Original Article

Pulmonary function tests in type 2 diabetes mellitus and their association with glycemic control and duration of the disease

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ABSTRACT

Background: Pulmonary complications of diabetes mellitus (DM) have been poorly characterized. Some authors have reported normal pulmonary functions and even concluded that spirometry is not at all necessary in diabetic patients. Some studies have shown abnormal respiratory parameters in patients of DM. Moreover, the duration of DM and glycemic control have varied impact on the pulmonary functions. **Aims and Objectives:** The study was undertaken to analyze the pulmonary function parameters in diabetic patients and compare them with age and gender matched healthy subjects. We correlated forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) in diabetic patients with duration of the disease and glycosylated hemoglobin (HbA1c). **Materials and Methods:** Pulmonary function tests (PFTs) were recorded in 60 type 2 diabetic male patients and 60 normal healthy male controls aged 40-60 years by using Helios 702 spirometer. The PFTs recorded were – FVC, FEV_1, FEV_1/FVC, FEF_{25}, FEF_{50}, FEF_{75}, FEF_{25-75}, $FEF_{0.2-1.2}$, and peak expiratory flow rate (PEFR). HbA1c of all the patients was estimated by ion exchange resin method, which is a very standard method of estimation. PFTs of diabetic patients and controls were compared by applying Student's unpaired *t* test. Associations between FVC and FEV_1 and HbA1c and duration of illness in diabetic patients were analyzed by applying Pearson's coefficient. **Results:** The PFTs were significantly decreased in diabetic patients compared with the healthy controls except FEV_1/FVC. There was no correlation found between FVC and FEV_1 and duration of illness as well as HbA1c. **Conclusion:** DM being a systemic disease, which also affects lungs causing restrictive type of ventilatory changes probably because of glycosylation of connective tissues, reduced pulmonary elastic recoil and inflammatory changes in lungs. We found glycemic levels and duration of disease are probably not the major determinants of lung pathology, which requires further research.

KEY WORDS: Diabetes, glycemic control, pulmonary function

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INTRODUCTION

The 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.[1] There is an alarming increase in the incidence and prevalence of diabetes mellitus (DM) in Asian Indians.[2] Diabetes is a micro-macrovascular disorder with debilitating effects on many organs. Pulmonary complications of DM have been poorly characterized with conflicting results. The alveolar capillary network in the lung is a large micro-vascular unit and may be affected by microangiopathy.[3] However, because of its large reserve, substantial loss of the microvascular bed can be tolerated without developing dyspnoea. As a result, pulmonary diabetic micro-angiopathy may be under-recognized clinically. In DM pulmonary functions have been studied frequently in countries other than India,[4] while in our country there are few studies concerning these abnormalities and their relationship with glycosylated hemoglobin (HbA1c) and duration of the disease.

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Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/0970-2113.110417

Reduced elastic recoil, reduced lung volume, diminished respiratory muscle performance, chronic low grade inflammation,[5,6] decrease in pulmonary diffusion capacity for carbon monoxide,[7] autonomic neuropathy involving respiratory muscles[8] are some of the important changes occurring in DM.

Despite the unclear nature, the relationship between DM and pulmonary function tests (PFTs) remains important because of potential epidemiological and clinical implications. The loss of pulmonary reserve may become clinically important.

Hence, we hypothesized that PFTs are affected in DM in Indian population and the changes may correlate with HbA1c and the duration of the disease.

Objectives

- The study aims to evaluate the PFTs in type 2 DM patients and compare them with the age and gender matched healthy controls.
- We also determine the co-relation of the HbA1c and duration of the disease with PFTs in type 2 DM patients.

MATERIALS AND METHODS

The study was carried out in collaboration with Diabetes Outpatient Department of Sassoon General Hospitals. The Institutional Ethics Committee approved the study protocol. Sixty male patients of type 2 DM diagnosed by the treating physician, of the age group 40-60 years taking oral hypoglycemics, were randomly selected from the Diabetes Outpatient Department.

Exclusion criteria

1. Patients having complaints of cough, sputum, or dyspnoea.
2. Smokers and patients with any cardio-respiratory illnesses or major diseases.

Sixty normal healthy males of the same age group and socioeconomic status from patient's relatives were selected as control group. The controls were also thoroughly examined clinically. Those with cardio-respiratory, musculoskeletal, or endocrine diseases were excluded from the study. Fasting and postprandial blood glucose levels were measured by glucose oxidase method to rule out type 2 DM in them.

Informed written consent was taken from patients as well as from controls. All the patients were handed a questionnaire that contained a detailed personal and medical history. PFTs of the patients as well as of the controls were performed with turbine flow sensor-based 702 Helios – Spirometer (Chandigarh, India) between 11 am and 12 pm. All the tests were conducted according to American Thoracic Society/European Respiratory Society (ATS/ERS guidelines) in a quiet room in sitting position by the trained personnel.[9] The controls and patients performed spirometry three times at the interval of 15 minutes and the best of the three was taken into account. Parameters recorded were – forced vital capacity (FVC) in liters, forced expiratory volume in 1 second (FEV_1), FEV_1/FVC in percentage (%), forced expiratory flow during 25% of FVC (FEF_{25}), forced expiratory flow during 50% of FVC (FEF_{50}), forced expiratory flow during 75% of FVC (FEF_{75}), forced expiratory flow during 25-75% of FVC (FEF_{25-75}), forced expiratory flow during 0.2-1.2 liters of FVC ($FEF_{0.2-1.2}$), and peak expiratory flow rate (PEFR). For all these parameters percentage of predicted values for the respective age, height, and weight were taken into consideration.

Nearly 2 ml of venous blood was collected in ethylenediamine tetra acetic acid (EDTA) bulb in all the diabetic patients with aseptic precautions. HbA1c of all the patients was estimated by ion exchange resin method by the diagnostic glycohaemoglobin kits of Asritha Diatech as per the guidelines provided.[10]

All data were collected in a data collection form and then transferred to an Excel sheet by two independent data entry operators. Discrepant values were corrected by checking the data collection form. Clean data was then analyzed statistically.

PFTs of diabetic patients and controls were compared by applying Student's unpaired '*t*' test. Correlations between FVC and FEV_1 and HbA1c and duration of illness in diabetic patients were analyzed by applying Pearson's coefficient. Statistical analysis was done by using SSPS version 11 and Graphic Prism Pad version 5 (Statistician, B.J. Medical College).

RESULTS

Table 1 depicts the physical characteristics of the normal controls as well as the patients of DM. Age, height, and weight of both the groups were comparable as statistically there was no difference between them ($P > 0.05$). Our study showed that all the pulmonary parameters, that is, FVC, FEV_1, FEF_{25}, FEF_{50}, FEF_{75}, FEF_{25-75}, $FEF_{0.2-1.2}$, and PEFR were significantly reduced except FEV_1/FVC in patients of type 2 DM as compared with the healthy controls ($P < 0.05$). The ratio FEV_1/FVC is almost equal in normal controls and diabetic patients ($P > 0.05$) [Table 2, Figure 1]. On correlating the FVC and FEV_1 with duration of illness and HbA1c, we found that there was no significant correlation

Table 1: Physical characteristics of subjects

Parameter	DM patients, *n*=60 Mean±SD	Controls, *n*=60 Mean±SD	*P* value
Age (years)	53.90±8.45	54.88±8.28	>0.05
Height (cm)	159.23±7.86	161.28±7.33	>0.05
Weight (kg)	61.57±7.38	64.42±8.70	>0.05
HbA1c (%)	7.12±1.36	-	-
Duration of DM (years)	6.56±5.86	-	-

DM: Diabetes mellitus

between them ($P > 0.05$) [Table 3, Figures 1 and 2].

DISCUSSION

Our study showed that all the pulmonary parameters, that is, FVC, FEV_1, FEF_{25}, FEF_{50}, FEF_{75}, FEF_{25-75}, $FEF_{0.2-1.2}$, and PEFR were significantly reduced except FEV_1/FVC in patients of type 2 DM as compared with the healthy controls. This is in accordance with previous studies.[11-15]

Some of the prospective and cross sectional studies have shown low vital capacity or restrictive pattern in type 2 DM.[16,17]

Meta-analysis by van den Borst, *et al*. showed that DM is associated with statistically significant, impaired pulmonary function in a restrictive pattern. Moreover, these results were irrespective of body mass index (BMI), smoking, diabetes duration, and HbA1c levels.[18]

Uchida, *et al*. found that there was decreased pulmonary diffusing capacity in patients with diabetes with perfusion defect on ventilation perfusion scintigrams.[19] It was not possible for us to analyze the pulmonary diffusing capacity because of practical difficulties.

Davis, *et al*. conducted a study in Western Australia in large number of patients of type 2 DM. They found that VC, FVC,

Table 2: Comparison of PFTs in patients with type 2 DM and healthy controls

Parameter % predicted values	Control subjects Mean±SD	DM subjects Mean±SD	*P* value
FVC	89.36±9.71	77.97±12.99	<0.05*
FEV_1	88.03±6.69	78.98±14.09	<0.05*
FEV_1/FVC	111.36±10.62	112.83±9.35	>0.05
PEFR	77.70±12.81	59.16±99.35	<0.05*
FEF_{25}	81.60±8.69	60.23±18.75	<0.05*
FEF_{50}	q	61.23±17.96	<0.05*
FEF_{75}	85.00±10.28	64.03±24.92	<0.05*
FEF_{25-75}	73.83±10.28	67.00±15.08	<0.05*
$FEF_{0.2-1.2}$	91.06±1.46	70.46±23.68	<0.05*

*P<0.05: Statistically significant, DM: Diabetes mellitus, PFTs: Pulmonary function tests

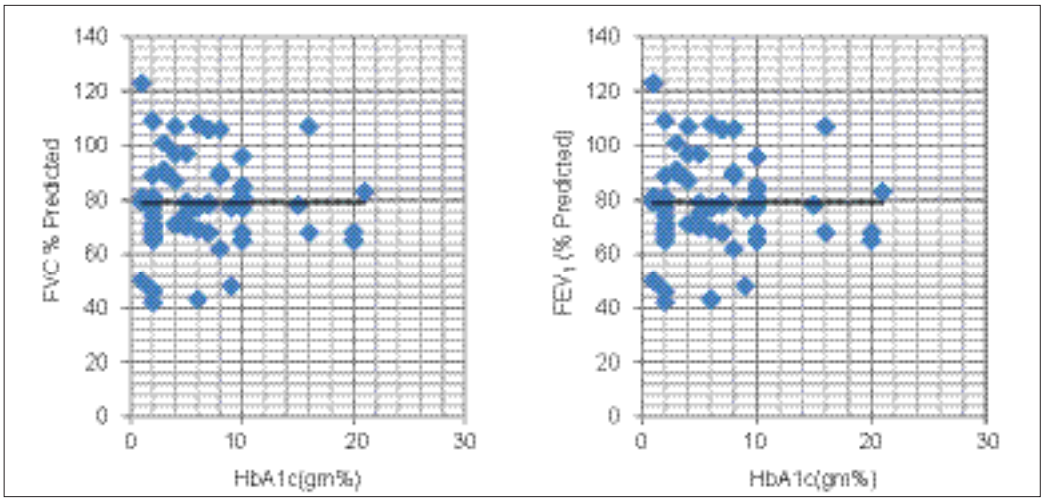

Figure 1: Correlation of HbA1c with PFTs. $P > 0.05$ - Statistically not significant

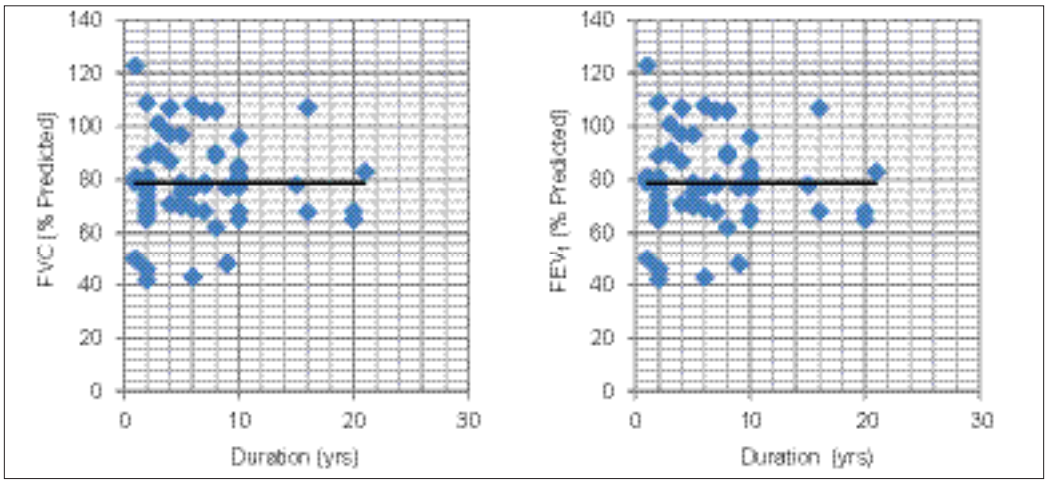

Figure 2: Correlation of PFTs with duration of diabetes. $P > 0.05$ - Statistically not significant

Table 3: Correlation of HbA1c and duration of DM with PFTs

Parameters	r^2	*P* value
FVC with HbA1c	0.019	0.289
FEV_1 with HbA1c	0.007	0.498
FVC with duration	8.809e-0.009	0.9994
FEV_1 with duration	0.007	0.518

DM: Diabetes mellitus, PFTs: Pulmonary function tests

FEV_1, and PEFR decreased at an average of between 1.1% and 3.1% of predicted values/year in type 2 DM patients.[11]

Ehrlich, *et al*. showed that patients with type 2 DM were at increased risk of several pulmonary condition like – asthma, Chronic Obstructive Pulmonary Disease (COPD), fibrosis, and pneumonia.[20]

Few studies have mentioned that no significant differences were observed in patients of type 2 DM.[21-23] Probably the small sample size is the reason behind these findings.

Pathophysiology of reduced lung function is still an interesting research issue. Normal lung mechanics and gas exchange are influenced by the integrity of the pulmonary connective tissue and microvaculature. Acceleration of aging process in connective tissue cross links and presence of nonenzymatic glycosylation and modification of alveolar surfactant action causes reduction in PFTs.[3] There have been reports of histopathological changes in the diabetic patients. In the study by Weynand *et al*.,[24] it was found that alveolar epithelium, endothelium capillary, and basal laminaes were thickened in lungs on electron microscopy, when compared with the controls. In addition, the thickening of basal laminae was of the same magnitude in lung and kidney. Diabetic microangiopathy might be existing in the pulmonary vascular bed. Moreover, reduced pulmonary capillary blood volume was found, favoring the evidence of microangiopathy. This could lead to redistribution of the pulmonary circulation, resulting in well ventilated areas to become underperfused.[25]

The thorax and lungs are rich in collagen and elastin. Stiffening of thorax and lung parenchyma can occur because of nonenzymatic glycosytion of these structural compounds. This may lead to restrictive pattern.[3] In our studies, since the FVC/FEV_1 ratio is statistically not significantly different in DM patients as compared with normal controls, other PFT values are lower in DM patients; this strongly suggests restrictive pattern in DM patients.

Studies have even shown diabetic polyneuropathy, which affects respiratory neuromuscular function and thus reducing pulmonary volumes.[26]

On correlating the FVC and FEV_1 with duration of illness and HbA1c, we found that there was no significant correlation between them [Table 3, Figures 1 and 2].

There are certain studies showing no correlationship between HbA1c and PFTs.[7,14,22] They argued that HbA1c levels are indicators of glycemic control for a short period of 1-2 months, it was not adequate to conclude that the plasma glucose level was not related to decreased PFTs. While some studies have shown that the decline in PFTs was negatively correlated with HbA1c.[11,13]

There are studies that have reported no significant correlation between PFTs and duration of diseases,[22] while some of the studies have reported a strong negative correlation of PFTs with duration.[14,15] Since DM is a disease, which involves multiple organs randomly, the study of the effect of duration of the disease on them requires further research.

Several studies have analyzed the association between impaired lung function and death and found that a 10% decrease in FEV_1 was associated with a 12% increase in all cause mortality in type 2 DM.[27]

Clinical implications

Pulmonary dysfunction should be regarded as a specific derangement induced by DM. Further studies may clarify whether this should be included as a long-term complication of diabetes. The role of strict glycemic control on pulmonary function in diabetic patients is another interesting aspect and needs further studies. The impairment in PFTs can lower the threshold for clinical manifestations of acute or chronic lung disease. Patients with DM admitted with pneumonia have increased risk of complications and mortality.[28]

Limitations and scope

It seems to be necessary to repeat PFTs and to assess the changes of pulmonary functions among the same subjects. Over a long observation course, the relationship between the plasma glucose concentration and the PFTs can be elucidated.

SUMMARY AND CONCLUSION

DM being a systemic disease, also affects lungs causing restrictive type of ventilatory changes probably because of glycosylation of connective tissues, reduced pulmonary elastic recoil, and inflammatory changes in lungs. We found that glycemic levels and duration of disease are probably not the major determinants of lung pathology, which requires further research.

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How to cite this article: Shah SH, Sonawane P, Nahar P, Vaidya S, Salvi S. Pulmonary function tests in type 2 diabetes mellitus and their association with glycemic control and duration of the disease. Lung India 2013;30:108-12.

Source of Support: Nil, **Conflict of Interest:** None declared.

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