Expiratory Flow. Table 4 compares the components of metabolic syndrome (MetS) and other traits among different ventilatory pattern subgroups: Normal, Mild Restrictive, Mild Obstructive, and Mixed. The table presents the mean values with standard deviations (SD) for each variable. For body mass index (BMI) in kg/m², there were minimal differences observed among the subgroups, with mean values ranging from 29.54 ± 5.90 to 32.25 ± 2.60. The differences were not statistically significant, as indicated by the t-values ranging from 0.775 to 0.50. Regarding waist circumference (West cir) in cm,

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significant differences were observed among the subgroups, with mean values ranging from 96.96 ± 40.58 to 109.75 ± 9.27. The differences were statistically significant, with a t-value of 6.027 and a p-value of 0.001.

For systolic blood pressure (SBP) and diastolic blood pressure (DBP) in mmHg, there were slight variations among the subgroups, but the differences were not statistically significant, as indicated by the t-values and p-values.For fasting blood glucose (FBG) in mg/dL, significant differences were observed among the subgroups, with mean values ranging from 130.83 ± 37.78 to 161.25 ± 23.30. The differences were statistically significant, with a t-value of 3.45 and a p-value of 0.017. Triglyceride levels (TG) in mg/dL showed no significant differences among the subgroups, as indicated by the t-values and p-values. Similarly, high-density lipoprotein cholesterol (HDL-C) levels in mg/dL and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) showed no significant differences among the subgroups, as indicated by the t-values and p-values. Overall, the results suggest that while there are some differences in metabolic and physiological parameters among the ventilatory pattern subgroups, significant variations were primarily observed in waist circumference and fasting blood glucose levels.

Table 4: Comparison of components of MetS and other trait among ventilatory pattern subgroups

Components of MetS	Normal (Mean ± SD) (n=100)	Mild Restrictive (Mean ± SD) (n=33)	Mild Obstructive (Mean ± SD) (n=13)	Mixed (Mean ± SD) (n=4)	t - Value	P-Value
BMI (Kg/M^2)	30.76 ± 4.58	31.00 ± 5.66	29.54 ± 5.90	32.25 ± 2.60	0.775	0.50
West cir (CM)	98.99±9.15	103.08±9.97	96.96±40.58	109.75±9.27	6.027	0.001
SBP(mmHg)	144.10±15.32	147.94±17.37	141.15±9.66	148.25±20.24	1.51	0.212
DBP (mmHg)	92.30±11.43	93.82±12.46	89.08±4.77	95.75±12.48	1.34	0.262
FBG(mg/dl)	130.83±37.78	132.85±31.41	148.54±30.74	161.25±23.30	3.45	0.017
TG(mg/dL)	161.97±69.11	175.74±62.74	174.38±61.55	181.00±75.62	0.745	0.527
HDL-C (mg/dL)	45.23±5.04	46.58±6.15	46.92±5.85	44.38±3.81	1.32	0.267
Homa-IR	8.45±7.35	8.44±6.45	10.65±6.81	11.75±5.70	1.23	0.29

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Values are presented as mean ± standard deviation. *F* value and *P* value derived from one-way analysis of variance with post hoc analysis according to Tukey that used to evaluate in the four subgroups. SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; FBG, fasting blood glucose; TG, triglyceride; HDL-C, high density lipoprotein cholesterol, HOMA-IR, Homeostatic Model Assessment of Insulin Resistance, BMI, Body mass index.

DISCUSSION

In this cross-sectional investigation, we found that 50% of the study group had ventilatory patterns. Among these patterns, the most common was moderate restrictive, which was detected in 66% of the cases. Obstructive patterns were observed in 13% of the cases, while mixed patterns were observed in 4% of the cases. The findings of this investigation were comparable to the outcomes documented in population-based research studies conducted by Lim et al. (2010) and Nakajima et al. (2008). The current investigation demonstrated a substantial decrease in lung function measures among individuals with Metabolic Syndrome (MetS) compared to those without metabolic conditions. Patients with Metabolic Syndrome (MetS) exhibited a notable elevation in insulin resistance. The results of this study are consistent with the findings from previous research conducted on Korean nonsmoking males (Lim et al., 2010) and the population of Taiwan (Chen et al., 2014). Furthermore, a separate study demonstrates a slight, although statistically significant variation in FEV1/FVC between individuals with and without Metabolic Syndrome (MetS) (van Huisstede et al., 2013). It is possible that the existence of Metabolic Syndrome (MetS) could have an impact on the impairment of lung function, which would confirm our hypothesis. A different study demonstrated an inverse association between metabolic factors and lung functioning. Furthermore, it was found that abdominal obesity is the strongest indicator of pulmonary function impairment, according to a study conducted by Leone et al. in 2009. An possible reason is that heightened abdominal obesity directly impacts diaphragm compliance, leading to a decrease in lung function (Salome et al., 2010). Furthermore, a study conducted in the United States discovered a detrimental association between FEV1/FVC and waist circumference (Chen et al., 2001). A study conducted in Australia found that there is a negative connection between forced vital capacity (FVC) and abdominal obesity in males (Lazarus et al., 1998a). A study conducted in Japan proposed that hyperglycemia and abdominal obesity may lead to a decline in lung function (Yoshimura et al., 2012). Furthermore, a separate study conducted in Korea shown a strong correlation between waist circumference, hypertension, hyperglycemia, and HDL-C levels and lung function (Choi et al., 2011). The study conducted by Lazarus et al. in 1998 b found a negative correlation between fasting serum insulin levels and FVC and FEV1. In addition, the study conducted by Lawlor et al. (2004) found a negative correlation between insulin resistance measured by HOMA and the occurrence of type 2 diabetes mellitus, and the forced vital capacity (FVC) and forced expiratory volume in one second (FEV1). The findings of our research were in line with the outcomes of prior investigations.Multiple hypotheses exist about the correlation between diminished pulmonary

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function and Metabolic Syndrome (MetS). Metabolic syndrome (MetS) is a collection of diseases characterized by several cardiovascular risk factors, including insulin resistance (IR), dyslipidemia, glucose intolerance, and hypertension. These risk factors are often associated with one common etiology, which is visceral obesity. Research has demonstrated that obesity contributes to physiological abnormalities in the respiratory system. Obesity leads to a restriction of airflow, resulting in a decrease in both FEV1 and FVC. It also affects lung capacities, particularly the expiratory reserve volume (ERV) and functional residual capacity (FRC). These modifications lead to a decrease in the diameter of the airways outside of the lungs, a decrease in the flexibility of the respiratory system, an increase in the amount of oxygen needed for breathing, and an increased sensitivity of the airways to stimuli. When obese individuals have low lung volume, the lung tissue exerts less force on the airways, resulting in a decrease in airway size and an increase in airway hyperresponsiveness (AHR). This can have a negative impact on lung function. The correlation between obstructive lung function and Metabolic Syndrome (MetS) can be attributed to obesity and the resulting systemic inflammation, as well as the influence of adipokines (Lim et al., 2010).

There are a limited number of constraints in this investigation. Initially, this study has a cross-sectional design, and it is necessary to conduct additional longitudinal studies to examine the connections between lung function, inflammation, insulin resistance (IR), metabolic syndrome (MetS), and their association with future cardiovascular disease. Furthermore, the analysis of the ventilatory patterns was insufficient due to the absence of total lung capacity measurement for diagnosing restrictive patterns and the lack of post-bronchodilator assessment for identifying obstructive patterns. This study did not test systemic inflammatory markers such as hs-CRP, TNF-α, Eotaxin IL-1, IL-6, and leptin, which could potentially contribute to insulin resistance, pulmonary function impairment, and an increased risk for cardiovascular illnesses.

Conclusion

To summarize, the study found that 50% of individuals with Metabolic Syndrome (MetS) exhibited a ventilatory pattern, with a particularly high incidence (33%) of a restrictive pattern. The presence of Metabolic Syndrome (MetS) and its individual components, as well as insulin resistance, have a major impact on and are closely associated with the decline in pulmonary function.

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