

Study of Pulmonary Function Test in Type 2 Diabetics and COPD with Diabetes

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Abstract

Introduction: The association of reduced lung functions and diabetes mellitus has been described for many years suggesting that the lung could be a target organ in diabetes mellitus. Chronic obstructive Pulmonary Disease is considered as a disease that goes beyond lung involvement giving it an expression of multisystem inflammatory disease. Diagnosis of Chronic Obstructive Pulmonary Disease in diabetics may have difficulties due to superimposition of restrictive abnormality associated with diabetes mellitus.

Aim: To study pulmonary function test in type 2 Diabetics and in COPD with type 2 Diabetes.

Materials and Methods: The study was conducted in Department of Pulmonary Medicine at Dr. Shankar Rao Chavan Govt Medical College, Nanded. After inclusion criteria were met, patients were divided into 3 groups (40 type 2 diabetes with COPD (Group A), 40 type 2 diabetics (Group B), and 40 healthy controls (Group C) who are non-smoker and having no history of any acute or chronic respiratory illness.) which underwent clinical evaluation and spirometry was performed.

Results: The spirometric parameters shows that among 40 patients of DM with COPD 22 (55%) had restrictive, 12 (30%) had obstructive, 06 (15%) had mixed and 0 patients were normal and among 40 patients of DM 26 (65%) had restrictive, 06 (15%) had obstructive, 06 (15%) had mixed and 02 (05%) patients were normal spirometric findings. We also compared duration of diabetes with spirometric findings (FEV₁, FVC, FEV₁/FVC) in both the groups so we found no correlation between them (p>0.05).

Conclusion: The finding in our study proved that patients with type 2 DM with COPD showed additional restriction pattern on spirometry with compared usual obstructive pattern, also further we found that in patients with Type 2 DM we also found restrictive pattern. So we can conclude that DM being a systemic disease, also affects lung causing restrictive type of ventilatory changes. The restrictive changes probably because of glycosylation of connective tissues reduced pulmonary elastic recoil and inflammatory changes in lungs.

Keywords: COPD; Type 2 diabetics; Pulmonary function test; Spirometry

Introduction

Diabetes mellitus type 2 is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency [1]. This is typically a multi-organ chronic disease and is associated with a ten-year-shorter life expectancy due to its complications [2]. World Health Organization estimates that more than 180 million people worldwide have diabetes, and by 2030 it is expected that this number will have doubled [3]. There is an alarming increase in the incidence and prevalence of diabetes mellitus (DM) in Indians [4]. Diabetes has micro-vascular and macro-vascular disorder with debilitating effects on many organs. The alveolar capillary network in the lung is a large micro-vascular unit and may be affected by microangiopathy [5]. However, because of its large reserve, substantial loss of the micro-vascular bed can be tolerated without developing dyspnoea. As a result, pulmonary diabetic micro-angiopathy usually remains under-recognized clinically.

Among these, Diabetes mellitus (DM) is one frequent comorbidity encountered in patients with COPD which can have a significant impact on the course of the disease. COPD and DM, both being pro-inflammatory conditions, they share relevant features in their genesis and course. COPD patients more prone to develop type 2 DM due to multiple risk factors like obesity, sedentary lifestyle, smoking, increased inflammation, oxidative stress and corticosteroid therapy. DM affects 2-37% of people with COPD, depending on the patient subgroup studied. In population studies, COPD is consistently associated with a 1.4-2.0 fold increased risk of DM [6]. Decrements in lung functions

in patients with type 2 DM are believed to be the consequence of biochemical alterations in the connective tissue constituents of the lung particularly elastin and collagen as well as micro angiopathy due to the non-enzymatic glycosylation of proteins and the extracellular matrix or lung parenchyma, thickening of basal lamina, increased susceptibility to infection and a modified sarcolemma with subsequent skeletal muscle weakness which are induced by chronic hypoglycaemia. Diabetic microangiopathy itself alters the alveolar diffusion capacity of the lungs [7-11].

The assessment of spirometric parameters is important in diagnosis of COPD. The diagnosis of COPD in patient with DM is difficult due to superimposed restrictive pattern on spirometry as obstructive pattern is predominantly found in these patients. In this study, we assessed and compared the spirometric parameters and duration of DM in patient with COPD with DM and DM without history of acute or chronic

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respiratory illness with that of healthy controls.

Materials and Methods

The study was conducted in Dept. Of Pulmonary Medicine, Dr. Shankarrao Chavan Govt. Medical College and Hospital, Nanded. The study was carried out after approval from the ethical committee and fully informed written consent from the subjects. A detailed case history proforma was filled out during the recruitment of the patients. This is a case control study carried from January 2016 to August 2017. The following three groups of subjects were included: 40 Type 2 DM patients with COPD (Group A), 40 Type 2 DM patients (Group B) and 40 non-diabetics, non-smoker controls (Group C) with no chest complaints. A total 120 consecutive subjects were included in the study depending on the criteria till the sample size of each group was met.

The patients were recruited as per the following criteria:

1) Type 2 Diabetes Mellitus: Symptoms of diabetes plus fasting plasma glucose \geq 126 mg/dl two-hour plasma glucose 200 mg/dl during an oral glucose tolerance test [12].

2) COPD: Postbronchodilator FEV1/FVC <70% post bronchodilator change in FEV1 <12% and clinical correlation (exposure to cigarettes or bidis and/or environmental or occupational pollutants; and/or presence of cough, sputum production or Dyspnoea) [13].

Inclusion criteria

1. Age >13 years.
2. Those subjects giving informed consent to participate in the study.
3. Inclusion of cases and controls will be:

Cases: Patients with Type 2 DM of at least 6 months' duration with-

Group A (DM with COPD)

- All the patients who are diagnosed as COPD according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) Criteria-2017 and suffering with type 2 Diabetes Mellitus (DM) will be enrolled in the study.
- Patients already on treatment for COPD by a chest physician or newly diagnosed COPD patients based on post-bronchodilator FEV1/FVC <0.7 on spirometry.

Group B (Only DM)

- Subjects who never smoked and no past history of acute and chronic respiratory illness.

Group C (Controls) (Healthy subjects)

- Subjects who are Non-diabetic and who never smoked and no past history of acute and chronic history of respiratory illness.
- Controls were selected from relatives of the cases who give informed Consent to participate in the study.

Exclusion criteria

1. Patients age less than 13 years.
2. Patients not willing to participate in the study.

Cases

Group A (DM with COPD)

- Patients having history of ILD, lung cancer, present or past

history of tuberculosis and decompensated cardiac disease.

- Patients with gross abnormalities of vertebral column or thoracic cage, Neuromuscular disease.
- Patients with major psychiatric illness and those who had gone major abdominal and chest surgery.

Group B (DM only)

- Present or past history of respiratory diseases that might affect lung function such as Asthma, COPD, tuberculosis, bronchiectasis, interstitial lung disease.
- History of occupational exposure to any substances that could affect the lung functions.
- Individuals with unacceptable spirometric technique. An unacceptable spirometry was that in which FEV1/FVC could not be correctly measured due to-Cough, Obstruction of teeth or tongue, air escape, lack of understanding of the procedure.

Group C (Controls) (Healthy subjects)

- Subjects who do not give informed consent and not ready to participate in study.

Patients were first evaluated on the basis of clinical parameters Age, Gender, Height (in meter), weight (in kg), systolic and diastolic blood pressure (in mm Hg) were noted along with detail history. Detail clinical examination was done for all the patients. Then all necessary investigations and spirometry and PEFr were done, in order to confirm the diagnosis of patient and also fasting and post prandial blood glucose is measured. Patients were categorized into Obstructive and restrictive respiratory PFT patterns.

Statistical analysis

All the data collected and filled in Microsoft office excel 2016 sheet. Data was tabulated, all the calculation done with software present in Microsoft office excel 2016. In this study Biostatistics calculations done with Statistical Package for the Social Sciences (SPSS)-16. The demographic, biochemical and spirometric parameters compared by Unpaired 't' test and the association with duration were estimated by one-way ANOVA test.

For spirometry

After physical examination and investigations, an informed consent was obtained from all the patients. Patients were informed regarding withholding bronchodilator medications and smokers were instructed for abstinence from smoking. Patients were also instructed about the maneuver thoroughly prior to testing and were also positioned in a proper way. In all patients' baseline Spirometry was done with computerized Medgraphics Spirometer. This Spirometer met American thoracic society criteria and was volume calibrated daily.

Measurement accuracy of Spirometer was +2%. The patient was subjected to Spirometric study in PFT lab. Bronchodilator response was assessed by giving nebulized salbutamol in a dosage of 2.5 mg (0.5 ml) diluted with 2 ml. 0.9% normal saline. Available as 5 mg/ml. 15 minutes after nebulization with salbutamol, Spirometry was performed. The best of three consecutive measurements were taken. Patients were categorized into Obstructive, restrictive, mixed and Normal respiratory diseases and also categorised according to their severity (Figure 1).

Results

The study included 120 patients who categorized in 3 groups.

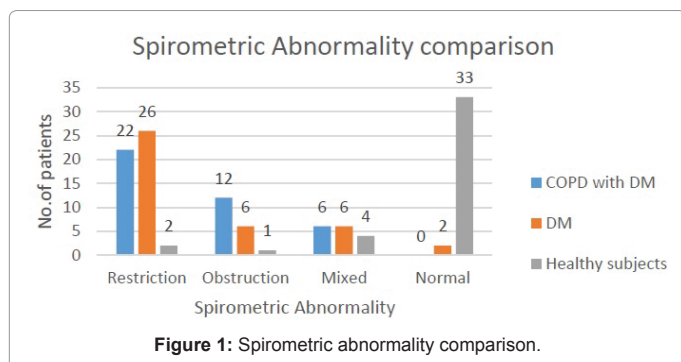


Figure 1: Spirometric abnormality comparison.

1. Group A – (DM with COPD)
2. Group B – (Only DM)
3. Group C – (Healthy subjects/Controls)

Their demographic and biochemical profiles are presented in Table 1 and Table 2. There was no significant difference in Height, Weight, age, sex and BMI distribution of individuals across the three groups. The mean fasting and post prandial blood sugar level was increased in Group A and Group B.

The Pulmonary function tests

The various parameters of Pulmonary function test have been presented in Tables 3 and 4. After comparing parameters, Table 3 shows that lung functions were reduced in Group A (COPD with DM) as compared to Group C (Healthy subjects), Also Table 4 shows that lung functions were reduced in Group B (DM) as compared to Group C (Healthy controls). It could be interpreted that the presence of DM worsens the lung functions including FVC, FEV1, FEF 25-75 and PEF and pushes the COPD patients to next severity stage.

Types of spirometric abnormality

As per Table 5 out of 40 Diabetes with COPD (Group A) patients 22 (55%) have restrictive pattern, 12 (30%) have obstructive pattern, 06 (15%) have mixed pattern. And in Diabetics (Group B) 26 (65%) have restrictive pattern, 06 (15%) have obstructive pattern, 06 (15%) have mixed pattern.

In the study association of Pulmonary Function Tests with duration of DM in Group A was shown in the above Table 6, There is no association between FEV1, FVC and FEV1/FVC with duration of diabetes as the P values for FEV1, FVC and FEV1/FVC were 0.658, 0.328 and 0.556 respectively which were statistically not significant.

In the study association of Pulmonary Function Tests with duration of DM was shown in the above Table 7. There is no association between FEV1, FVC and FEV1/FVC with duration of diabetes as the P values for FEV1, FVC and FEV1/FVC were 0.921, 0.360 and 0.112 respectively which were statistically not significant.

Discussion

In this study 40 patients with DM with COPD (Group A) and 40 patients with DM (Group B) satisfying inclusion criteria attending outpatient and indoor patients of a tertiary care government hospital were compared with 40 healthy subjects (Group C) which were matched with Group A and B on basis of age, height, weight and BMI from January 2016 to August 2017 over a period of 18 months.

All the patients included in this study were subjected to detail

Variables	Diabetics with COPD (Group-A) (Mean ± SD)	Healthy subjects (Group-C) (Mean ± SD)	p value
Height	163.55 ± 2.78	161 ± 3.02	0.16
Weight	67.38 ± 5.51	62.42 ± 5.59	0.06
BMI	25.35 ± 2.08	23.91 ± 2.52	0.07
Age	52.82 ± 8.24	52.25 ± 9.98	0.78
FBS (mg/dl)	118.95 ± 11.24	107.05 ± 31.73	0.002
PPBS (mg/dl)	177.40 ± 32.15	129.45 ± 8.96	<0.05

Table 1: Demographic and biochemical profile of DM with COPD with healthy subjects.

Variables	Diabetics with COPD (Group-B) (Mean ± SD)	Healthy subjects (Group-C) (Mean ± SD)	p value
Height	162.0 ± 3.60	161.95 ± 3.02	0.947
Weight	66.73 ± 5.60	62.42 ± 5.59	0.42
BMI	25.45 ± 2.50	23.91 ± 2.52	0.087
Age	53.90 ± 9.46	52.25 ± 9.98	0.45
FBS (mg/dl)	134.65 ± 17.12	107.05 ± 31.73	<0.05
PPBS (mg/dl)	182.05 ± 23.54	129.45 ± 8.96	<0.05

Table 2: Demographic and biochemical profile of DM with healthy subjects.

Parameter		Diabetics with COPD (Group A)	Healthy Subjects (Group C)	Unpaired 't' test p value
FVC	Absolute(L) (Mean ± SD)	1.88 ± 0.5	2.72 ± 0.52	<0.05
	% Predicted (Mean ± SD)	61.35 ± 11.52	79.02 ± 4.92	
FEV1	Absolute(L) (Mean ± SD)	1.16 ± 0.32	2.31 ± 0.31	<0.05
	% Predicted (Mean ± SD)	49.30 ± 12.99	78.35 ± 6.41	
FEV1/FVC	Absolute(L) (Mean ± SD)	67.05 ± 14.85	62.8 ± 6.42	0.31 (>0.05)
	% Predicted (Mean ± SD)	81.90 ± 17.25	78.80 ± 8.35	
FEF 25-75%	Absolute(L) (Mean ± SD)	0.96 ± 0.59	3.62 ± 1.32	<0.05
	% Predicted (Mean ± SD)	1.31 ± 0.51	3.67 ± 0.46	
PEFR (Mean ± SD) (L/min)		208 ± 68.77	338 ± 64.32	<0.05

Table 3: Comparison of PFT in type 2 DM with COPD (Group A) and healthy controls (Group C).

history, physical examination, basic and specific investigation. For the purpose of meticulous data collection, a proforma was prepared and filled for every patient. Collected data was entered regularly in the MS EXCEL 2016 sheet and then by using SPSS the demographic, biochemical and spirometric parameters compared by Unpaired 't' test and the association with duration was estimated by one-way ANOVA test. Observations and results were compared with other similar studies done in India and across the World.

DM being a systemic disease, which also affects lungs causing restrictive type of ventilatory changes, because of glycosylation of connective tissues, reduced pulmonary elastic recoil and inflammatory changes in lungs. The histopathological changes in the lungs of diabetics are associated with the thickening of the alveolar epithelium and the pulmonary capillary basal lamina and also due to the reduced recoiling of the lung [14]. This is caused by biochemical alteration of connective

Parameter		Diabetics Mellitus (Group B)	Healthy Subjects (Group C)	Unpaired 't' test p value
FVC	Absolute(L) (Mean ± SD)	1.92 ± 0.62	2.72 ± 0.52	<0.05
	% Predicted (Mean ± SD)	57.80 ± 13.03	79.02 ± 4.92	
FEV1	Absolute(L) (Mean ± SD)	1.35 ± 0.43	2.31 ± 0.31	<0.05
	% Predicted (Mean ± SD)	53.55 ± 16.98	78.35 ± 6.41	
FEV1/FVC	Absolute(L) (Mean ± SD)	69.2 ± 14.65	62.88 ± 6.42	0.175 (>0.05)
	% Predicted (Mean ± SD)	83.90 ± 17.29	78.80 ± 8.35	
FEF 25-75%	Absolute(L) (Mean ± SD)	1.08 ± 0.74	3.62 ± 1.32	<0.05
	% Predicted (Mean ± SD)	1.08 ± 0.73	3.67 ± 0.46	
PEFR (Mean ± SD) (L/min)		219 ± 74.29	338 ± 64.32	<0.05

Table 4: Comparison of PFT in type 2 DM (Group B) and healthy controls (Group C).

Sr. No	Spirometric abnormality	Diabetics with COPD (Group A)		Diabetes Mellitus (Group B)		Healthy subjects (Group C)		Total	
		No	%	No	%	No	%	No	%
1	Restriction	22	55%	26	65%	2	5%	50	41.66%
2	Obstruction	12	30%	6	15%	1	2.50%	19	15.83%
3	Mixed	6	15%	6	15%	4	10%	16	13.33%
4	Normal	0	0%	2	5%	33	82.50%	35	29.16%
	Total	40	100%	40	100%	40	100%	120	100%

Table 5: Spirometric abnormality comparison.

Duration	FEV1(L) (Mean ± SD)	FVC(L) (Mean ± SD)	FEV1/FVC (Mean ± SD)
<5 yrs. (n=13)	1.18 ± 0.22	2.01 ± 0.59	78.28 ± 20.23
5-9 yrs. (n=15)	1.09 ± 0.43	1.69 ± 0.42	86.22 ± 19.01
10-15 yrs (n=8)	1.28 ± 0.26	2.07 ± 0.45	74.25 ± 11.84
>15 yrs. (n=4)	1.04 ± 0.21	1.72 ± 0.39	84.24 ± 17.24
ANOVA p value	F=0.429, p=0.658, NS	F=1.191, p=0.328, NS	F=0.607, p=0.556, NS

Table 6: Association of spirometry parameters with duration of DM in group A (n=40).

Duration	FEV1(L) (Mean ± SD)	FVC(L) (Mean ± SD)	FEV1/FVC (Mean ± SD)
<5 yrs. (n=6)	1.45 ± 0.41	2.01 ± 0.59	78.28 ± 20.23
5-9 yrs. (n=18)	1.35 ± 0.29	1.69 ± 0.42	86.22 ± 19.01
10-15 yrs (n=12)	1.40 ± 0.58	2.07 ± 0.45	74.25 ± 11.84
>15 yrs. (n=4)	1.60 ± 0.79	1.72 ± 0.39	84.24 ± 17.24
ANOVA p value	F=0.162, p=0.921, NS	F=1.147, p=0.360, NS	F=5.073, p=0.112, NS

Table 7: Association of spirometry parameters with duration of DM in group B (n=40).

tissue constituents, particularly collagen and elastin. There is increased cross-linkage formation between polypeptides of collagen which leads to thickening, leading to restriction of lung volume and alveolar gas transport, reduced membrane diffusion capacity and pulmonary

capillary blood volume [15,16].

Mishra et al. [17] in a study of 15 patients with COPD with DM demonstrated that 73% patients had the probability of restrictive pattern of spirometry. In the present study, the high proportion (55%) of patients having the restrictive pattern of spirometry. Possible reason for such high proportion of restrictive component in these patients could be the independent decline in FEV1 and FVC known to be associated with diabetes which causes pulmonary microangiopathy. In present study FEV1, FVC, FEF 25-75 and PEFR reduced as compared to healthy controls but FEV1/FVC was nearly same as that of controls, it correlates with other studies done by Kinney et al. [18] and Adiodi et al. [19].

Irfan et al. [9], studied spirometric parameters in 64 diabetics and showed that there was significant reduction in FEV1, FVC when compared with healthy controls. Davis et al. [20] also showed that reduced lung volume is result of chronic complications of diabetes. Sreekumar et al. [21] also studied spirometric parameters in 100 diabetics and found that diabetics had decreased lung volumes (FVC, FEV1, FEV1/FVC and PEFR) as compared to healthy controls. Also the possible mechanisms are micro-vascular changes in the lung tissue will lead to impairment in lung functions studies also shown that T2DM with microangiopathy show reduced diffusion capacity. Yadav et al. [22] also studied pulmonary parameters in 30 DM type 2 and found that FVC, FEV1, FEF 25-75, PEFR were significantly reduced except FEV1/FVC as compared to healthy controls, this study also found that there are 22 (73.33%) cases out of 30 show restrictive pattern on spirometry. The FEV1/FVC% in our study was lower than normal and was found to have restrictive pattern. This is in concordance Boulbou et al., [23], Sreeja et al. [24], Fimognari et al. [25]. PEFR was also reduced in our study which was similar to Sreeja et al. [24]. In present study of cases with type 2 DM shows that FVC, FEV1, FEF 25-75, PEFR were significantly reduced except FEV1/FVC as compared to healthy controls and It correlates with other studies done by Sanjeev Verma et al. [26] Irfan et al. [9], El-Azeem et al. [27], Kalappan et al. [28], Shah et al. [29].

In the study group of COPD with DM, There is no association between mean absolute FEV1, FVC and FEV1/FVC and duration of diabetes as the P values for FEV1, FVC and FEV1/FVC were 0.658, 0.328 and 0.556 respectively which were statistically not significant. It means mean absolute values of FEV1, FVC and FEV1/FVC does not related to duration of DM and there was no change in above parameters in relation to increase in duration of DM.

In the study group of DM There is no association between FEV1, FVC and FEV1/FVC and duration of diabetes as the P values for FEV1, FVC and FEV1/FVC were 0.921, 0.360 and 0.112 respectively which were statistically not significant. It correlates with other studies done by El-Azeem et al. [27] Shah et al. [29] in these studies they found no statistical significance. As per our present study duration of DM was probably not the major determinant of lung pathology, which needs further research.

Our study has some limitations such as due to resource limited setup we could not go into the details of risk factors of type 2 Diabetes Mellitus and effect of poor glycaemic control (HbA1c) on lung function tests, the study size was small and we cannot analyse the result in different ethnic groups and Large, long term, prospective, randomized controlled studies are necessary to more fully evaluate effect of type 2 Diabetes Mellitus and Duration of DM on lung function tests.

This study showed that lung functions in term of FEV1, FVC, FEF

25-75 and PEFr were reduced in Group A (DM with COPD) and Group B (DM) but FEV1/FVC didn't show any change as compared to healthy subjects in both the study groups.

It has been shown that DM is multisystem disease which is associated with continuous damage and dysfunction of various organs and also affects the lung functions. It seems prudent to add spirometry to the monitoring tool for DM associated lung involvement and sequelae.

Conclusion

We conclude that COPD with DM and only DM patients showed a decrease in Pulmonary Function Test (spirometry) values compared to healthy subjects. The finding in our study proved that patients with type 2 DM with COPD (Group A) showed additional restriction pattern on spirometry with compared usual obstructive pattern, also further we found that in patients with Type 2 DM (Group B) we also found restrictive pattern. So we can conclude that DM being a systemic disease also affects lung causing restrictive type of ventilatory changes. The restrictive changes probably because of glycosylation of connective tissues reduced pulmonary elastic recoil and inflammatory changes in lungs. As the type 2 DM was predominantly associated with restrictive pattern, Routine spirometry screening in all diabetic patients will help to identify the pulmonary function changes earlier which is often detected late or missed. Duration of DM was probably not the major determinant of lung pathology, which needs further research. There is a need for periodically assessing the pulmonary functions in COPD with type 2 DM patients and DM patients as spirometry remains a cost effective and simple diagnostic tool and its use can give warning signal for patients to take early therapeutic measures to control progression.

Hence we can recommend doing periodic spirometry to the patients of Type 2 DM with COPD and Isolated Type 2 DM to monitor the reduction in lung functions and prevent further progressive lung volume reduction.

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